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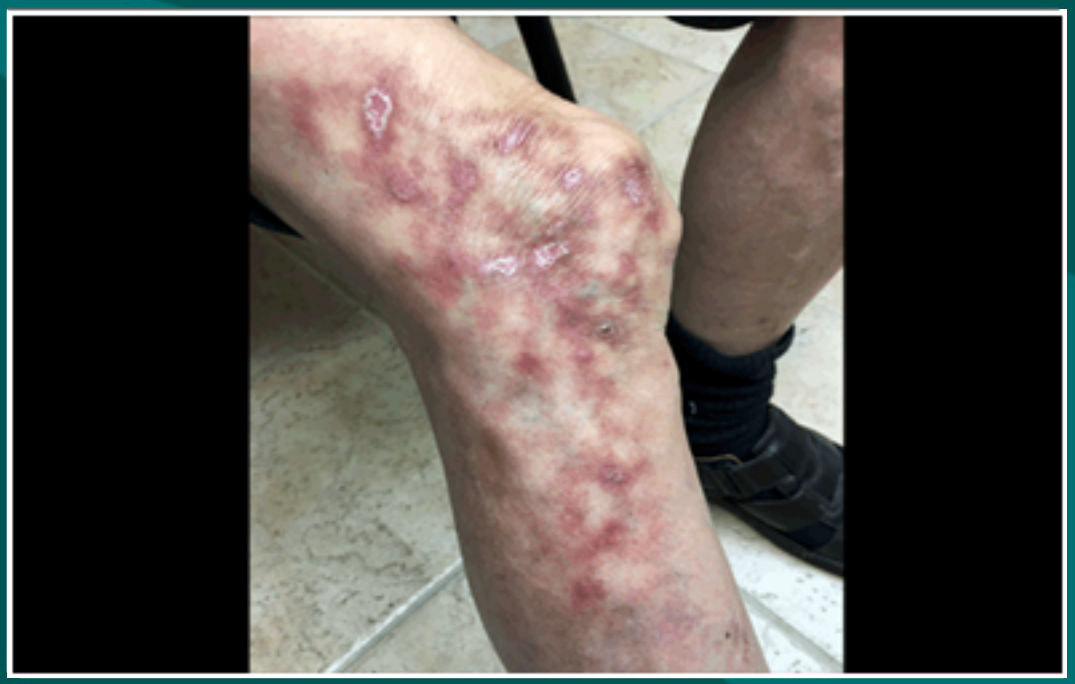

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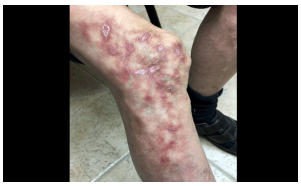

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CASE SERIES

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Ultrasound imaging of tongue malignancy

Margaret Eseza Kisansa, Savvas Andronikou

ABSTRACT

Introduction: Squamous cell carcinoma of the tongue is a common malignancy associated with risk factors like excessive alcohol consumption, heavy tobacco smoking and human papilloma virus. Magnetic resonance imaging (MRI) scan is considered to be the gold standard in investigating these tumors. However, MRI equipment is expensive to buy and is not readily available in some centers. Computed tomography scan has also been used in imaging these patients but this modality carries a radiation burden. Patient's five-year survival is dependent on early diagnosis. It is, therefore, important to diagnose early and image accurately to ensure good outcomes. Case Series: Two male patients with confirmed carcinoma of the tongue are reported. The first patient was 65-year-old and the second patient was 40-year-old. They both presented with odynophagia. Clinical examination revealed ulcerating lesions involving the base of the tongue. Axial CT scans and ultrasound imaging were performed on these patients through the floor of the mouth. This case report focused on comparing the ability of the two modalities, in delineating margins and depicting tumor thickness. Conclusion: Ultrasound gives excellent information with regards to tumor thickness, margins and vascularity. This highlights the value of using ultrasound as an additional tool in imaging of these patients especially in regions where CT and MRI scans are not readily available.

Keywords: Carcinoma, Tongue malignancy, Ultrasound, Ulcerating lesions

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INTRODUCTION

The prevalence of oral cancers is high in the world, and the risk factors cited are: excessive alcohol consumption, heavy tobacco smoking as well as human papilloma virus (HPV). Smoking tobacco and smoke less products have contributed to an increased incidence in some countries like Taiwan [1].

Computed tomography (CT) scan and magnetic resonance imaging (MRI) scan are the current modalities of choice in imaging of oral cavity tumors because of good tissue differentiation and excellent nodal mapping [2]. However, MRI machines are expensive to buy and maintain, and are not readily available in the most

developing nations. Computed tomography scanners, although more available compared to MRI scanners, do use ionizing radiation which is known to carry risks. On the other hand, ultrasound machines are relatively inexpensive, readily available and easy to use. This makes a combination of ultrasound with CT, an important one in investigating patients with oral cancers in areas where MRI machines are not available.

Since early detection and treatment of oral cancers is crucial for good outcomes, it makes imaging a very important component in the management of these patients. Patient's five-year survival was found to be dependent on tumor depth, with invasion greater than 2 mm being predictive of poor outcomes and a 3.7-fold increase in the risk of regional recurrence. It is therefore very crucial to measure the tumor depth accurately [3].

In this case series, imaging was done using Aloka SSD 5500 Ultrasound Unit (Aloka Japan) with a convex probe at 5.0 MHz frequency. The tongue was imaged through the sub-mandibular region (axial and sagittal planes) in these patients who had also undergone prior contrasted CT scanning of floor of the mouth. Computed tomography images were acquired on a spiral CT scanner (Spiral 4 slice Asteion CT scanner Toshiba Japan).

A long axis control ultrasound of an individual with no tongue pathology is included to demonstrate the normal sonographic appearance of the tongue (Figure 1). Selected ultrasound images were compared with the corresponding axial CT images in the two patients at similar anatomic levels.

CASE SERIES

This case series presents two patients with confirmed diagnosis of carcinoma of the tongue who had undergone CT imaging both before and after intravenous contrast injection and were subsequently taken to ultrasound for further imaging. Comparisons of imaging findings, obtained from ultrasound and CT in the two patients are presented.

Case 1

A 65-year-old male presented with base of the tongue lesion of a long duration, which on ultrasound was seen as a hypo-echoic mass involving the base of the tongue. This lesion demonstrated lobulated, but well delineated margins on both sagittal and axial images respectively (Figure 2A–B).

In comparison, the post contrast axial CT images shown in Figure 3A–B demonstrated an ill-defined hypodense lesion involving the base of the tongue on the right side. This lesion showed distortion of the oropharynx, but the margins were poorly defined. Distortion and infiltration of the right floor of the mouth and para-pharyngeal spaces was evident but the margins of the entire lesion were difficult to determine and depth of the tumor could not be measured accurately.

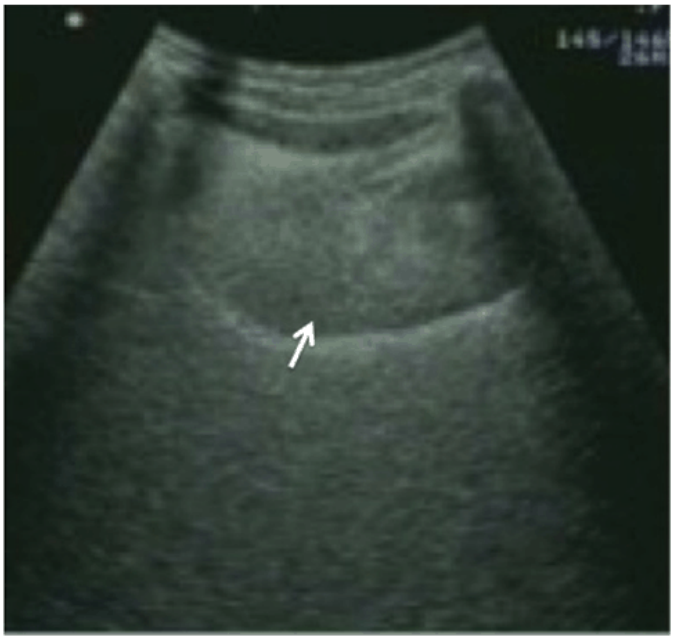

Figure 1: Longitudinal ultrasound image of the tongue in a control performed via the submandibular approach, showing the normal homogenous sonographic appearance.

Case 2

A 40-year-old male presented with odynophagia. On examination there was an ulcerating mass involving the base of the tongue. The lesion was locally invasive and documented as stage 4 with local nodal spread. Patient had lung metastases. Biopsy results showed a mucoepidermoid carcinoma. Ultrasound demonstrated a hypoechoic lesion with clearly delineated scalloped margins (Figure 4A). The lesion was further interrogated on Doppler, where the lesion showed high vascularity which was evidenced by the mosaic pattern of flow (Figure 4B). Computed tomography scan showed an enhancing lesion involving the base of the tongue but failed to clearly delineate the tumor margins (Figure 5).

DISCUSSION

Although computed tomography (CT) and magnetic resonance imaging (MRI) scan are the modalities commonly utilized in imaging of intra-oral tumors, for accurate measurement and evaluation of the tumor margins [4], there have been some publications which clearly documented the use of intra-oral ultrasound for evaluation of these tumors. Yuen et al. showed that intra-oral ultrasonography was accurate in measuring tumor thickness and they also cited its usefulness in pre-treatment staging and prognosis [5]. A study done in Japan using intraoral ultrasound also showed that ultrasonography is an excellent imaging modality in delineating tumor margins and tumor thickness [6]. Yesuratnam et al. went further to advocate that ultrasound should be used as a first-line modality of choice for

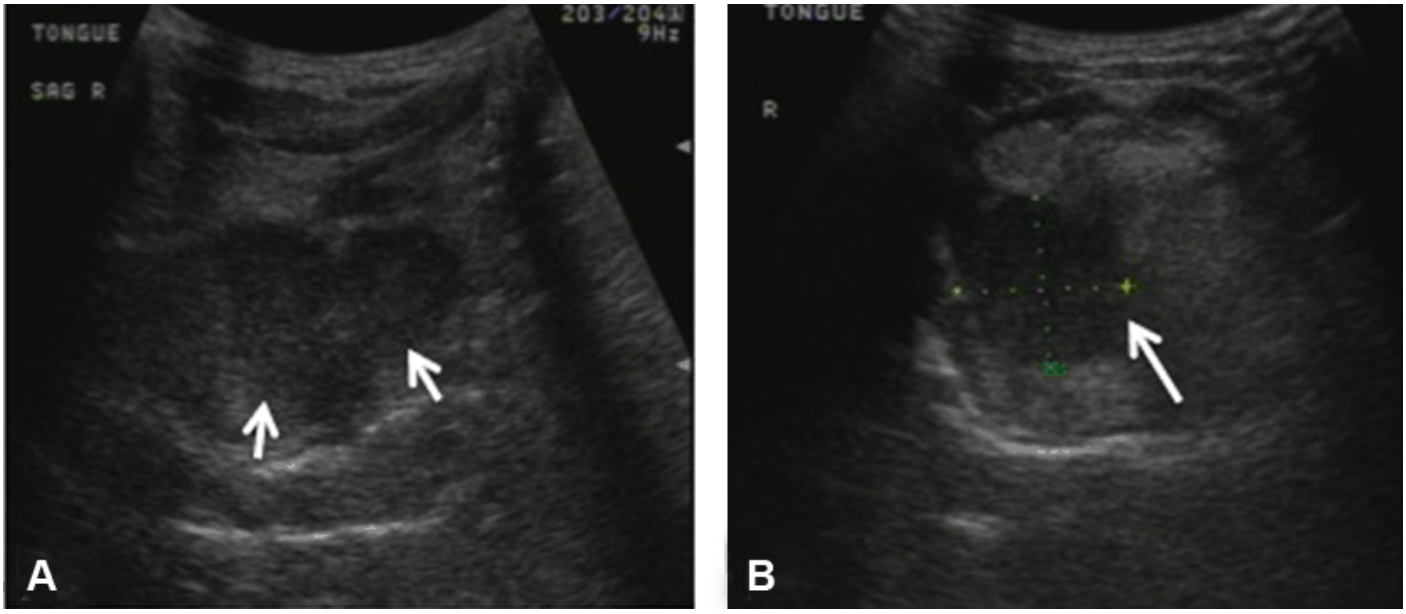

Figure 2: (A) Longitudinal ultrasound image showing a hypoechoic lesion involving the base of the tongue. The margins of the lesion (arrows) are scalloped and well delineated from the surrounding normal tongue, (B) Transverse plane showing a peripheral hypoechoic lesion which measured 2.5x2.3 cm (crosses) (Case 1).

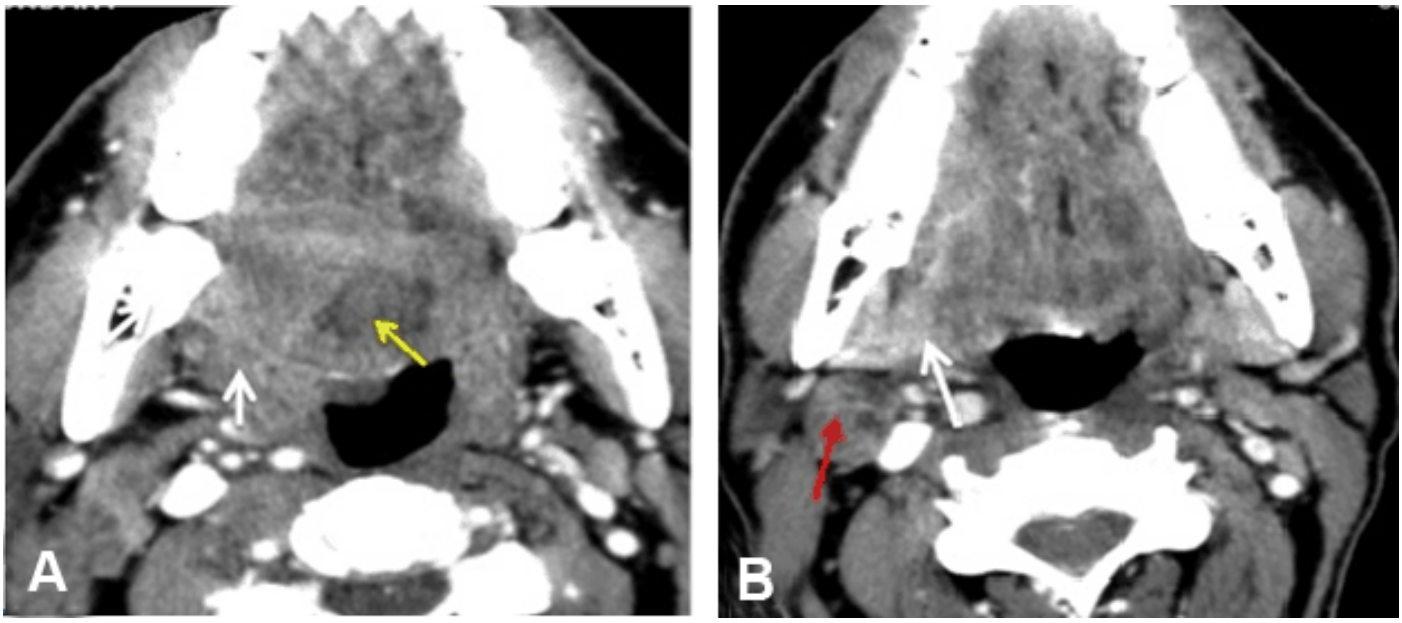

Figure 3: (A) Comparative axial post contrast CT images showing a mass (white arrow) infiltrating the right base of the tongue, with a hypo-dense central component (yellow arrow) causing distortion of the oropharynx and crossing the midline. The margins of the entire lesion are difficult to determine, (B) Right cervical lymphadenopathy is evident (red arrow) (Case 1).

preoperative assessment of tumor thickness. This study too was based on intra-oral ultrasound imaging [7]. Doppler ultrasound has been found to be very useful in predicting grades of malignancy both in the tumor and cervical lymph nodes [8]. The sublingual approach has also been used before, with positive results. It is noted to be safe, relatively cheap and readily available [9]. In our experience, the sublingual route is comfortable, tolerable and less invasive in patients with tongue tumors, as these lesions may be ulcerated and painful. It was also found to be more tolerable for the imager, as these patients had marked halitosis.

We demonstrated that ultrasound shows the primary lesion as a hypo-echoic mass with clear delineated margins and that Doppler ultrasound is useful in demonstrating the vascularity of the lesion, which aids in determining tumor staging. The tumor can be measured accurately and the tumor margins can be assessed adequately. In

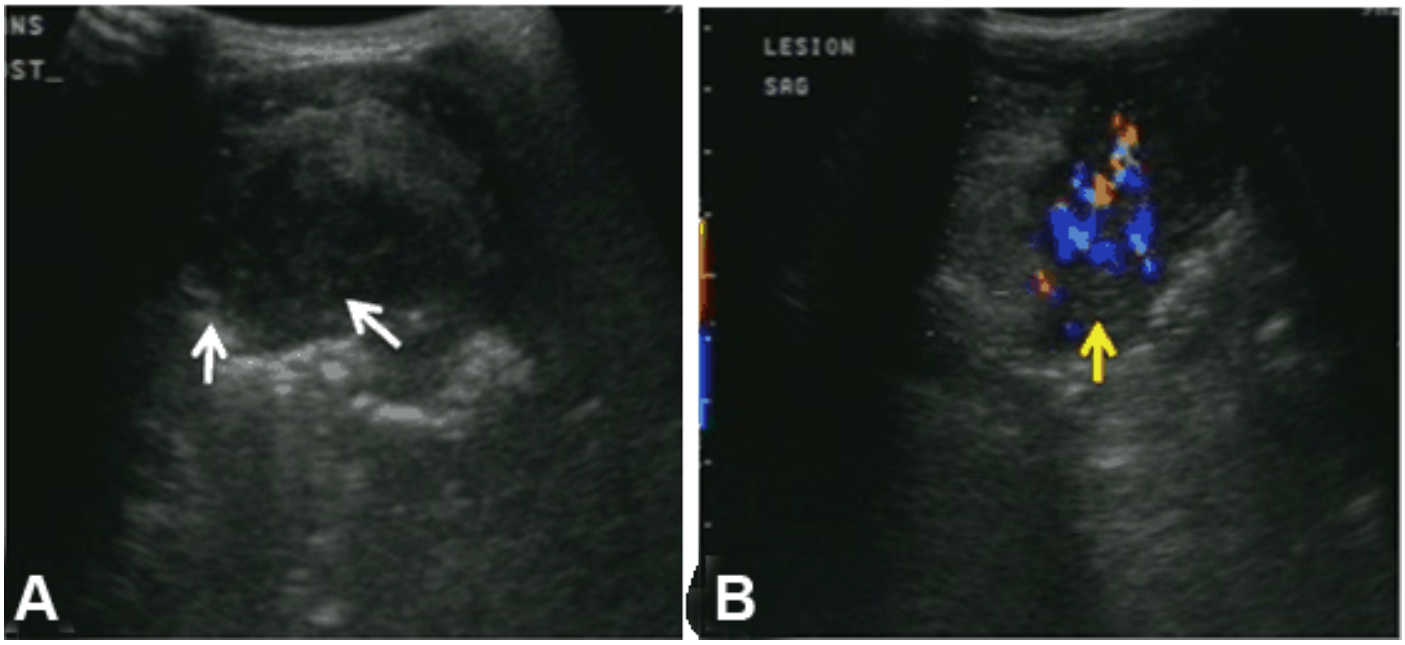

Figure 4: (A) Transverse ultrasound of patient demonstrating a hypoechoic lesion at the base of the tongue (arrows), with clearly delineated margins, (B) Color Doppler ultrasound of the tongue in the same patient showing marked vascularity of the lesion (arrow) compared to the surrounding normal tongue tissue (Case 2).

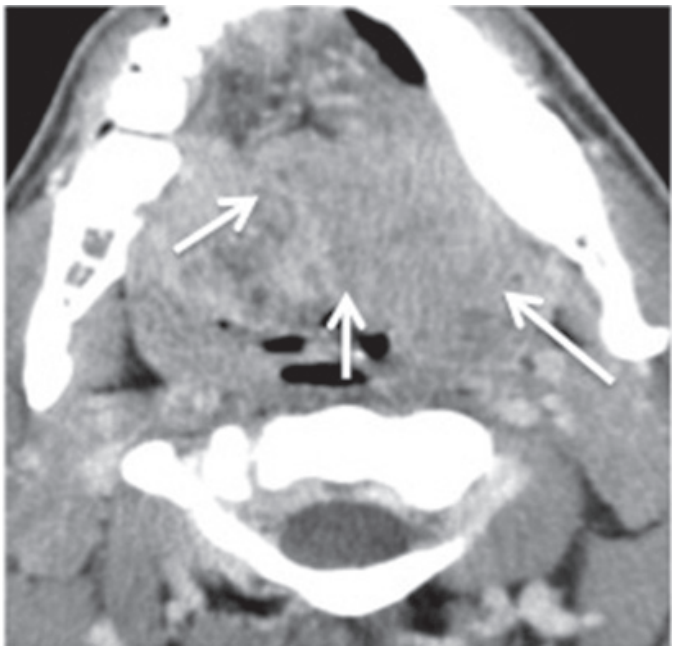

Figure 5: Axial post contrast CT image, demonstrating the large mass left the base of the tongue as indicated with white arrows. The exact size of the lesion cannot be determined accurately due to the poorly defined margins. There is post contrast enhancement confirming the vascularity of the tumor.

both the patients, CT scan failed to demonstrate the tumor edge clearly, whereas ultrasound demonstrated the tumor edge effectively. Evaluation of neck lymphadenopathy is also possible with ultrasound.

CONCLUSION

This case series highlights the importance of ultrasound as a modality that should be embraced and used more frequently in imaging of intraoral tumors than the presented case. We are only recommending adding ultrasound to the protocol of imaging and not replacing any of the gold standard modalities MRI and CT scans. There are no reports comparing the use of sub-lingual ultrasound and CT scan in imaging of tongue malignancies and this is an area that needs further investigation.

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Margaret Eseza Kisansa – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Savvas Andronikou – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

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Conflict of Interest

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CASE SERIES

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The role of gastrocnemius muscle flap for reconstruction of large soft tissue defects after infected total knee arthroplasty

Ingo Schmidt

ABSTRACT

Introduction: The surgical management of infected total knee arthroplasty remains a challenging therapeutic problem. The two-stage management has proven to be the reliable method of choice. The use of the gastrocnemius muscle flap has become a great "classic" for coverage of large soft tissue defects of the knee and proximal third of lower leg. A short review of literature including two short case presentations will highlight that procedure with or without required removal of implant and the specificities of the use of medial or lateral gastrocnemius muscle head are shown.

Keywords: Coverage, Gastrocnemius muscle flap, Infection, Soft tissue defect, Total knee arthroplasty

How to cite this article

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INTRODUCTION

The Surgical management of infected total knee arthroplasty (TKA) remains a challenging therapeutic problem, and severe infections with large soft tissue defects in elderly high-risk patients can potentially lead to limb amputation. The infection rate in patients sustaining a primary TKA is normally below 2%, but it increases up to 40% in patients who underwent a revision TKA [1], and infections with multiresistant bacteria have been shown to increase the rate of relapses up to 19% [2]. Early non-infected wound complications after primary or revision TKA, that is significantly associated with a history of diabetes mellitus, and resulting in exposure of bone or implant may have a risk of subsequent infection up to 20% [3, 4].

If a soft tissue defect after TKA with or without infection is present, a surgical intervention should follow as soon as possible. The one-stage management can be done in patients with no reduced general state of health, absence of multiresistant bacteria, adequate bone stock, and non-chronic infection. For the other patients, the two-stage management (TSM) is to be considered as the method of choice and can avoid limb amputation in 85% of patients who underwent a revision TKA [5].

CASE SERIES

Case 1

A 76-year-old male presented with a chronic and deep high-grade TKA. Assessment by culture and

histology revealed bacterial load with multiresistant Staphylococcus aureus. First: the implant was removed, accompanied with multiple debridements and incorporation of a polymethyl methacrylate (PMMA) spacer containing vancomycin, and multiple negative-pressure vacuum assisted closure (VAC) therapies of the resulting large soft tissue defect (Figure 1A). Second: after consolidation of deep infect, assessed by culture and histology, the defect was covered with the use of a medial gastrocnemius muscle flap (Figure 1B), and additional split-thickness skin grafts. After that, the wound healing was uncomplicated (Figure 1C); and eight weeks after the first step of surgical intervention, a new TKA could be performed. Six months after insertion of the new TKA, the function was satisfactory (Figure 1D), and the patient could be mobilized with full weight-bearing on the affected leg (Figure 1E).

Case 2

A 85-year-old female presented with an acute and low-grade revision TKA infection right, assessment by culture and histology revealed bacterial load with *Staphylococcus epidermidis*. The TKA was done six weeks ago due to a pronounced primary osteoarthritis.

Primary surgical treatment consists of multiple debridements, incorporation of collagen drug carriers containing gentamycin, multiple negative-pressure VAC therapies, and the revision TKA was not removed (Figure 2A). Second: after consolidation of low-grade infect, assessed by culture and histology, the defect was covered with the use of a lateral gastrocnemius muscle flap (Figure 2B), and additional split-thickness skin grafts. After that, the wound healing was uncomplicated (Figure 2C), and the patient could be mobilized with full weight-bearing on the affected leg.

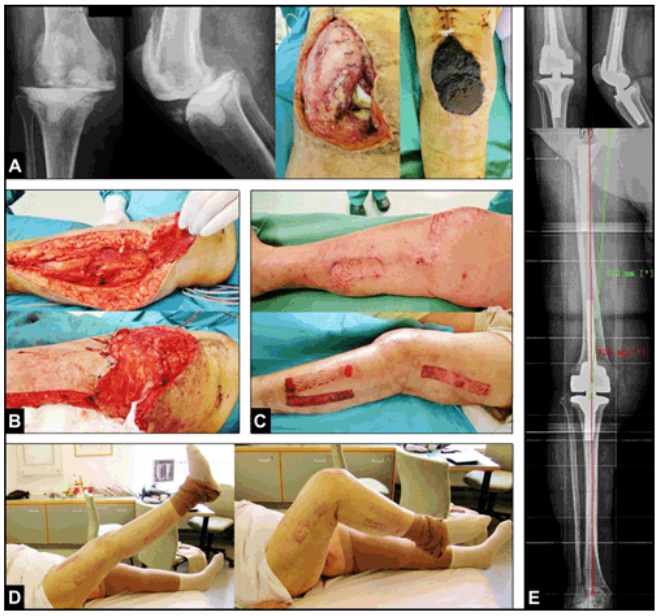

Figure 1 (Case 1) : (A) Posteroanterior and lateral radiographs demonstrating removal of implant and PMMA spacer incorporation that includes vancomycin, and clinical photographs showing large soft tissue defect treated with VAC therapy, (B) Clinical photographs showing harvesting and transposition of medial gastrocnemius muscle head over an incision of the adjacent skin bridge, (C) Clinical photographs showing wound healing medial and lateral after the required multiple procedures, (D) Clinical photographs demonstrating function of knee after re-implantation of a TKA with an extension-flexion motion arc of 90°, (E) Posteroanterior and lateral radiographs demonstrating correct alignment of re-implanted TKA, note that the patient had a history of total hip replacement of the same lower extremity.

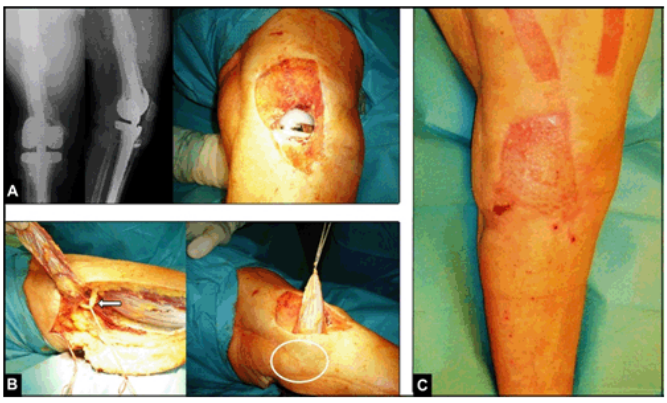

Figure 2 (Case 2) : (A) Posteroanterior and lateral radiographs demonstrating TKA, and clinical photograph showing large soft tissue defect with exposure of implant and without any signs of deep infection after multiple debridements and VAC therapies, (B) Clinical photographs showing harvesting and transposition of lateral gastrocnemius muscle head with preserving of the adjacent skin bridge (oval circle), the implant was not removed, note the lateral muscle head for transposition must be shifted under the peroneal nerve (arrow), and (C) Clinical photograph showing uncomplicated wound healing.

DISCUSSION

The first step of TSM includes radical debridement of soft tissue combined with negative-pressure VAC therapy, and systemic and/or local antibiosis using drug carriers such as collagen [2, 6], followed by coverage of soft tissue defect. The VAC therapy before coverage provides a sterile and controlled environment that can lessen the duration of wound healing, promotes better capillary circulation, and decreases the bacterial load [7]. The implant should be removed in patients with chronic or high-grade infection [5], accompanied with incorporation of a PMMA spacer containing antibiotics such as gentamycin or vancomycin. Implant preservation can be achieved when an acute low-grade infect is consolidated, assessed by culture and histology, and early closure of defect can be done [8].

The use of local flaps for coverage of soft tissue defects around the knee joint is an option for treatment in patients who are not willing or healthy enough to undergo free microvascular tissue transplantation, and do not

require microsurgical expertise. Muscle flaps promotes better capillary circulation and decreases the bacterial load, hence, muscle flaps are not contraindicated when superficial bacterial contamination or infection is present. However, muscle flaps generally are not free of complications. Neale et al. [9] reported on major and minor complications in 32% of a total of 95 muscle flaps and they agreed that the causes were mainly technical errors, inadequate debridement, use of diseased and traumatized muscle, and unrealistic objectives.

The gastrocnemius muscle flap has proven to be a suitable and reliable option for coverage of soft tissue defects after TKA or posttraumatic conditions, and it is probably one of the safest flaps [5, 10–13]. There is only one vasculonervous pedicle for each of both muscle heads composed of a sural artery and one or two veins, and is classified as type I according to the classification of Mathes and Nahai [14]. The blood supply allows to divide the muscles in two sections longitudinally according to the needs. The lateral muscle head must be rotated around the proximal fibula, therefore, it has a lower rotation angle than the medial head. Hence, the lateral muscle must be shifted under the peroneal nerve to prevent nerve compression. According to local specificities, the transposition each of both muscle heads can be done over an incision of the adjacent skin bridge, or with preserving of the adjacent skin bridge. There is an option to safely harvest a skin paddle overlying the muscle [15]. Additionally, the use of gastrocnemius muscle flap allows the reconstruction of knee ligaments or extensor tendon [12, 16]. Fansa et al. [12] reported on a flap survival of 100% in 11 patients after primary TKA, and TSM for re-implantation of implants was superior to a single-stage procedure. Suda et al. [5] reported on a required revision rate of 15,8% in 38 patients after revision TKA. If gastrocnemius muscle flap is not possible, simple random pattern skin flaps can be an option for coverage. Haroon-Ur-Rashid et al. [17] published results of 21 patients treated with distally pedicled random skin flaps for coverage of the upper two-thirds of the lower leg, all flaps survived, and the maximum size of flap was 15x7 cm.

The second step of TSM includes re-implantation of an implant or knee arthrodesis. Essential prerequisite for re-implantation of an endoprosthesis is sufficient exclusion of persistent bone infection, assessed by culture and histology. Knee arthrodesis is indeed an alternative to achieving stable lower limb with reduced pain [5].

CONCLUSION

The use of gastrocnemius muscle flaps for coverage of large soft tissue defects following primary or revision total knee arthroplasty is an excellent surgical option. The removal of implant depends on the grade of local infection.

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CASE SERIES

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Superficial siderosis following trauma to the cervical spine: Case series and review of literature

Pranab Sinha, Sophie Jane Camp, Harith Akram, Robin Bhatia, Adrian Thomas Carlos Hickman Casey

ABSTRACT

Superficial siderosis is a rare progressive disease associated with chronic hemosiderin deposition on the surfaces of the central nervous system (CNS). It typically manifests clinically in sensorineural hearing loss, cerebellar ataxia, and pyramidal signs. Recurrent or continuous bleeding into the cerebrospinal fluid is implicated in the disease process. The magnetic resonance imaging gradient-echo T2-weighted images have high sensitivity for hemosiderin deposits that bathe the CNS, giving the characteristic black rimmed area of hypointensity apparent on these images. The natural history and its treatments are still not clearly defined in literature. Our report details the clinical course and management of three cases of superficial siderosis following either cervical spine or brachial plexus injury. All of them underwent surgical intervention. In two of the cases, positive cessation of the intradural bleeding was achieved through surgery but clinical and radiological improvement occurred in only one of the cases. One patient had a negative intradural exploration. To date, 30 cases of superficial siderosis reported in the literature have undergone surgical intervention. Cessation of disease progression or neurological improvement has been documented in 18 of these cases. Our cases reveal that patients with superficial siderosis often develop severe functional impairment due to the progressive nature of the disease. On balance, we are of the opinion that early craniospinal imaging and surgical exploration should be undertaken, at least to attempt to halt neurological deterioration.

Keywords: Cervical Spine, Review, Superficial Siderosis, Trauma

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INTRODUCTION

Superficial siderosis of the central nervous system (CNS) is a rare progressive disease entity associated with chronic hemosiderin deposition in the leptomeninges and sub-pial parenchyma [1]. It typically presents with sensorineural hearing loss, cerebellar ataxia, and pyramidal signs [1–3]. Other features include cognitive impairment, bladder dysfunction, anosmia, myelopathy, back pain, bilateral sciatica, and lower motor neuron signs [4–6].

Recurrent or continuous bleeding into the cerebrospinal fluid is implicated in the aetiology of superficial siderosis. This may be as a result of intracranial or spinal neoplasm, subarachnoid hemorrhage, subdural hematoma, hemorrhagic meningitis, head injury, and spinal trauma with nerve root avulsion [3, 6]. Iatrogenic damage during surgery is a further possible cause [1, 5].

The natural history and treatment paradigms for superficial siderosis are not clearly defined. It is unknown why only a proportion of patients with hemosiderin deposition after subarachnoid hemorrhage develop the condition. Heme metabolism within the blood-brain barrier underpins the aetiology.

The following report details the clinical course and subsequent management of three cases of superficial siderosis following cervical spine or brachial plexus injury.

CASE 1

A left handed patient was referred with a seven year history of progressive deterioration in gait and balance, and a two-year history of left sided hearing loss with associated tinnitus and dysarthria. On further questioning, the patient had been involved in a motorcycle accident at the age of 23, sustaining a partial right C7 and complete right C8 and T1 nerve root avulsions.

The patient had a broad based ataxic gait, and exhibited a cerebellar dysarthria. Examination of the cranial nerves revealed hypometric saccades, a mild left facial weakness, and a sensorineural hearing loss on the left. The intrinsic muscles of the right hand were atrophied, with clawing of the digits. Sensation was absent in the right C7, C8, and T1 dermatomes. The right triceps reflex was absent, but all other upper limb reflexes were brisk. Reflexes were slightly reduced in the lower limbs, with bilaterally down going plantars.

Magnetic resonance imaging scan of brain demonstrated superficial siderosis, most markedly over the superior cerebellum, which was grossly atrophic (Figure 1A). These findings were also noted over the posterior aspect of the midbrain and around the calcarine sulci. Imaging of the cervical spine showed only degenerative changes, with a right-sided ventral longitudinal intraspinal fluid filled collections (VLISFC) at the C6/7 level. A CT myelogram to identify the dural defect was carried out and it confirmed a well-defined 20x15 mm lesion expanding into the right C7/T1 intervertebral foramen, consistent with a VLISFC. Routine blood tests revealed mild iron deficiency anemia, whilst examination of the cerebrospinal fluid (CSF) showed an increased ferritin concentration (100 IU/L). Microtrauma to the internal venous plexus in the epidural space by CSF leak may be the a reason for red blood cells seen in the cervical spine.

The patient underwent a C6 to T1 laminectomies and exploration of the VLISFC in March 2008. Following a durotomy, the right C8 nerve root was inspected, and the VLISFC was also explored. There was obvious staining on inspection of the cord. A small intradural bleeding vessel was identified, this was in close proximity to the site of dural aberration but separate from dissection site. This was coagulated. The defect in the dura was then repaired.

Postoperative imaging taken three months after the surgery showed that the intramedullary signal change had become less conspicuous (Figure 1B). The patient's radiological changes postoperatively were mirrored by clinical improvement in his postoperative symptoms over the course of the two years following the surgical repair.

CASE 2

A right handed patient was referred with a six year history of a worsening left hemiparesis, progressive gait ataxia, dysarthria, increasing urinary urgency, complex double vision in all directions, and declining cognitive function. The patient's symptoms followed recurrent thunderclap headaches eighteen months previously, which had been investigated at his local hospital, without a conclusive diagnosis. The patient's background history revealed that they had sustained a C1/2 hangman fracture following a cycling accident 24 years earlier. As a consequence the patient was left with a Brown-Sequard syndrome, with left pyramidal signs and a right spinothalamic sensory level from C3 down. During the accident the patient also sustained a right C5 and C6 brachial plexus avulsion injury, with resultant right upper limb weakness. Cranial nerve examination showed disconjugate eye movements with convergence nystagmus, scanning dysarthria, and cerebellar signs.

Brain MRI scan revealed susceptibility artefacts along the surface of the cerebellum bilaterally, which were thought to represent superficial siderosis (Figure 2). There was an appearance of a VLISFC at the level of C6 and C7. There was also an incidental finding of tonsillar ectopia in keeping with a Chiari I formation, and general non-significant cervical degenerative changes. Intracerebral and spinal angiography did not show any obvious vascular pathology.

The patient's symptoms displayed signs of intracranial hypotension. There is a close association with superficial siderosis with the underlying mechanism being a dural tear [7]. Given the patient's progressive neurological deterioration, and the imaging findings consistent with superficial siderosis, the patient agreed to a surgical

exploration of the VLISFC. This was undertaken in August 2008.

Through a posterior spinal approach, a unilateral partial facetectomy at C6/C7 revealed the capsule of the VLISFC. The capsule was opened and the cavity fully explored using the microscope. Staining of the spinal cord was observed. No bleeding point was identified. Artificial dura and tissue glue were applied, followed by layered closure.

Over the two weeks following surgery, the patient's cognitive function deteriorated. However, the patient then slowly recovered to their preoperative baseline. Subsequently, the patient experienced worsening episodes of postural headache, and their preoperative symptoms failed to improve. Postoperative imaging did not reveal a surgical complication as a cause of the headaches. Local occupational and speech and language therapists were enlisted to facilitate his activities of daily living. In addition, a local hematologist commenced deferiprone in place of trientine, to aid improvement in the patient's functional state.

CASE 3

A right-handed patient was referred with a 10 year history of deteriorating gait and an eight-year history of slurring of speech, dysphagia, and diplopia, with worsening bilateral sensorineural hearing loss worse on the left side. The patient had sustained a C2 and a C3 vertebral body and left forearm fractures following a road traffic accident 33 years earlier. At this time, the patient had undergone and open reduction and internal fixation of the forearm fractures, and posterior cervical fixation. The patient had no other significant past medical history. The patient's medications comprised baclofen and detrusitol for bladder dysfunction.

On examination the patient had anosmia, horizontal nystagmus on lateral gaze, and diplopia on right and left gaze. The patient had a complete sensorineural hearing loss on the left and partial loss on the right. The patient exhibited poor co-ordination of the right upper limb, with past pointing and dysdiadochokinesia. The tone, power, and reflexes were normal throughout all four limbs, with down going plantars. The patient walked with a wide based gait and their higher mental functions were intact.

A cervical spine x-ray revealed fusion of the spinous process of C1 and C2, with interspinous wires. A cervical spine CT scan showed the wiring through the posterior elements of C1 and C2, with bony fusion. There was fusion of the peg anteriorly at C1 and fusion of C2 and C3.

An MRI scan of the head revealed evidence of superficial deposition of blood degradation products primarily affecting the posterior fossa (Figure 3A). These were predominantly surrounding the midbrain, extending down the cervicomedullary junction to the superior cervical cord and lining the posterior lateral, and the fourth ventricles. Similar findings, but to a lesser degree, were seen on the surfaces of both cerebral hemispheres. There was some signal attenuation affecting the left lateral semicircular canal which was most obvious on the axial high resolution images. An MRI scan of the spine showed that the odontoid peg was malformed and posteriorly inclined. However, no thecal sac compression was reported. Metallic artefact was seen in the soft tissues posteriorly. The visualized spinal cord was normal in contour. The cervical cord also showed siderosis on its surface but otherwise was of normal signal intensity. Intracerebral and spinal angiography did not show obvious vascular pathology. This could be due to craniospinal hypovolemia, which may lead to prominent vasculature on the MRI but negative results on angiography.

The patient underwent C1-C3 laminectomy through a posterior spinal approach in March, 2009. A microscopic intradural exploration revealed a bleeding point, which was separate from the dissection site. This was cauterized. The dura was then repaired.

In the postoperative period, the patient noted worsening headaches, numbness of the right side of his body, and he became doubly incontinent. A subsequent MRI scan revealed a large irregular VLISFC in the

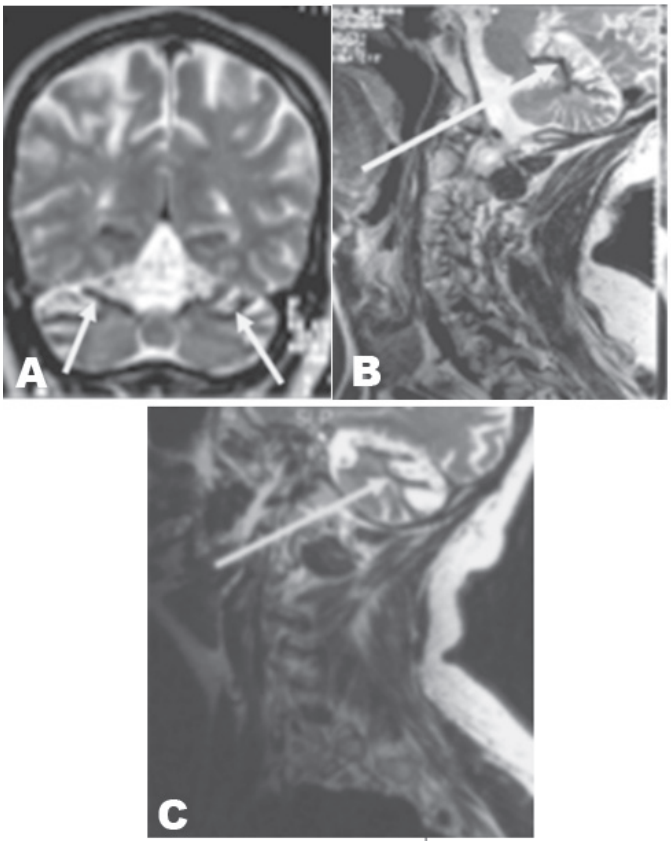

Figure 1: Showing black rimmed hypointensity in the superior cerebellum due to hemosiderin deposits on the (A) T2 coronal and (B) T1 sagittal MRI views, (C) Showing postoperative T2, sagittal MRI views three months later with less conspicuous signal change in the superior cerebellum.

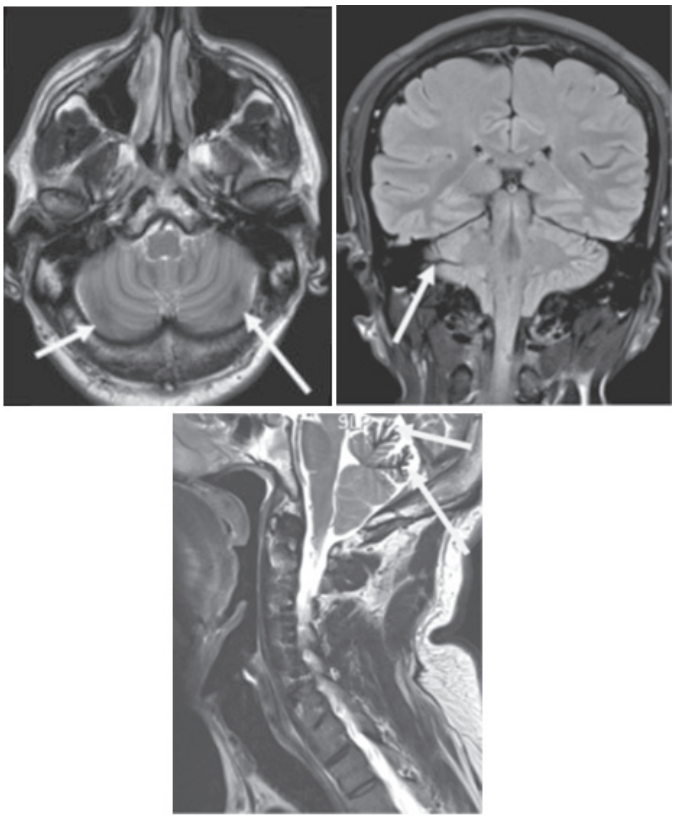

Figure 2: Showing area of black rimmed hypointensity along the surface of the cerebellum bilaterally T2, axial, coronal and sagittal MRI views respectively

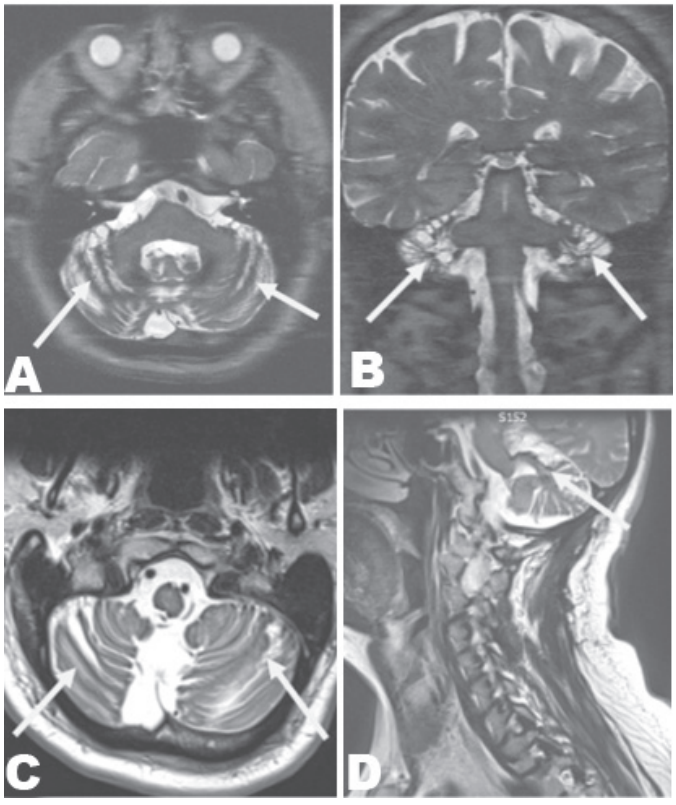

Figure 3: Showing black rimmed hypointensity of the cerebellum on T2 (A) axial and (B) Coronal MRI views. Showing no significant change in the area of black rimmed hypointensity postoperatively on T2 (C) Axial and (D) Sagittal views.

posterior extraspinal tissues. The patient underwent a re-exploration of the surgical site and the VLISFC was repaired.

With intense neurorehabilitation the patient regained fecal continence and the patient's urinary sphincter control improved. However, the patient's right-sided sensory loss persisted. The patient's most recent MRI showed focal cord atrophy at the level of C2. The previously noted VLISFC was no longer visualized (Figure 3B). The patient was subsequently transferred to his local neurorehabilitation unit.

DISCUSSION

Superficial siderosis is a rare condition [3, 8], due to chronic hemorrhage into the subarachnoid space [1]. Historically, the diagnosis of superficial siderosis was made by histological examination of biopsied tissue, or at autopsy. However, in the modern era, MRI scan can facilitate the diagnosis, especially the gradient-echo T2-weighted images which have a high sensitivity for hemosiderin deposition [8].

Macroscopically, superficial siderosis is apparent by the brownish discoloration of the leptomeninges and adjacent parenchyma, with a predilection for the superior vermis, crest of the cerebellar folia, basal frontal lobe, temporal cortex, brainstem, spinal cord, nerve roots, and cranial nerves I, II, V, VIII, and X [6]. At a microscopic level, hemosiderin deposition occurs within macrophages in the perivascular spaces, and along the pial vessel walls. This may lead to neuronal loss, gliosis, and demyelination [6]. The hemosiderin is derived from the breakdown of heme within the glia and the microglia. These cells will synthesize ferritin, however, once their biosynthesis capabilities have been exceeded, hemosiderin is produced. Unbound ferric ions mediate apoptosis by free radical mechanisms [8]. The iron deposits on the CNS surfaces bathed by cerebrospinal fluid have a paramagnetic effect on gradient echo sequences on MRI (T2-weighted images), giving a characteristic black rimmed area of hypointensity [9, 10].

The aim of treatment is to prevent progression of the neurological deficit. Medical and surgical options have been proposed. Medical management includes the use of iron chelators, with variable success [3, 8, 11]. Trientine has been associated with iron and copper chelation, but may cause increased iron levels within the liver, presumably due to its interference with ceruloplasmin [3].

Surgical management of superficial siderosis involves identifying and terminating the source of chronic bleeding [3]. Posti et al. reported that of 27 cases undergoing surgical intervention, disease progression was halted in 13 patients, four patients clinically improved, five patients had further clinical deterioration, whilst five patients sustained other complications [12]. Kumar et al. reported a case of superficial siderosis where intradural

exploration did not identified a bleeding source [7, 9, 10, 13, 14]. Egawa et al. reported two cases of superficial siderosis where the patients had dural defects with fluid-filled collections in the spinal canals, which were successfully closed [2]. One of the patients had cessation of further neurological deterioration, whilst the other partially deteriorated after surgery.

To date, 30 cases of superficial siderosis reported in the literature have undergone surgical intervention, and in five individuals no source of bleeding was identified intraoperatively. Disease progression has either been halted or there has been neurological improvement in 18 of these cases thus far.

All our three cases were referred late to our quaternary centre from other hospitals, this was perhaps due to delay in presentation together with difficulty in diagnosing this rare and obscure disease. All three cases had negative angiography. Previous studies of patients with cranial cerebellar superficial siderosis have shown to have negative angiography [3, 15]. The authors recognize that angiography seems to have limited sensitivity.

Post-traumatic VLISFC was deemed a potential target for a bleeding vessel and therefore explored. Intraoperatively all three patients had obvious staining of the spinal cord. Authors considered biopsy of the pia arachnoid but believed it to be hazardous and of no additional benefit to the patients. The two cases which revealed the intradural microscopic bleeding vessel were entirely separate from the dissection site. The intradural spinal artery after the arachnoid layer opened is usually bloodless and were not damaged intraoperatively in these cases. The intradural microscopic bleeding vessels were likely bleeding over a period of years. This is clearly unusual and the authors cannot explain this as the normal coagulation cascade should have stopped this process. However, Tapscott el al. have previously described of a case where superficial siderosis developed more than a decade after the traumatic brachial nerve root avulsion [16]. Angiography was not able to locate a specific bleeding source but surgical repair of the meningeal diverticulum and venous cauterization helped reduce the overall central nervous system bleeding.

Our cases reveal that patients with superficial siderosis often develop severe functional impairment due to the progressive nature of the disease. This may significantly compromise their quality of life. The first case showed a positive outcome at two years. However, the second case highlights the possibility of a negative intradural exploration. The third case demonstrates that quality of life is not necessarily improved even if there is confirmed cessation of an intradural bleeding point. On balance, we are of the opinion that early craniospinal imaging and surgical exploration should be undertaken, at least to attempt to halt neurological deterioration.

CONCLUSION

Patients with superficial siderosis often develop myriad of neurological symptoms and signs that lead to severe functional impairment due to its progressive nature. On balance, we are of the opinion that early craniospinal imaging and surgical exploration should be undertaken, at least to attempt to halt neurological deterioration.

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Author Contributions

Pranab Sinha – Substantial contributions to concept and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the paper to be published
Sophie Jane Camp – Substantial contributions to concept and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the paper to be published
Harith Akram – Substantial contributions to concept and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the paper to be published
Robin Bhatia – Substantial contributions to concept and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the paper to be published
Adrian Thomas Carlos Hickman Casey – Substantial contributions to concept and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the paper to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE SERIES

PEER REVIEWED | OPEN ACCESS

The distally pedicled peroneus brevis muscle and fasciocutaneous sural artery flap for reconstruction of the distal third of lower leg

Ingo Schmidt

ABSTRACT

Introduction: The use of distally pedicled peroneus brevis muscle and fasciocutaneous sural artery flap for coverage of the distal end of lower leg is recommended for soft tissue defects with exposure of bones and/or tendons in patients who are not willing or healthy enough to undergo free microvascular tissue transplantation, and do not require microsurgical expertise. Case Series: A short presentation of six cases including a short review of literature will highlight current knowledge and complications of these procedures. Conclusion: The distally pedicled peroneus brevis muscle and fasciocutaneous sural artery flaps are useful for coverage of soft tissue defects of the distal third of lower leg. In our patients, the complication rate of distally pedicled neurofasciocutaneous sural artery flap is higher than the distally pedicled peroneus brevis muscle flap.

Keywords: Distal third lower leg, Distally pedicled peroneus brevis muscle flap, Distally pedicled sural artery flap, Soft tissue defect

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INTRODUCTION

Anatomical features of the distal third of lower leg and heel like subcutaneous bone surrounded by tendons with no muscles, vessels in isolated compartments with little intercommunication between them make the coverage of the wounds in the region a challenging problem. Options for coverage of soft tissue defects are free flaps, perforator flaps, reverse flow flaps, muscle flaps, cross leg flaps, and axial pedicled fasciocutaneous flaps such as the distally pedicled sural artery flap [1–3]. Quality debridement is the key to success for the healing of wounds in this region. Negative-pressure vacuum assisted closure (VAC) therapy before soft tissue coverage provides a sterile and controlled environment that can lessen the duration of wound healing, promotes better capillary circulation, and decreases the bacterial load [4]. The use of distally pedicled peroneus brevis muscle and neurofasciocutaneous sural artery flap for coverage of the distal end of lower leg is recommended for soft tissue defects with exposure of bones and/or tendons in patients who are not willing or healthy enough to undergo free microvascular tissue transplantation, and do not require microsurgical expertise.

CASE SERIES

Case 1

A 66-year-old female presented with chronically destroyed left Achilles tendon (Figure 1A) that was treated with an open augmented repair (Figure 1B). The patient developed early wound healing problems

resulting in a large necrotizing soft tissue defect (Figure 1C). The defect was covered with the use of a distally pedicled peroneus brevis muscle flap and additional split-thickness skin grafts (Figure 1D-E). The wound healing was uncomplicated (Figure 1F).

Case 2

A 67-year-old male presented with primary osteoarthritis of left ankle that was treated by total ankle arthroplasty, and resulting in soft tissue defect with exposure of anterior tibial tendon (Figure 2A). The tendon was covered with the use of a distally pedicled peroneus brevis muscle flap (Figure 2B) and additional split-thickness skin grafts. The wound healing was uncomplicated (Figure 2C).

Case 3

A 58-year-old male presented with a highly comminuted open intra-articular complete fracture of the right distal lower leg treated by external fixation and internal plating (Figure 3A). The resulting defect of medial malleolus was initially treated with VAC therapy (Figure 3B). After that, the defect was covered with the use of a distally pedicled sural flap (Figure 3C). The wound healing was uncomplicated (Figure 3D).

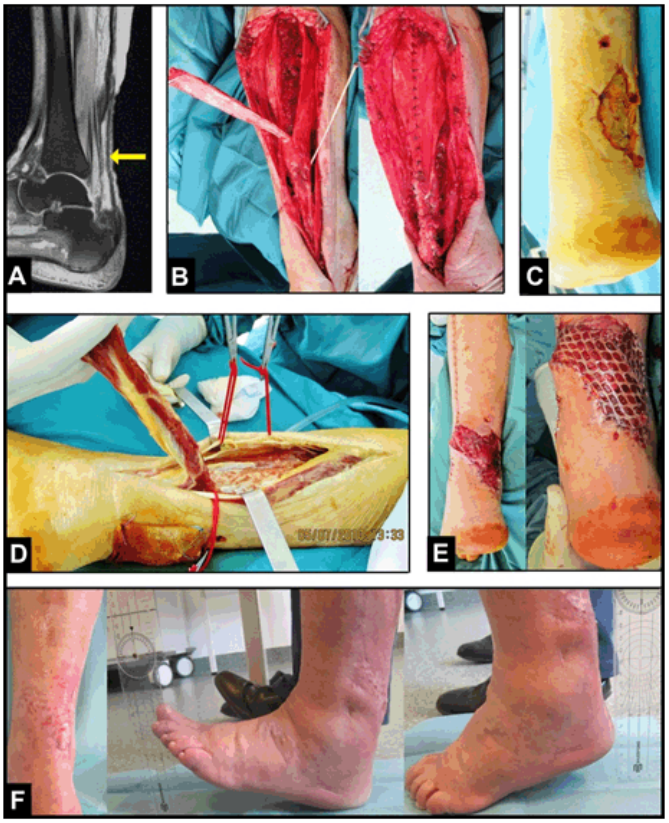

Figure 1: (A) Magnetic resonance image demonstrating chronically destroyed Achilles tendon (arrow), (B) Clinical photographs showing open augmented repair of Achilles tendon intraoperatively, (C) Clinical photograph showing large necrotizing soft tissue defect postoperatively, (D) Clinical photograph demonstrating harvesting of distally pedicled peroneus brevis muscle flap intraoperatively, (E) Clinical photographs showing transposition of peroneus brevis muscle before and after skin grafting intraoperatively, and (F) Clinical photographs postoperatively showing uncomplicated wound healing with preserving of eversion and plantar flexion of foot.

Case 4

A 61-year-old female presented with a posttraumatic soft tissue defect of the left heel that was successfully treated with the use of a distally pedicled sural flap, the pivot point was primarily closured (Figure 4A).

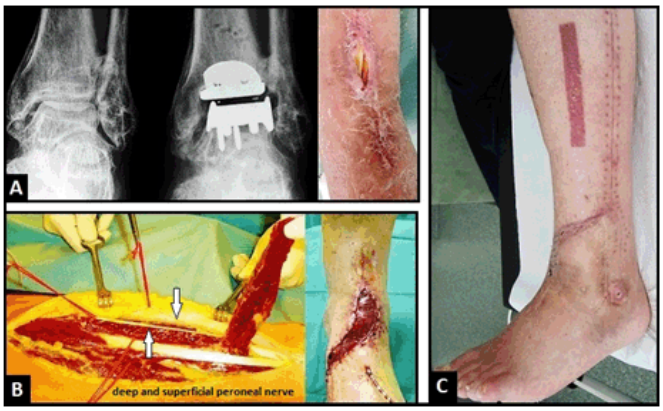

Figure 2: (A) Posteroanterior (PA) radiographs and clinical photograph showing pronounced osteoarthritis of ankle treated by total ankle arthroplasty, and postoperatively resulting in soft tissue defect with exposure of anterior tibial tendon, (B) Clinical photographs demonstrating harvesting and transposition of distally pedicled peroneus brevis muscle flap, note that both peroneal nerves were preserved (arrows), and (C) Clinical photograph postoperatively showing uncomplicated wound healing.

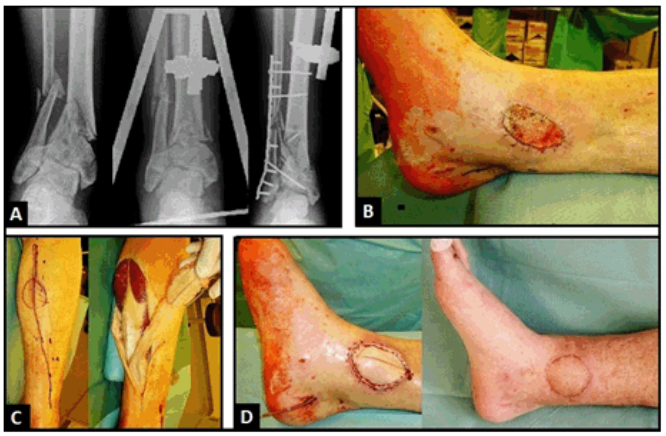

Figure 3: (A) Posteroanterior radiographs demonstrating highly comminuted open intra-articular complete fracture of the distal lower leg primarily treated by external fixation, and clinical photograph showing VAC therapy of pre-tibial soft tissue defect, (B) Clinical photographs showing harvesting and transposition of distally pedicled sural flap intraoperatively, and (C) Lateral radiograph demonstrating open reduction and internal fixation after complete an uncomplicated wound healing.

Case 5

A 74-year-old male presented with a chronic ulcer of the left heel that was treated with the use of a distally pedicled sural flap. The pivot point was primarily closured, resulting in flap loss due to venous congestion (Figure 4B).

Case 6

A 84-year-old female presented with an chronic ulcer of the right heel that was treated with the use of a distally pedicled sural flap in another hospital. The flap was failed (Figure 5A) due to selection of an unacceptable too short vascular pedicle (Figure 5B). The resulting defect was covered with skin grafts in the further course.

DISCUSSION

Originally, the peroneus brevis was a type II muscle flap according to the classification by Mathes and Nahai [5] with a dominant pedicle from the peroneal artery which is located proximally, and distal minor pedicles from the peroneal or tibial vessels, but it was reclassified as a type IV [6]. When harvesting the muscle with the proximal segmented pedicles, it can be used as flap for coverage of the middle third of lower leg. When harvesting the distal segmented pedicles which are found within six cm from the tip of lateral malleolus (approximately three fingerbreadths), it can be used in a distally pedicled manner for the distal third of lower leg. Lorenzetti et al. reported on a flap survival of 100% of 10 patients, and the ankle functionality and stability were maintained due to preservation of peroneus longus muscle [7]. The advantage is that the donor site can always be closed primarily and the flap is relatively reliable even in high-risk patients with a number of comorbidities, but care must be taken when using this flap in patients with peripherial arterial disease [8].

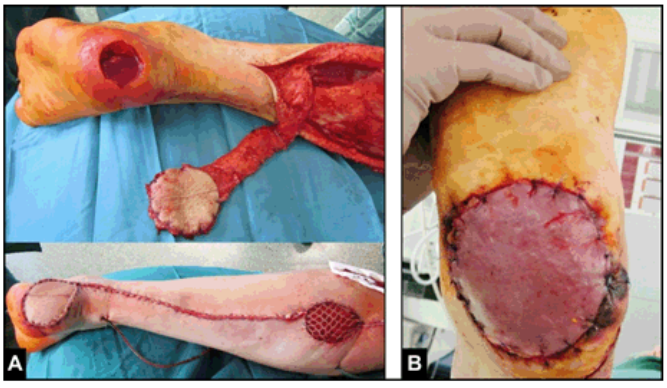

Figure 4: (A) Clinical photographs showing harvesting and transposition of distally pedicled sural flap for coverage of chronic ulcer of the heel, the pivot point was primarily closured and the donor site was primarily covered with a split-thickness skin graft, this flap survived, (B) Clinical photograph demonstrating venous congestion of a distally pedicled sural flap after coverage of the heel leading to complete flap loss.

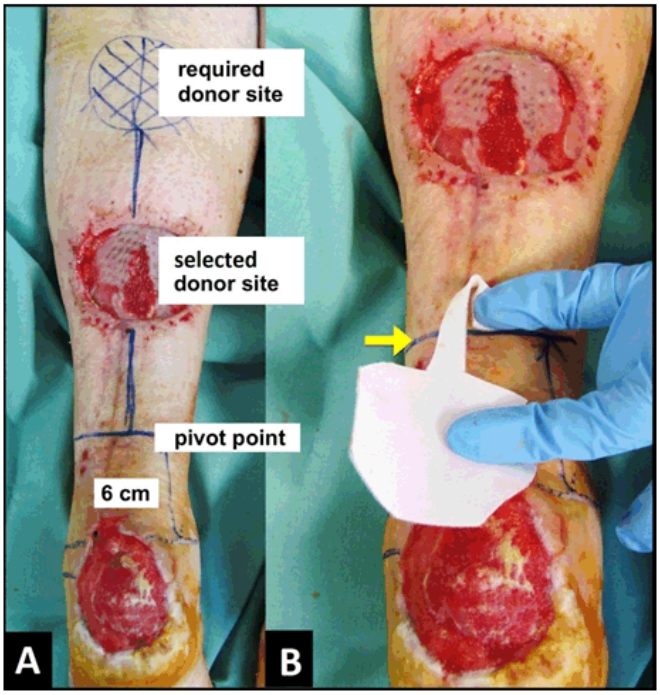

Figure 5: (A) Clinical photograph demonstrating a result after excision of a failed distally pedicled sural flap due to selection of an unacceptable too short vascular pedicle, and (B) The same patient in a retrospective reconstruction: if the correct pivot point (arrow) had been applied coverage of existing heel defect would not have been possible (imitation of the required 180° turned manner in this special situation), the primary procedure was performed in another hospital.

The distally pedicled neurofasciocutaneous sural artery flap was first described by Masquelet et al. [2], it is a skin island flap which is retrograde supplied by at least three perforator vessels from the peroneal artery within approximately six cm from the tip of lateral malleolus. However, this flap is not free of any complications mostly based on venous congestion, and the weakness can be the pivot point. The flap's arterial inflow is robust and constant, but the venous congestion is susceptible, occurring in up to 21.4% of cases [9], and it is mostly detected if the flap was used in a 180° turned manner [10]. To prevent venous stasis intra- and early postoperatively, the pivot point of vascular pedicle including the short saphenous vein can be covered temporary with a skin substitute and covered secondary with a skin graft. Another options to prevent venous congestion are the flap's use in a two-stage manner, supercharged or superdrained manner, and/or intermittent short saphenous vein phlebotomy [10–13]. Schmidt et al. [14] reported on a survival rate of flap's use in an adipofascial manner with additional skin grafting in 87.5% of 104 cases. In cases in which the short saphenous vein cannot be found, the flap should not be utilized; and in older, high-risk, and critically multimorbid patients including peripherial arterial disease, a considerable necrosis rate of 36% of a total of 70 procedures was found by Baumeister et al. [15]. An unacceptable failure leading

to a loss of flap is when the vascular pedicle was elected too short and no sufficient arterial supply exists.

CONCLUSION

The distally pedicled peroneus brevis muscle and fasciocutaneous sural artery flaps are useful for coverage of soft tissue defects of the distal third of lower leg. In our patients, the complication rate of distally pedicled neurofasciocutaneous sural artery flap is higher than the distally pedicled peroneus brevis muscle flap.

****

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Author Contributions
Ingo Schmidt – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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CASE SERIES

PEER REVIEWED | OPEN ACCESS

Breast augmentation using injectable materials

Olayinka Gbolahan, Sonal Halai, Steven Goh

ABSTRACT

Introduction: Breast augmentation using injectable materials are widely used around the world. Most commonly used materials include collagen and silicone. These materials are associated with detrimental effects and although this method of augmentation is banned in UK, due to medical tourism and immigration we still encounter such patients in our practice. It is hence important to understand how best to manage the complications associated with these practices. We discuss three of such cases. Case Series: A 30-year-old female presented with bilateral painful breasts with history of previous augmentation with silicone injections in Thailand. A 57-year-old female recall from breast screening due to presence of bilateral multifocal nodular densities with history of previous bilateral collagen augmentation. A 41-year-old female presented with lump in right breast with previous history of silicone injection in Dubai. Conclusion: Awareness of potential imaging complications in this group of patients with ensure safe practice in their management.

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INTRODUCTION

Breast augmentation by means of injectable materials such as collagen and silicone are widely used around the world, particularly in Asian countries. The minimally invasive nature of injectable materials makes it appealing to patients. Collagen, either bovine or recombinant human, is a widely used filler substance since 1977 [1] with cosmetic effects are thought to last 6–22 months depending on the product. Collagen is also not histologically detected six months following injection [2]. Liquid silicone has been used since 1940; its involvement into the tissue varies. Complications following the injection of liquid silicone on average are thought to occur nine years following injections with extensive breast tissue involvement [3, 4]. Both materials are associated with detrimental effects. However, not all patients present with complications. Liquid silicone is displayed on mammography as either multiple cystic lesions or large areas of opacity [4]. Symptomatic presentation following such procedures is rare in the UK, we discuss three such cases.

CASE SERIES

Case 1

A 30-year-old Thai female presented with bilateral painful breast lumps. She had undergone bilateral breast augmentation with silicone injections in Thailand six years prior to presentation. On examination she had extensive bilateral breast nodularities and induration. Ultrasound and MRI (Figure 1) scan confirmed widespread silicone granulomata. Patient was discussed in the MDT and subsequently referred to plastic surgeons for consideration for piecemeal excision of the silicone deposits with possible augmentation, or mastectomy and reconstruction, if skin continued to have significant inflammation. The patient was seen over a four-month period prior to subsequent referral.

Case 2

A 57-year-old Asian female was recalled from breast screening following the presence of bilateral multifocal nodular densities. In 2007, the female had undergone breast augmentation in Dubai with three sessions of collagen injections into the breast parenchyma. She was asymptomatic and clinical examination revealed no suspicious features. Mammography images (Figure 2) were difficult to interpret and will consequently make future screening challenging. Following an MDT discussion routine clinical examination should be used to screen the patient. It was also subsequently decided by the local breast screening director that mammographic screening would not be useful and the patient should present to clinic if symptomatic. The patient was seen over a two-year period prior to this decision being made.

Case 3

A 41-year-old female presented with lump in right breast with a previous history of silicone injection in Dubai in 2012. On examination she was found to have an indeterminate lump in the medial aspect of right breast. Mammogram showed unusual appearance (Figure 3) with well-defined opacity seen medial to right nipple

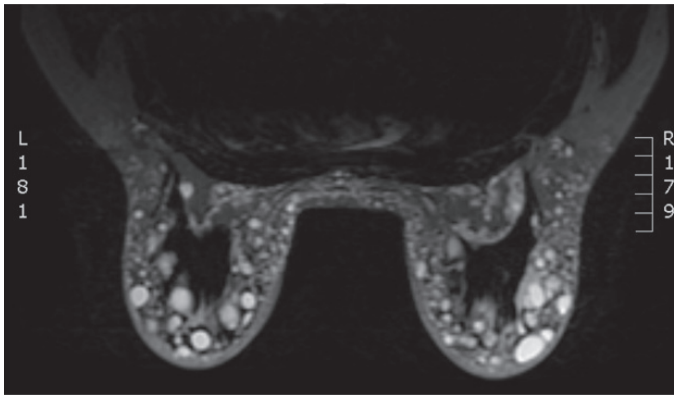

Figure 1: Bilateral magnetic resonance imaging breast showing widespread silicone granulomata.

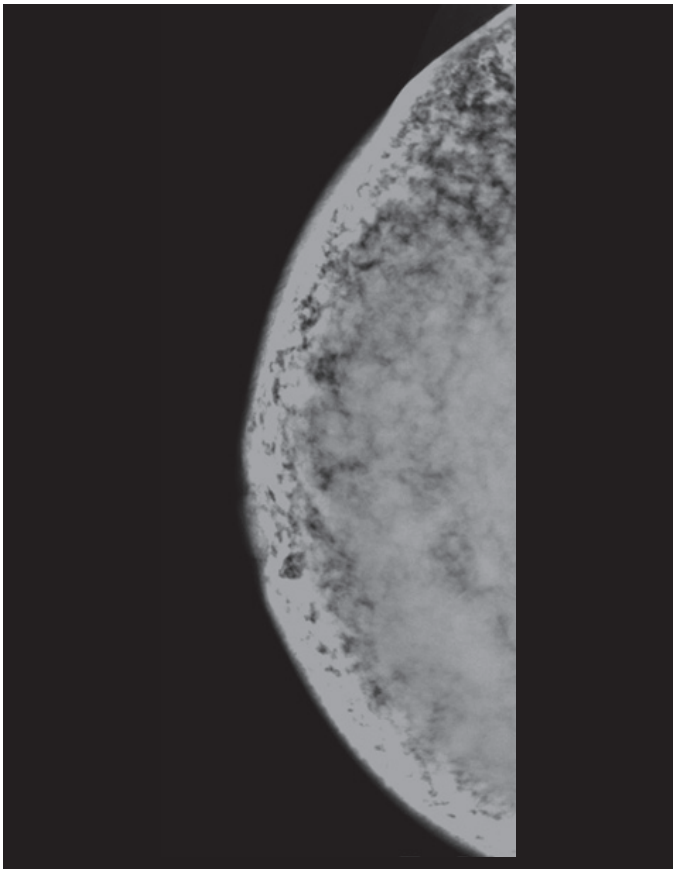

Figure 2: Right breast mammography post collagen injections to breast parenchyma.

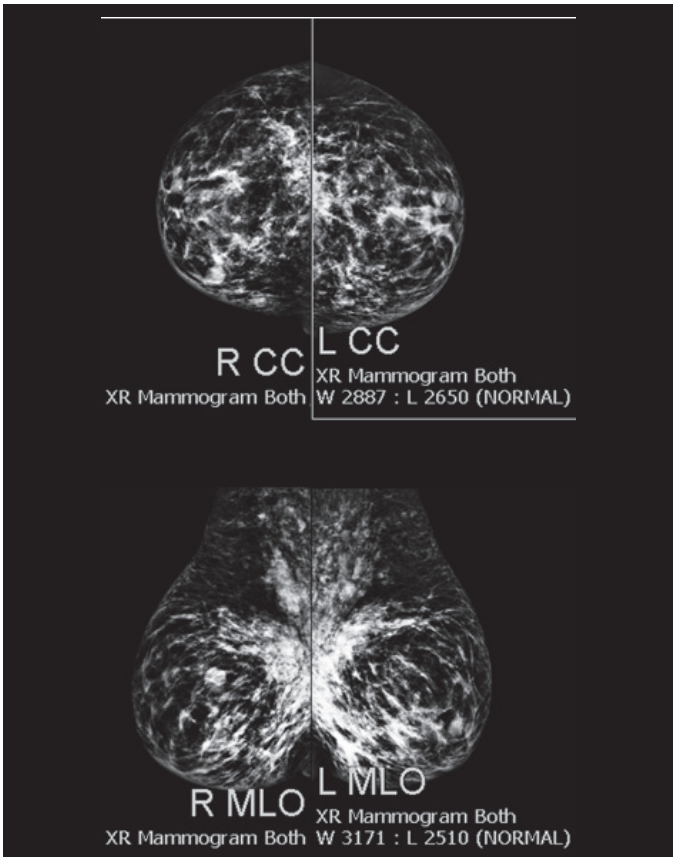

Figure 3: Bilateral mammography showing well defined opacities in both breasts.

and deep to left nipple. Ultrasound imaging was severely impaired by the silicone. MDT discussion concluded that MRI would not be useful and FNA was advised which showed silicone reaction. The patient was seen over a two-month period, re-assured and discharged.

DISCUSSION

There are some studies describing the long-term effects of injectable materials such as collagen and silicone with one case report of a patient undergoing total expiration of the injected material, affected skin, pectoralis major and breast parenchyma with immediate reconstruction using rectus abdominis muscle [5]. Augmentation with injectable materials poses a challenge to the interpretation of mammograms and thus can reduce the effectiveness of screening. MRI scan has been shown to be a more useful imaging modality in these patients [6] although as in Case 3, FNA is most conclusive in solitary nodules. This, therefore, makes effective screening in these patients time consuming and costly. As in Case 2, patients may have to forfeit their mammographic screening rights and may have to self-present if symptomatic. Awareness of potential complications and the presence of these fillers in the breast parenchyma rendering mammography ineffective will ensure safe practice during breast screening of these patients.

CONCLUSION

Although breast augmentation using injectable material is currently banned in the UK with increased immigration of individuals, it is important to understand how to deal with local complications that may arise. The cases described give some potential solutions to these complications including patients forfeiting routine mammographic screening and self-presenting when symptomatic.

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Author Contributions

Olayinka Gbolahan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Sonal Halai – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Steven Goh – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Cytomegalovirus transverse myelitis in a non-immunocompromised patient

Binju Bose, Sonia Gera, Tasfia Hoque, Gaurav Kapoor, Hamza Khalid, Michelle El-Hajjaoui, Philippe Vaillancourt, Sandeep A. Gandhi, Mahmood Afghani

ABSTRACT

Cytomegalovirus (CMV) is known to be an opportunistic infection that causes a diverse clinical spectrum of disease states including retinitis, pharyngitis, adenitis, pneumonitis, hepatitis, and cystitis. We present a rare case of transverse myelitis in a non-immunocompromised patient found to be caused by cytomegalovirus. The patient's serum CMV titer was found to be very elevated and his initial magnetic resonance imaging scan revealed a signal abnormality in the spinal cord consistent with a transverse myelitis. This case report is intended to highlight the significance of developing a standard protocol to efficiently identify and treat transverse myelitis caused by cytomegalovirus in immunocompetent hosts and to reduce poor outcomes.

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INTRODUCTION

Transverse myelitis is a neurological disorder characterized by inflammation of the spinal cord. The inflammation traverses the spinal cord across one or multiple levels and results in destruction of myelin [1]. Cytomegalovirus (CMV), most commonly infects immunocompromised hosts. Its clinical spectrum includes retinitis, pneumonitis, hepatitis, and may cause transverse myelitis in some cases [2, 3]. We present a rare case of a transverse myelitis in a non-immunocompromised patient secondary to CMV infection.

A previously healthy 34-year-old Filipino male with no significant past medical history presented to the emergency department with fever 103.7°F, nausea, urinary retention, and bilateral hip pain for eight hours. He denied taking any medications. His social history was negative. His family history was not contributory. On physical examination, the patient was alert and in some

distress. The only significant finding on examination was a boggy, non-tender prostate and an enlarged bladder. The neurologic examination was unremarkable. The white blood cell count was 8,700/uL, hemoglobin 14.4 g/dL, platelets 175,000/uL, international normalization ratio (INR) was 1.1. and C-reactive protein was 0.78 mg/dL. Serum electrolytes were remarkable for sodium of 134 mmol/L and chloride of 97 mmol/L.

CASE REPORT

On hospital day-1, the patient developed a rapidly ascending weakness from his toes to the lower abdomen along with diplopia, perioral numbness, and urinary retention. He was started on levofloxacin, acetaminophen, tamsulosin, and intravenous (IV) hydration. A Magnetic resonance imaging of the spine showed a non-enhancing T2 signal abnormality in the cord extending from level C5 to the upper endplate of C7 without cord expansion or edema (Figure 1) and an increase in signal intensity in the mid-thoracic and upper lumbar spinal cord regions (Figure 2). Methylprednisolone 1000 mg IV was administered three times a day for four days. A few hours later, slurred speech and facial numbness were noted with progression to pinprick sensation loss up to T11 dermatome, bilateral leg weakness of 0/5, and diminished tone in lower extremities. There was also mild dysmetria on finger-to-nose testing and loss of rectal tone. Human immunodeficiency virus antibody I and II, Human T-Lymphocyte virus I and II were negative. Urinalysis and urine toxicology screen were negative. No enteric pathogens were detected in the stool culture. Blood cultures showed no growth. Direct flu antigen A and B, herpes simplex virus 1 and 2 DNA were undetectable. Serum Epstein–Barr virus IgG was 1, 270 mg/dL (normal: <0.90). Epstein–Barr virus Antibody Vca IgG titer was 1.84 (normal: <0.90). Epstein–Barr virus antibody Vca IgM titer was 2.96 (normal: <0.90). Serum antibody Lyme titer was undetectable. Cerebrospinal fluid analysis was significant for a non-reactive venereal disease research laboratory test (VDRL). The white blood count was 26/mm^3; polynuclear cells 32% and mononuclear cells 68%. Lyme antibody titer was negative. Protein was 150 mg/dL. It also contained well defined gamma restriction bands that were also in the corresponding serum sample, but some bands in the cerebrospinal fluid (CSF) were more prominent. The CSF IgG titer was 20.7 mg/dL and IgG synthesis rate was 25.3 mg/24 hours. Cytomegalovirus DNA titer by rapid polymerase chain reaction (PCR) was 40, 787. This suggested a transverse myelitis secondary to CMV. Thereafter, five plasmapheresis treatments were undertaken every other day. Ganciclovir 375 mg IV q12h for four days was also given. Despite such measures, his respiratory status started to decline and he was placed on bilevel positive airway pressure (BiPAP) support. Also, intravenous immune globulin 40 g IV every other day for a total of five treatments was prescribed. Subsequently, the respiratory status improved and he no longer required BiPAP support. On hospital day 18, paraplegia persisted with urinary and fecal incontinence and he was transferred to a rehabilitation facility. After 10 weeks, he was able to ambulate with a walker.

DISCUSSION

Transverse myelitis is characterized by inflammation of the spinal cord resulting in the destruction of myelin. The scar formation results in neuronal signal disruption [1]. Cytomegalovirus (CMV), a herpes virus, typically affects immunocompromised hosts. It may cause retinitis, pneumonitis, and hepatitis [2].

Transverse myelitis may result in weakness, sensory loss, and autonomic dysfunction below the level of the spinal cord lesion [3]. The signs and symptoms in the case described above are urinary retention, loss of

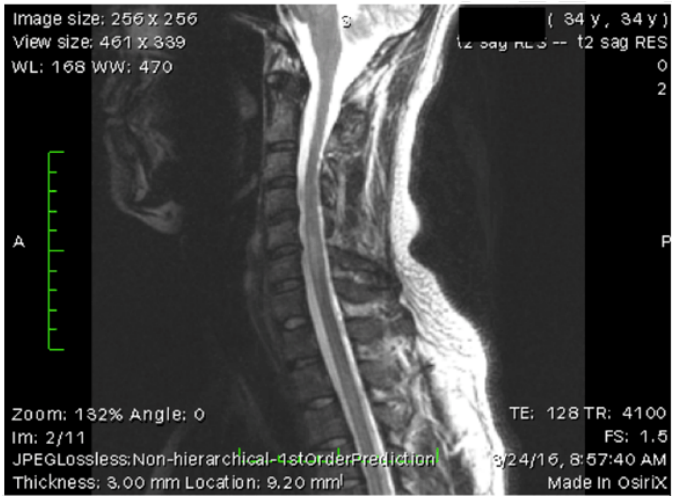

Figure 1: Magnetic resonance imaging of cervical spine: Non-enhancing T2 signal abnormality in the cord extending from level C5 to the upper endplate of C7.

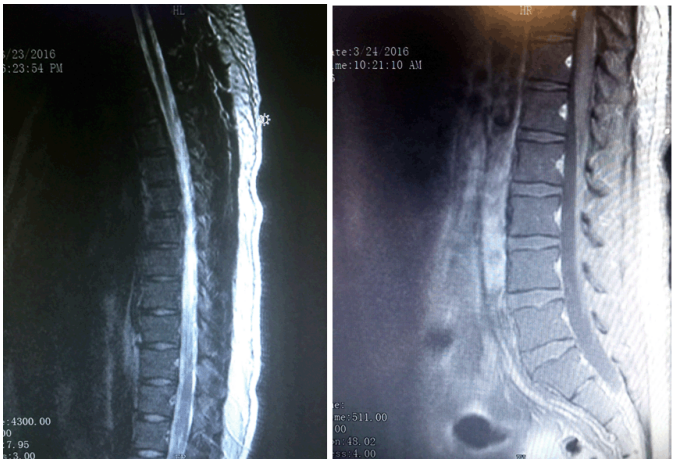

Figure 2: Magnetic resonance imaging of thoracic and lumbar spine: Non-enhancing T2 signal abnormality in the mid-thoracic and upper lumbar spinal cord.

sensation from the umbilicus to the toes, and paraplegia in the lower extremities. Magnetic resonance imaging results revealed a non-enhancing T2 signal abnormality involving spinal segments C5 to C7, mid-thoracic and upper lumbar region consistent with transverse myelitis. Our patient met the criteria of the variant longitudinally extensive transverse myelitis (LETM) [4, 5]. Recent literature suggests that 40–50% of transverse myelitis cases may present without significant CSF findings [1, 6, 7]. Additionally, transverse myelitis may not meet diagnostic criteria for signs of inflammation [8]. The absence of inflammatory markers does not rule out the possibility of transverse myelitis when the clinical picture is suggestive of transverse myelitis [8].

There is a reported case of CMV transverse myelitis in a 40-year-old immunocompetent Sri Lankan male who presented with a two-day history of fever with bilateral lower extremity flaccid paralysis without urinary retention, but within five days, the paralysis progressed proximally with significant urinary retention [9]. A spinal MRI scan demonstrated hyperintensities on C5 and T2 cord segments and the CSF had WBC of 350/mm^3 (92% lymphocytes). The patient's lower extremity strength improved from flaccid paralysis to anti-gravity muscle strength after 21 days of intravenous ganciclovir treatment. Of note, both patients were Asian men. This group may be prone to CMV transverse myelitis [10, 11] (Table 1).

Table 1: Diagnostic Criteria for Transverse Myelitis.

Diagnostic Criteria for Transverse Myelitis
• Sensory, motor or autonomic dysfunction attributable to the spinal cord
• Bilateral signs and/or symptoms
• Clearly define sensory level
• No evidence of compressive cord lesion
• Inflammation define by cerebrospinal fluid pleocytosis or elevated IgG index or gadolinium enhancement
• Progression to nadir between fours and 21 days

CONCLUSION

Transverse myelitis is a potentially debilitating disease. Approximately one-third of patients with transverse myelitis experience full recovery, one-third experience partial recovery, and the remaining have no recovery. Our patient's neurological symptoms have improved since initial presentation approximately three months ago. Future studies on pathophysiology of transverse myelitis may be required to develop a standard medical management protocol to prevent morbidity and mortality associated with cytomegalovirus associated transverse myelitis.

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Author Contributions

Binju Bose – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Sonia Gera – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
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The corresponding author is the guarantor of submission.

Conflict of Interest

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Rare presentation of a massive intermittent upper gastrointestinal bleed

Bonnie Patek, Matthew Sullivan, Shashin Shah

ABSTRACT

Introduction: Hemosuccus pancreaticus is a rare cause of upper gastrointestinal bleeding defined as bleeding from the ampulla of Vater through the main pancreatic duct, commonly caused by a ruptured aneurysm in the setting of acute or chronic pancreatitis. Bleeding is often intermittent and repetitive, but can be massive. Endoscopy rarely reveals active hemorrhaging. Case Report: We present a 35-year-old male with complaints of progressive fatigue and generalized weakness over two weeks. He denied melena, hematochezia, and hematemesis. History revealed prior alcohol abuse and hospitalization for pancreatitis. Laboratory studies revealed hemoglobin of 2.8 g/dL. Initial esophagogastroduodenoscopy (EGD) revealed actively bleeding mass at the major papilla and absence of gastric/esophageal varices. Colonoscopy revealed no pathology. Bleeding continued and patient developed mild epigastric tenderness. Repeat EGD revealed a clean based ulcer in the distal esophagus and thickening of the duodenal mucosa, but no bleeding. Duodenal biopsies showed signs of chronic inflammation. Abdominal computed tomography scan revealed pancreatitis and splenic artery pseudoaneurysm. Patient underwent an abdominal aortogram, revealing an 8 mm splenic artery pseudoaneurysm with no active bleeding. The pseudoaneurysm was embolized and repeat imaging confirmed no residual pseudoaneurysm. Conclusion: Pseudoaneurysm resulting from a pseudocyst secondary to pancreatitis forms most commonly in the splenic artery. Mortality can be as high as 90–100% if left untreated. Although rare, hemosuccus pancreaticus should be included in the differential diagnosis for any patient presenting with severe anemia, in the absence of endoscopically visualized bleeding and with a history of pancreatitis.

Keywords: Hemosuccus pancreaticus, Pancreatitis, Splenic artery pseudoaneurysm, Upper gastrointestinal bleeding

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INTRODUCTION

Hemosuccus pancreaticus is a rare cause of upper gastrointestinal bleeding defined as bleeding from the ampulla of Vater through the main pancreatic duct, commonly caused by a ruptured aneurysm in the setting

of acute or chronic pancreatitis. This terminology was described in 1970 by Dr. Sandblom and characterized by gastrointestinal bleeding leading to the cause of anemia and possible sharp episodic epigastric pain that can easily be overlooked, originating from a splenic artery aneurysm that ruptured into the main pancreatic duct [1]. Aneurysms and pseudoaneurysms are commonly formed in the setting of both acute and chronic pancreatitis [2]. However, these are not the only causes of hemosuccus pancreaticus (Table 1) [2–7].

Bleeding in these cases is often intermittent and repetitive, but can be massive. The intermittent bleeding of hemosuccus pancreaticus, despite being from an arterial source, rarely presents with hemodynamic instability, unless the cause is from a pseudoaneurysm or aneurysm that has ruptured [2]. The intermittent bleeding makes the diagnosis difficult with the possible need for multiple imaging modalities and high index of clinical suspicion to continue to look for a bleeding source. Endoscopy rarely reveals active hemorrhaging and often CT scan or angiography is needed to locate the source of the hemorrhage. If the source is located, interventional radiology should be consulted and proceed with embolization [5].

If these are unsuccessful or the patient is hemodynamic unstable, surgical intervention with the use of intraoperative pancreatoscopy is necessary to determine and treat the hemorrhagic source [6].

CASE REPORT

A 35-year-old male presented with a past medical history pertinent only for an occult gastrointestinal bleed one year ago during a bout of pancreatitis. Patient complained of generalized weakness and progressive fatigue for the last two weeks. He denied melena, hematochezia, hematemesis, nausea/vomiting, jaundice or chronic ibuprofen usage. Further history revealed prior alcohol abuse discontinued two years ago and a hospitalization for acute pancreatitis about four years ago. Laboratory studies revealed hemoglobin of 2.8 g/dL, which was followed by a blood transfusion of four packed red blood cell (pRBC) units.

An actively bleeding mass was seen at the major papilla during the initial esophagogastroduodenoscopy (EGD). No other sources of bleeding were noted as the patient had a non-bleeding ulceration at the gastroesophageal junction and lacked gastric or esophageal varices. A colonoscopy was performed that was unremarkable for a bleeding source. These procedures were performed prior to transfer to our institution. Bleeding continued with a continued drop in hemoglobin.

Upon arrival to our institution, the patient was noted to have spiking fevers and developed acute epigastric tenderness. Repeat hemoglobin was 7.1 g/dl leading to another two units of pRBC being transfused. An elevated lipase level at 803 U/L was noted.

A repeat EGD was performed at our institution and revealed no mass at the major papilla or source of bleeding. Mild thickening of the duodenal sweep and a clean based ulcer at the distal esophagus were the only findings. Duodenal biopsies exhibited only signs of chronic inflammation. A computed tomography scan of the abdomen/pelvis revealed pancreatitis consistent with splenic artery pseudoaneurysm (Figure 1), splenomegaly and 10x12 mm pancreatic head lesion (Figure 2) that was non-specific.

The patient was evaluated by interventional radiology and underwent an abdominal angiography, revealing an 8 mm splenic artery pseudoaneurysm from the proximal-mid splenic artery with no active bleeding. Coil embolization with six clips (Figure 3) and repeat imaging confirmed no residual pseudoaneurysm (Figure 4). After the procedure, the patient experienced mild abdominal

Table 1: Hemosuccus pancreaticus etiology

Acute Pancreatitis
Chronic pancreatitis (more common than in acute setting and more common in alcoholics)
Vascular Malformations
Pancreatic tumors (cystadenocarcinoma, pancreatic carcinoma, serous cystic neoplasm, neuroendocrine tumors and osteoclastoma)
Blunt Abdominal Trauma
Iatrogenic (laparoscopic surgery with vessel manipulation and EUS-FNA)
Pancreatic Divisum (Chronic pancreatitis); Pancreatolithiasis
Rupture of true aneurysm (atherosclerosis, vasculitis, fibromuscular dysplasia, syphilitic affection, hereditary dystrophy of elastic tissue (Marfan syndrome, Ehlers-Danlos syndrome), alpha-1 antitrypsin deficiency)

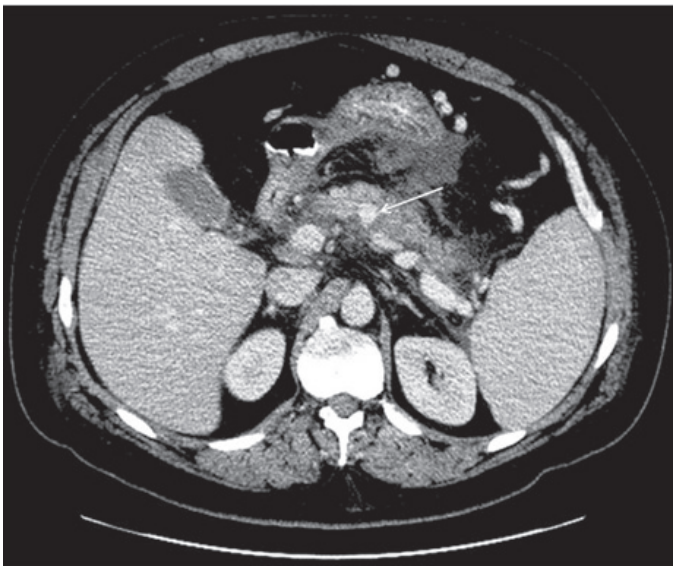

Figure 1: Computed tomography scan of abdomen/pelvis with contrast revealing pseudoaneurysm (arrow) located in the proximal-mid splenic artery and splenomegaly (not fully appreciated in this cut)

discomfort, fevers, leukocytosis which could be secondary to a splenic infarction (Figure 5) that was also observed on CT scan status post embolization or from resolving pancreatitis.

Follow-up MRI scan to evaluate the pancreatic mass showed an ill-defined area of decreased attenuation measuring 1.3 cm in addition to fatty infiltrates within the liver and splenic infarct. Patient was advised to follow-up for endoscopic ultrasound to evaluate this lesion after his acute issue had resolved. At time of discharge, patient was afebrile with no abdominal tenderness, stable hemoglobin and was vaccinated for encapsulated bacteria secondary to his asplenic condition status post splenic infarct.

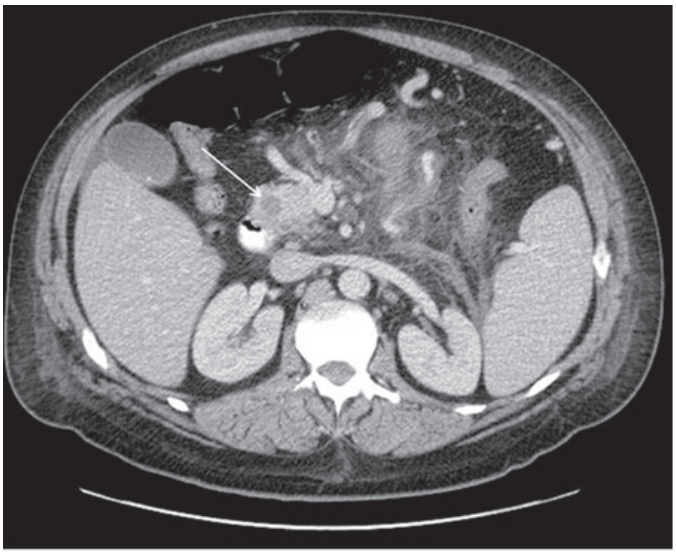

Figure 2: Computed tomography scan of abdomen/pelvis that visualizes the non-specific pancreatic mass (arrow) located in the head of the pancreas.

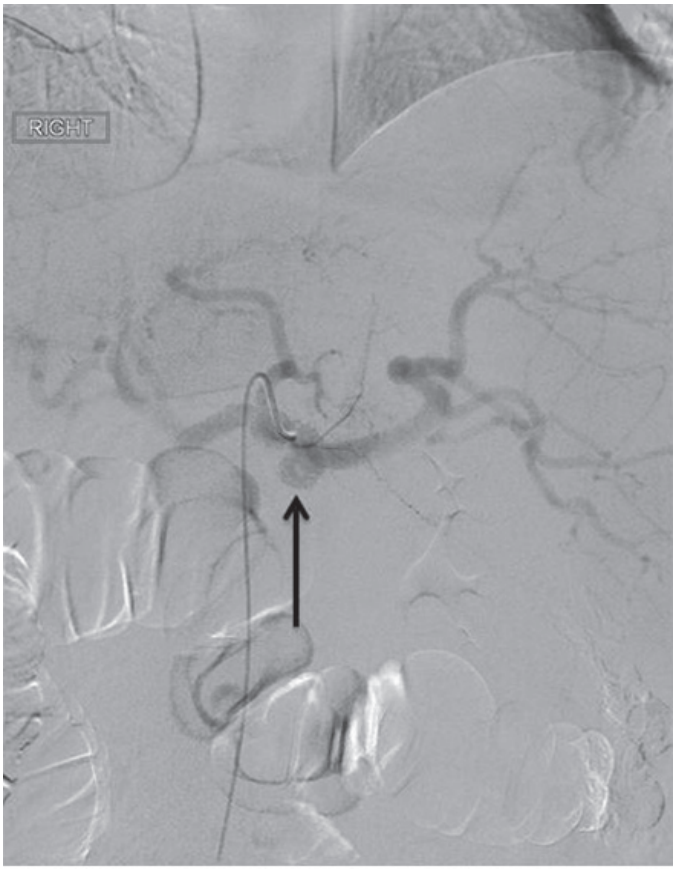

Figure 3: Angiography of the splenic artery and the pseudoaneurysm (arrow) prior to coil embolization.

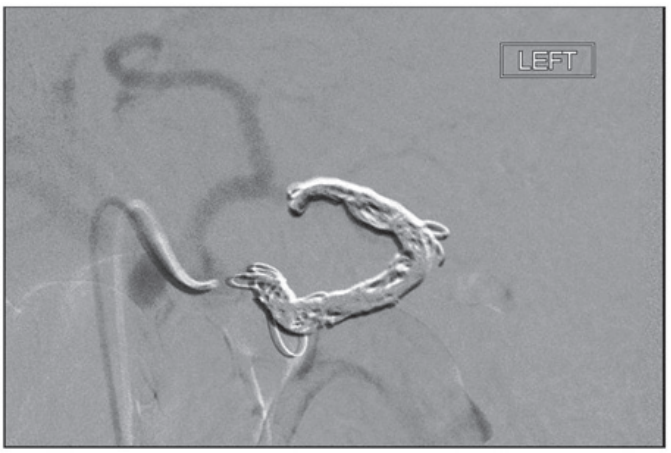

Figure 4: Angiography status post coil embolization indicating no filling of the splenic artery pseudoaneurysm after coil placement.

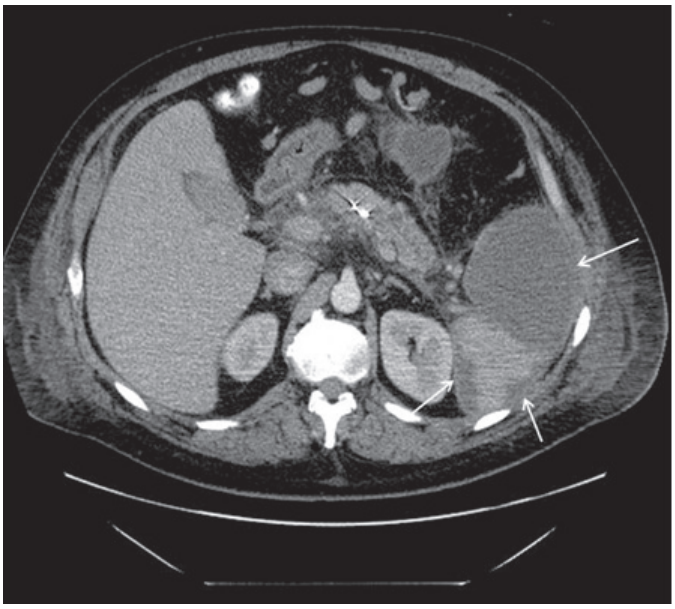

Figure 5: Computed tomography scan of abdomen/pelvis status post coil embolization with several areas of infarction within the spleen (white arrows). Coils within the splenic artery are visualized.

DISCUSSION

Hemosuccus pancreaticus is a rare cause of upper gastrointestinal bleeding. There is a male predominance (7:1) associated with this disease. Pathophysiology is either from direct rupture of the aneurysm or

pseudoaneurysm (PA) into the main pancreatic duct or indirect communication between the artery and duct with the pseudocyst. Weakening of the vessel wall forms the PA and is due to constant pressure necrosis (pseudocyst) and autodigestion from leakage of pancreatic enzymes from the pancreatitis [2].

Pseudoaneurysms commonly form in the setting of chronic (most common) or acute pancreatitis. Pseudoaneurysms form most commonly in the splenic artery (60%) followed by gastroduodenal (20%), pancreaticoduodenal (10%), hepatic (5%) and left gastric (2%) arteries in descending frequency. Complications of aneurysms and PAs include rupture leading to hemorrhage into the gastrointestinal tract, a pseudocyst, peritoneal cavity, retroperitoneal space or adjacent organs. The risk of rupture for an aneurysm is dependent on size, but there is no correlation in size with rupture of PAs or predictability therefore, all PAs should be treated. Frequency of rupture in the setting of pancreatitis is 5–10% and with a pseudocyst present, this can rise up to 20%. Mortality of a ruptured PA can be as high as 90–100% and if treated, the mortality risk is reduced to 12–57% [7–10].

Bleeding is often intermittent, possibly due to clotting occurring within the main pancreatic duct, consequentially making diagnosis with endoscopy difficult [9]. Esophagogastroduodenoscopy is the first modality in order to rule out other more common causes of upper gastrointestinal bleeding. If bleeding is observed from the major ampulla, this is a strong indicator of hemosuccus pancreaticus, though seldom seen. Other signs may include residual blood clots located near the ampulla, which may be difficult to visualize with no signs of peptic ulcer disease, varices or gastritis [7]. If no clear bleeding source, CT scan of the abdomen is the first line imaging modality of choice to identify pancreatic pathology followed-by angiography, which is considered the gold standard for detecting PAs and first line treatment [5, 10].

Embolization is first line therapy in hemodynamically stable patients. Coil embolization has a 79–100% success rate and a mortality rate of 12–33%. Both coils and glue are acceptable, coiling having less success if the vessel has increased tortuosity. Complications include embolization of undesired vessel, ischemia of organs with a lack of collateral circulation, infection and splenic infarct in the specific case of splenic artery involvement. Some of these complications can be avoided with the use of a non-coated metallic stent and the stent can be used as bridge to surgery in high risk patients or those with pancreatic disease that is in need of surgical treatment. The advantages to embolization include precise location, assessment of proper collateral flow, and excellent alternative for patients that are poor surgical candidates [7–10].

If hemodynamically unstable or embolization has failed or re-bleeding has occurred, surgery is recommended. Surgery depends on the location of the bleeding but most common procedures include bipolar arterial ligation, direct intra-pseudocystic ligation with pseudocyst drainage [9]. Pancreatic resection maybe necessary to control the pancreatic disease and the arterial bleeding with such operations as pancreaticoduodenectomy or splenopancreatectomy preferred in the setting of chronic pancreatitis [5].

The incidence of hemosuccus pancreaticus may rise in the future as a result of increasing alcohol use, primarily in males in the western countries consequentially causing more cases of pancreatitis, which could possibly, in turn, cause more occurrence of PAs leading to cases of hemosuccus pancreaticus [11]. Hemosuccus pancreaticus should rank higher on a differential diagnosis in the presence of chronic or even acute pancreatitis especially in the setting of chronic alcohol use in males. Given that the most common etiology for pancreatitis in the United States is alcohol induced and with the incidence continuing to rise, the increase in laparoscopic surgeries and the use of EUS-FNA for suspicious lesions residing in the pancreas, the incidence of hemosuccus pancreaticus may increase in the future.

CONCLUSION

Hemosuccus pancreaticus is a rare cause of an upper gastrointestinal bleed that is difficult to diagnose with endoscopy alone and often requires multiple imaging modalities to visualize. It should be included in a differential for any patient that presents with melena, generalized weakness and fatigue with low hemoglobin that cannot be explained by more common causes such as peptic ulcer disease, varices, gastritis or iron deficiency anemia with colon cancer ruled out if the patient is over the age of 50. Treatment is based on the hemodynamic stability of the patient and the ability to identify the bleeding source, but embolization should be attempted prior to surgical interventions.

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Author Contributions
Bonnie Patek – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Matthew Sullivan – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Shashin Shah – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Intraosseous acinic cell carcinoma: A rare case report

Lakshmana N., Vamsi Pavani B., Abhishek Singh Nayyar, Kartheeki B., Kalyana Chakravarthy B., Kameswara Rao A.

ABSTRACT

Introduction: De-differentiated acinic cell carcinoma of salivary glands is an uncommon variant of acinic cell carcinoma characterized by the co-existence of both low grade acinic cell carcinoma and a high-grade de-differentiated component as well as an aggressive clinical course. Case Report: Herewith, we are reporting a case of de-differentiated acinic cell carcinoma which was present in mandibular region. A 35-year-old female patient reported with a chief compliant of a swelling since one month and pain since 15 days in the lower left back tooth region. To the best of our knowledge, this location has never been described in de-differentiated acinic cell carcinoma as parotid is the most common site for its occurrence. Conclusion: Despite the rarity of intraosseous acinic cell carcinomas, one should be well aware of this diagnostic possibility, emphasizing the need for histopathological analysis, a clearly defined and guided treatment strategy, and an adequate follow-up to check for the possibility of any recurrences.

Keywords: De-differentiation, Low grade acinic cell carcinoma

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INTRODUCTION

Acinic cell carcinoma is a neoplasm of low grade malignancy and composed of cells that have got differentiated towards serous acinar cells. It was originally described by Nasse in 1892 as a low grade, benign lesion with later studies confirming its malignant behavior which was in between that of adenoma and carcinoma [1]. Hence, it was initially termed acinic cell tumor in the earlier WHO classification in 1972 which was later revised

to acinic cell carcinoma in 1991. Acinic cell carcinoma is considered to be the third most common major salivary gland tumor/malignancy [2].

De-differentiation or, high-grade malignant transformation (HGT) has been described in a variety of salivary gland tumors although the phenomenon is reported to be a relatively rare event. Authors preferably use the term HGT rather than de-differentiation for such cases [3]. De-differentiation is the progression of cells towards a less differentiated state in which the original line of differentiation is no longer evident. The first acinic cell carcinoma with high grade malignant transformation of salivary gland was reported by Stanley et al. in 1988. Thirty-five cases have been described in literature so far and most of them showed poor clinical outcome. Also, all cases reported to date were of parotid gland origin with involvement of both the superficial and/or, deep lobes. These tumors have a slight male predisposition, high recurrence rates, and a high propensity for cervical lymph node metastasis, suggesting a role for neck dissection in the management of affected patients [4]. Furthermore, vascular and peri-neural invasions are typically observed in acinic cell carcinomas.

The diagnosis is usually confirmed with a fine needle aspiration cytology (FNAC) procedure, while radical surgical excision of the tumor is the mainstay of treatment of this malignant neoplasm. Other treatment modalities include radiotherapy which might be indicated in some cases. Acinic cell carcinomas have a significant tendency to recur, to lead to metastases in cervical lymph nodes, and lungs rarely, and may have an aggressive evolution, therefore, making long-term follow-up, mandatory, post-treatment.

CASE REPORT

A 35-year-old female reported with a chief compliant of a swelling since one month and pain since 15 days in the lower left back tooth region. The swelling actually had an insidious origin and progression and started as a small imperceptible growth which was painless initially and gradually increased in size and became painful with the pain being continuous, dull, throbbing in nature which used to get aggravated on brushing and other mechanical trauma/provocation and on taking hard foods. Pain used to get temporarily relieved with medication. There was shedding of a tooth in the left lower back tooth region 15 days prior to the reporting of the patient. Since then, patient gave a history of increase in the size of the swelling. Patient had multiple, palpable submental and submandibular lymph nodes, present which were firm, mobile and tender. On clinical examination, there was a single, unilateral, ovoid-shaped, swelling present irt left lower third of face measuring approximately 4x5 cm in greatest dimensions (Figure 1). The skin overlying the swelling was normal in appearance without signs of any erythema and/or, discharge or, ulceration. The swelling had well-defined edges and the borders extended from 2 cm away from corner of the mouth anteriorly to 2 cm ahead of the angle of mandible posteriorly, and from below the imaginary line drawn from the corner of the mouth and lobule of ear superiorly to approximately 1 cm below the inferior border of the mandible inferiorly (Figure 2). On palpation, the swelling was well-defined, firm to hard in consistency, slightly tender and fixed to the underlying bone. On intra-oral examination, there was an ulcero-proliferative, exophytic growth seen irt teeth #35, #36, #37 region on the lingual side. The mucosa was perforated due to expansion of the buccal and lingual cortical plates with exposure of the white, necrosed bone (Figure 3). On palpation, tenderness and vestibular obliteration were present. Orthopantomograph (OPG) revealed a solitary, irregular radiolucency extending from the distal surface of tooth #34 till the mesial surface of tooth #37. (Figure 4). Incisional biopsy was performed and sent for histopathological examination which showed neoplastic cells arranged in solid, lobular pattern, separated by thin, fibrous connective tissue septae (Figure 5). Epithelial

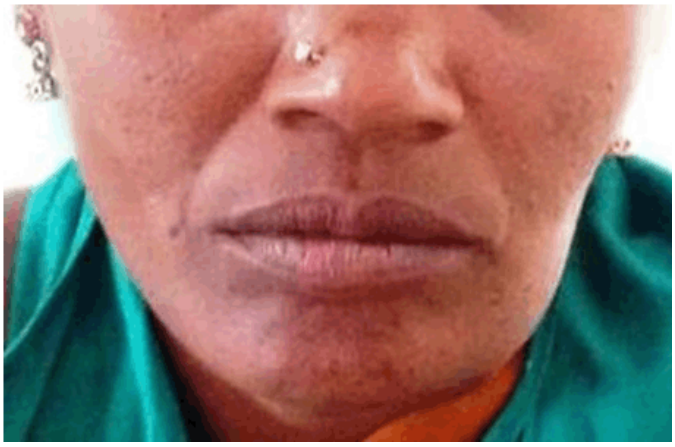

Figure 1: A single, unilateral, ovoid shape swelling present irt left lower middle third of face measuring approximately 4x5 cm in dimensions.

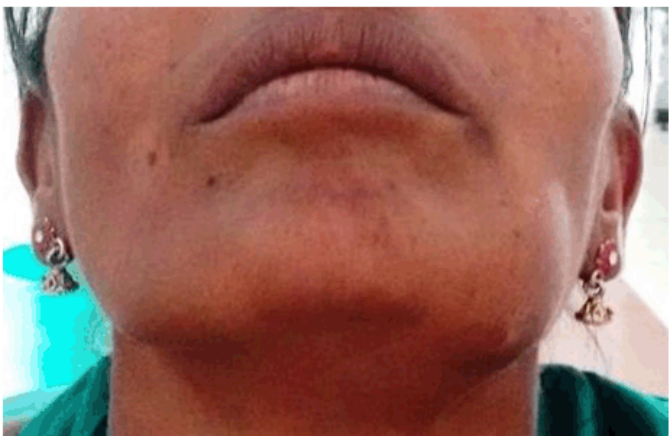

Figure 2: Well-defined edges of the swelling extending anteriorly 2 cm away from corner of the mouth, to posteriorly 2 cm ahead of the angle of mandible, superiorly below the imaginary line drawn from corner of the mouth and lobule of ear, to inferiorly 1 cm below the inferior border of mandible.

cells were pleomorphic in nature with increased mitotic activity and with keratin pearl formation suggestive of a de-differentiated acinic cell carcinoma (Figure 6). Based on the said clinical, radiological and histopathological features, a final diagnosis of a primary intraosseous salivary gland carcinoma was arrived-at. The patient was, then, referred for hemimandibulectomy and re-construction followed by radiotherapy and chemotherapy under guidance.

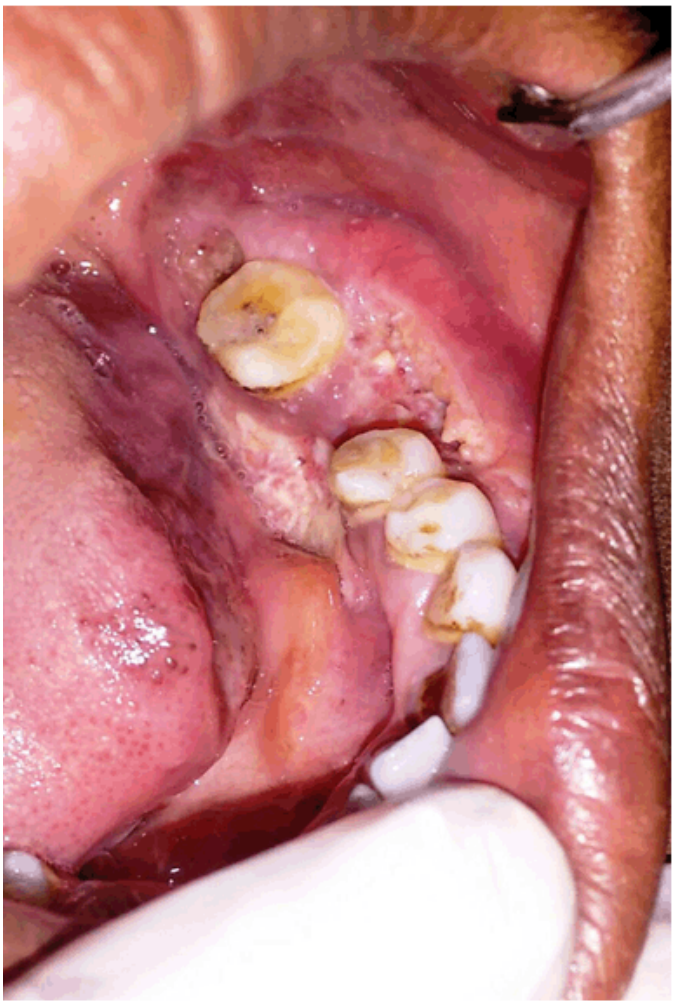

Figure 3: A ulceroproliferative, exophytic growth, seen irt teeth #35, #36, #37 on the lingual side.

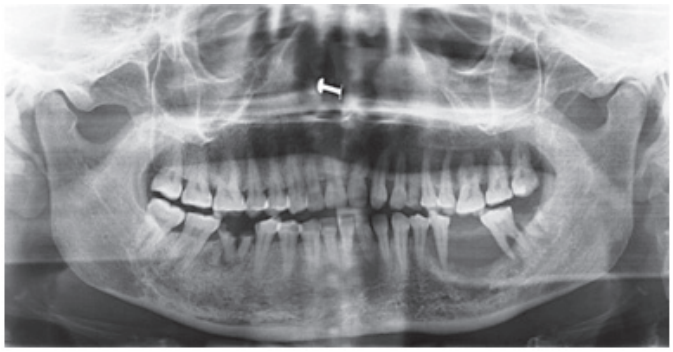

Figure 4: Orthopantomograph revealing a solitary, irregular radiolucency extending from the distal surface of tooth #34 till the mesial surface of tooth #37.

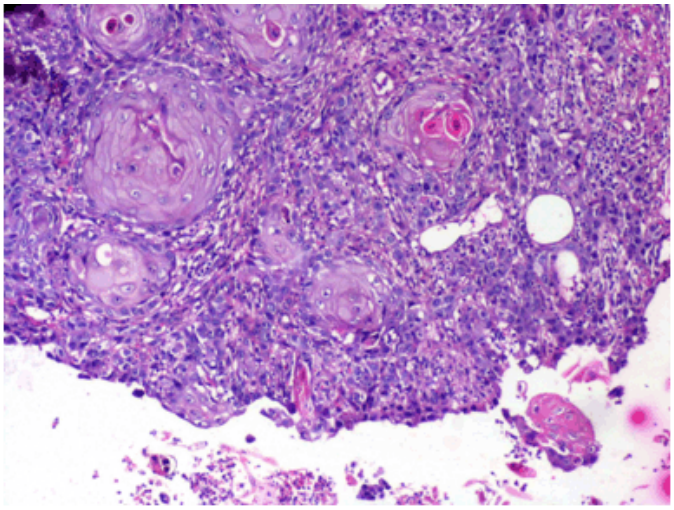

Figure 5: Neoplastic cells arranged in solid, lobular pattern, separated by thin, fibrous connective tissue septae (H&E stain, x100).

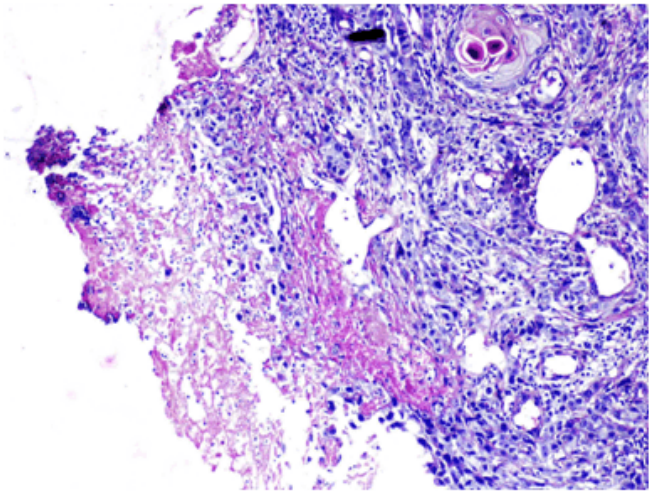

Figure 6: Epithelial cells, pleomorphic in nature, and with increased mitotic activity and keratin pearl formation suggestive of a de-differentiated (x10).

DISCUSSION

Acinic cell carcinoma is a low grade malignant epithelial neoplasm of salivary gland tissue origin in which at least few of the neoplastic cells demonstrate serous acinar differentiation characterized by the presence of cytoplasmic zymogen secretory granules. These carcinomas account for about 4% of all salivary gland neoplasms with around 7–17.5% going for malignant transformation [5]. Numerous reports indicate primary salivary gland neoplasms to be completely intra-bony, yet, non-neoplastic salivary gland tissues have rarely been found in such locales, with few reports suggesting odontogenic origin of such tumors, although, the rate of occurrence of salivary gland choristomas, hamartomas, embryonic rests, and aberrant salivary gland tissues within the alveolar bone, is less than 2.6 of

every 1000 marrow samples biopsied with this providing an additional and quite seemingly logical histogenetic explanation for the presence of intraosseous salivary gland neoplasms [6]. Neoplastic transformation of intra-bony salivary gland tissues, in particular, is an uncommon phenomenon with mandible being one of the most common sites for such neoplasia, accounting for around 75% of all the cases seen [7]. Entrapment of salivary gland tissue within the jaw bones during initial stages of development and metaplastic transformation of the epithelial lining of odontogenic cysts are the two significant hypotheses that have been proposed for such rare, intraosseous salivary gland neoplasms [8]. Acinic cell carcinomas may be found in all age groups, including children and early adolescence, with the peak incidence noted in the fifth and sixth decades of life. The most important clinical features include slow-growing lesions with an insidious onset and progression, most of the times, and which are attended by pain, later, in the course of development due to secondary changes and/or, as a result of mechanical trauma after they reach sufficient sizes [9]. Histopathologically, large lobules or, nests of tumor cells with little intervening stroma are characteristic. The arrangement of neoplastic cells is quite variable. Generally, cells are arranged in solid masses with blunted or, pushing margins. Other variants include microcystic, papillary, and follicular forms. Radical surgical excision of the tumors is the preferred treatment although recurrences are not uncommon [10].

CONCLUSION

To conclude, despite the rarity of intraosseous acinic cell carcinomas, one should be well aware of this diagnostic possibility, emphasizing the need for histopathological analysis, a clearly defined and guided treatment strategy, and an adequate follow-up to check for the possibility of any recurrences.

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Author Contributions

Lakshmana N. – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Vamsi Pavani B. – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Abhishek Singh Nayyar – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
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CASE REPORT PEER REVIEWED | OPEN ACCESS

An unusual cause for syncope: Pericardial paraganglioma causing right ventricular outflow obstruction

Kailyn Mann, Mahek Shah, Naumann Islam, Ronald Freudenberger, Matthew Martinez, Larry Jacobs

ABSTRACT

Introduction: Metastases are the most common cardiac neoplasms with primary cardiac tumors being rare. Cardiac paragangliomas constitute <5% of primary cardiac tumors. They tend to remain asymptomatic until discovered incidentally or grow to a size large enough to cause symptoms. Symptoms of cardiac tumors are generally secondary to local invasion, mass effect or embolization. Case Report: A case of pericardial paraganglioma leading to right ventricular outflow obstruction and subsequent hypotension and syncope is presented. Due to its large size, slow growth and proximity to large vessels, the tumor considered to be at a very high risk for resection and conservative management was chosen. Conclusion: Though rare, cardiac tumors must be among the differential for cardiovascular symptoms. Size and location of the tumor may determine the characteristics of symptoms produced, ranging from syncope, angina or dyspnea to cardiovascular collapse.

Keywords: Cardiac MRI, Cardiac tumor, Compression, Hypotension, Paraganglioma, Pericardial, Syncope

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INTRODUCTION

Primary cardiac tumors may be benign or malignant but are extremely rare with post-mortem studies reporting rates under 0.3% [1–3]. Secondary spread of the tumors to the heart i.e., cardiac metastasis is far more common with reported incidence as high as 18.3% [4, 5]. Most of these cases are asymptomatic and discovered either at autopsy or incidentally while using a myriad of imaging techniques including but not limited to echocardiography, magnetic resonance imaging (MRI) and computed tomography (CT) scans [6, 7]. Considering that the symptoms from tumors usually overlap those with cardiac conditions such as myocardial infarction, heart failure, primary arrhythmias among others, early diagnosis and effective treatment of cardiac tumors remains a clinical challenge [8].

We present a case of cardiac paraganglioma presenting as syncope in a patient from extrinsic compression of the right ventricular outflow tract (RVOT) causing obstruction.

CASE REPORT

A 54-year-old male with past medical history of hypertension, cryptogenic liver cirrhosis, a benign pericardial mass and prior pheochromocytoma presented to the hospital with weakness and diarrhea. The mass was initially incidentally discovered at another hospital in 2003, when imaging showed the presence of a pericardial and abdominal periaortic mass. High suspicion of a neuroendocrine etiology for the tumors was confirmed by a positive metaiodobenzylguanidine (MIBG) scan and elevated catecholamine levels. The masses were deemed inoperable at the time of diagnosis and a presumed diagnosis of pericardial paraganglioma was made in light of available evidence. The patient failed to manifest any significant symptoms attributable to excessive hormone secretion and underlying hypertension was treated using alpha- and beta-blockers.

At home prior to presentation at current visit, the patient had a single episode of syncope that lasted a few seconds. His blood pressure at presentation was noted to be 60/40 mmHg with significant bradycardia at a heart rate of 40 beats per minute. An electrocardiogram revealed a junctional rhythm. The patient was responsive to two doses of atropine but remained hypotensive requiring admission to the intensive care unit for aggressive fluid resuscitation in combination with pressor support.

Computed tomography scan of the chest demonstrated a large heterogeneously enhancing mass, abutting the main pulmonary artery and ascending aorta measuring up to 7x7.8 cm in the greatest transverse and antero-posterior dimension respectively (Figure 1). 2D echocardiogram showed an estimated left ventricular ejection fraction ≥75% and a large vascularized anterior mediastinal mass abutting the aortic root, ascending aorta partially obstructing the right ventricular outflow tract (RVOT) and pulmonary artery (Figure 2). Doppler data was significant for the presence of increased velocities across the RVOT with a peak velocity of 35 mmHg and mean gradient of 17 mmHg. A cardiac MRI scan was then ordered to better assess the anatomy of the mass and its relation to the great vessels.

Cardiac MRI scan (Figure 3) showed a large (65x74 mm) highly vascular anterior mediastinal paraganglioma between the right pulmonary artery and aorta causing extrinsic compression of the RVOT without intra-cardiac involvement. The patient was considered a poor candidate for surgery due to proximity of the mass to the major vessels of the heart, parasitization of cardiac blood supply and the anatomical challenges it posed for partial or complete resection. With continued supportive treatment, the patient's symptoms improved and his junctional bradycardia resolved. Comparative imaging from 2003 was acquired, which showed that the mass had been stable in size over the years with no evidence of invasion in the absence of related symptoms. The underlying hypertension controlled with cautious reintroduction of anti-hypertensive medications to avoid precipitation of hypotension. He was eventually discharged with close outpatient follow-up where he remained asymptomatic.

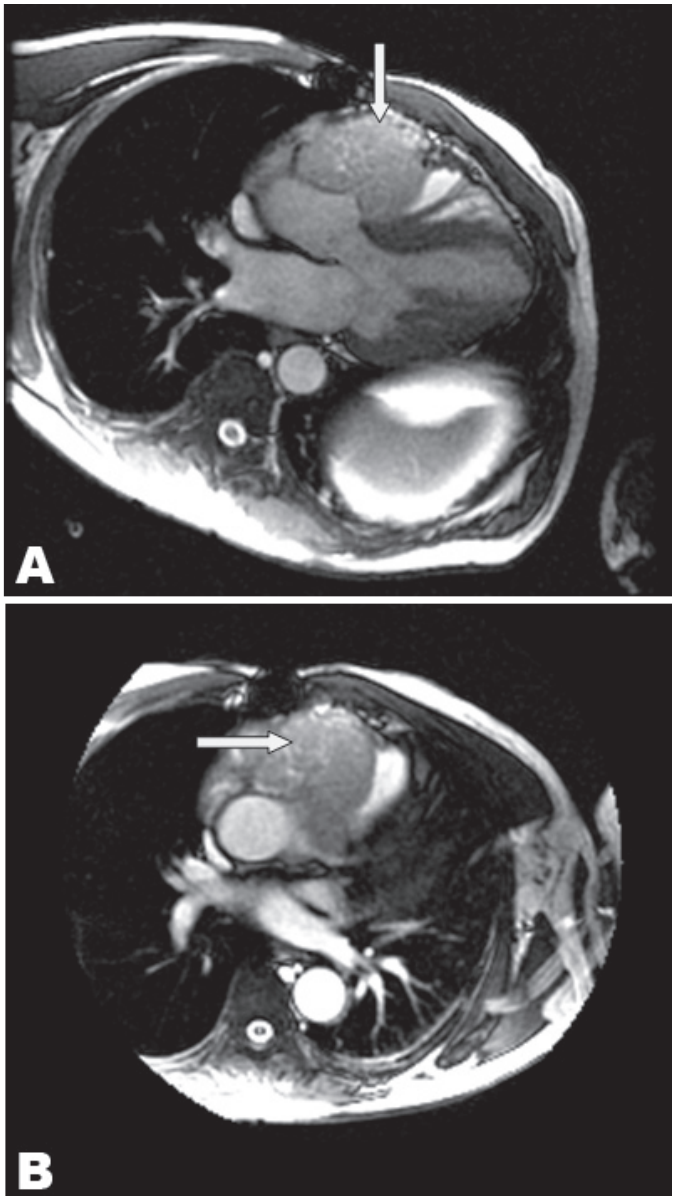

Figure 1: (A, B) Computed tomography scan of the chest demonstrated a large heterogeneously enhancing mass (arrow), abutting the main pulmonary artery and ascending aorta measuring up to 7x7.8 cm in the greatest transverse and antero-posterior dimension.

DISCUSSION

Our case describes a unique case where initial use of an MIBG scan, commonly used for detection of adrenergic tissue such as pheochromocytomas helped in the incidental discovery of a large cardiac mass due to inherent pathological properties of the underlying tumor. Catecholamine-secreting tumors arise from the

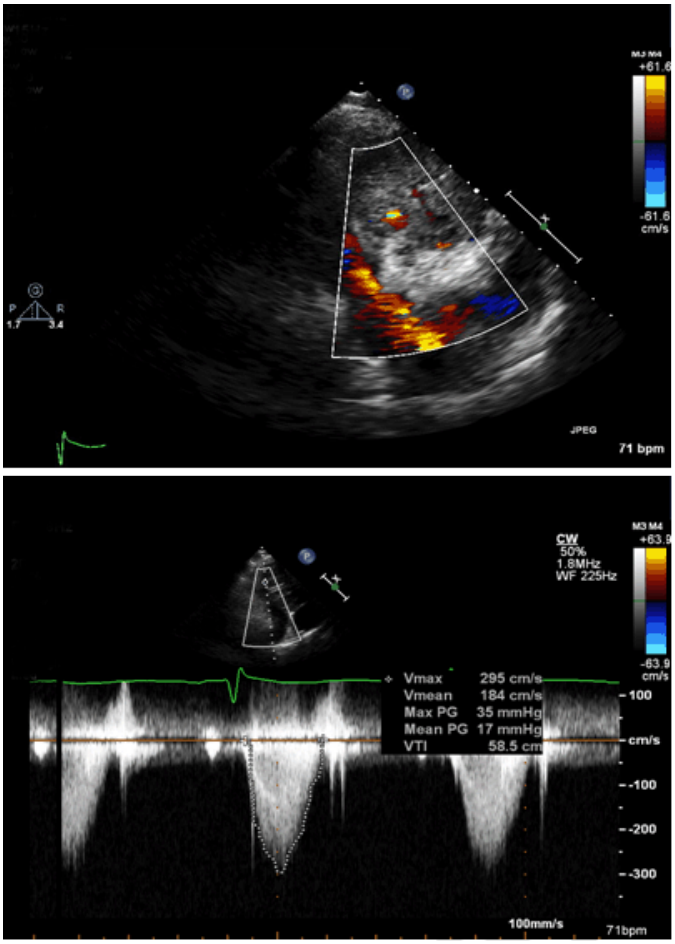

Figure 2: Two-dimensional echocardiogram showed an estimated left ventricular ejection fraction ≥75% and a large vascularized anterior mediastinal mass abutting the aortic root, ascending aorta partially obstructing the right ventricular outflow tract (RVOT) and pulmonary artery.

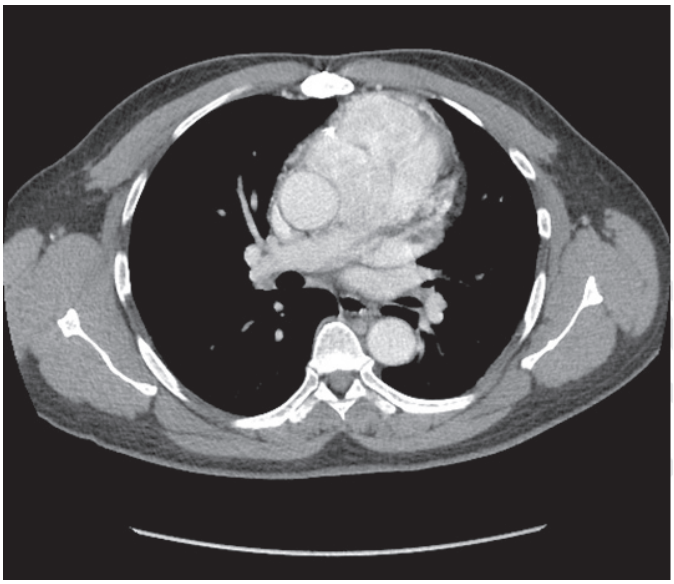

Figure 3: Cardiac magnetic resonance imaging showed a large (65x74 mm) highly vascular anterior mediastinal paraganglioma between the right pulmonary artery and aorta causing extrinsic of the RVOT without intra-cardiac involvement.

neural crest cells and have an annual incidence of 1 to 2 per 100,000. Eighty percent arise within the adrenal glands and present as pheochromocytomas with the remaining 20% being extra-adrenal in origin. The majority of the mediastinal paragangliomas are found in the anterior or posterior aorto-pulmonary groove and are largely nonfunctioning [9]. A functional catecholamine-secreting tumor can cause hypertension, diaphoresis or palpitations. Cardiac paragangliomas are rare and constitute <5% of all primary cardiac tumors. They tend to remain asymptomatic until discovered incidentally or grow to a size large enough to cause symptoms [10]. These tumors also tend to be locally invasive and can affect the cardiac conduction system [11]. When it comes to cardiac tumors, cardiac output can be compromised from several mechanisms contributing to direct flow obstruction (intrinsic or extrinsic), interference with valvular function, myocardial infiltration diminishing contractility, advanced heart block and the development of hemodynamically significant pericardial effusions and/or arrhythmias [12]. Our patient suffered from a paraganglioma led RVOT obstruction, which became clinically relevant due to the presence of significant dehydration resulting in a reduced preload, a drop in cardiac output, hypotension and transient cerebral hypoperfusion with syncope.

Many different imaging modalities can be used when evaluating cardiac tumors. MRI scan is presently the modality of choice in evaluating cardiac tumors, however, its results should be combined with data from coronary angiography. Cardiac MRI scan can access the extent of myocardial infiltration, pericardial involvement and/or extra cardiac extension. It also allows the differentiation of tumor from other non-tumor masses such as the fibro muscular elements of the posterior wall of the right atrium [13]. On MRI imaging, cardiac paragangliomas are typically iso or hypo intense to myocardium on T1-weighted imaging and hyperintense on T2-weighted imaging. They enhance with contrast given their hyper vascularity [13]. Coronary angiography can be useful to help determine the hypervascularization of the tumor by defining its feeding particles. This information is valuable when considering surgical resection and in its preparation [14].

The best therapy for paragangliomas is complete surgical excision, and remains the mainstay of treatment [15]. Surgical resection carries significant risks such as intraoperative hemorrhage given the tumor's hypervascular blood supply. Resection usually requires cardiopulmonary bypass and full thickness tissue resection due to lack of tumor encapsulation [15]. The removal of tumor usually requires reconstruction of the resected sites involving the right atrium, inferior venacava and RVOT [16]. A surgical approach was abandoned in our case due to its considerably high risk nature resulting from large size of the tumor and its anatomical proximity of the tumor with the large vessels. During our assessment a conservative approach was considered

appropriate, considering the indolent nature of the paraganglioma, transient nature of exacerbation and the improvement in patient condition with simple supportive measures and correction of the underlying hemodynamic abnormalities. Prior reports have documented situations when surgical resection is not feasible. They note that the prognosis is usually guarded in such cases since the course of disease is typically slowly progressive [11].

CONCLUSION

Cardiac paragangliomas account for <5% of all primary cardiac tumors. They tend to remain asymptomatic, however, they can grow to a size large enough to cause symptoms that are generally secondary to local invasion, mass effect or embolization. Different imaging modalities can be used, with magnetic resonance imaging scan the diagnostic modality of choice. The surgical excision remains the mainstay of treatment however, there are cases such as ours that a conservative approach is more appropriate.

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Author Contributions

Kailyn Mann – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Mahek Shah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Naumann Islam – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ronald Freudenberger – Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published
Matthew Martinez – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Larry Jacobs – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

The case of an extensive primary extramammary Paget's disease diagnosis and treatment

Apostolos Sarivalasis, Cécile Triboulet, Sandro Anchisi

ABSTRACT

Introduction: Extramammary Paget's disease (EMPD) is a rare neoplasm commonly related with underlying malignancy. It mainly affects intimate body areas and presents with eczema like lesions. Due to the rarity, the indolent natural history and the anatomical distribution of this disease, the diagnosis is difficult and often delayed. Treatment can be challenging especially since the majority of patient are elderly and frail. Case Report: A 91-year-old male suffering from coronary disease and myelodysplastic syndrome presented with a slowly evolving scrotal eruption. A differential diagnosis was established and a punch biopsy was performed. An EMPD was diagnosed. The known relation of EMPDs with underlying malignancies mandated further complementary examinations. An underlying malignancy was excluded and a personalized treatment was undertaken. Conclusion: Extramammary Paget's disease diagnosis and treatment are challenging. A comprehensive differential diagnosis is essential for integrating this rarity in the diagnostic assessment of persistent eczematous eruptions. A skin biopsy is paramount for diagnosis. A guided workout with multimodal examinations to rule out underlying malignancies is strongly recommended. The gold standard of EMPD treatment is surgery. Nevertheless, alternative less invasive treatments should be considered, depending on patient's comorbidities.

Keywords: Elderly, Extramammary Paget's disease, Skin rash

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INTRODUCTION

Cutaneous Paget's disease is a rare intraepithelial neoplastic condition [1, 2]. The breast Paget's disease can be associated with invasive and in situ breast cancer and is a well-defined entity. The same histological pattern (Paget's cells) [3] can be found in other body areas with abundance of apocrine glands such as the perineum, scrotum, vulva, penis, and axilla [4]. In such cases it is

called extramammary Paget's disease (EMPD). The EMPD affects mostly elderly persons and can be primary or secondary. Primary EMPD originate from intraepidermal cells. Secondary EMPD is associated with underlying malignancy and accounts for 10–30% of all EMPD cases series [1, 5, 6]. The most common associated neoplasms arise from the bladder, urethra, prostate and rectum. The involved body area can help guide diagnostic procedures since the bladder, urethra, and prostate cancers are associated with EMPDs of the external genitalia, while rectal adenocarcinoma is commonly related with perianal EMPD [6].

The relatively indolent natural history, the lack of specific symptoms and the body distribution (most frequently in the anogenital region followed by the axilla) often delays diagnosis, resulting in extensive lesions. The treatment of those lesions can be challenging. Different procedures have been reported effective with surgery being considered the standard of care [5, 7, 8]. This radical approach cannot be considered in every clinical setting. Hence, alternative local treatments have been evaluated. Imiquimod 5% topical cream [9–11], photodynamic therapy [12, 13] and radiation therapy [14] are the most frequently applied alternative treatments.

CASE REPORT

A 91-year-old male known for refractory cytopenia myelodysplastic syndrome and coronary disease, presented with a slowly evolving scrotal and perineal eruption. The onset of the eruption could not be dated. Previously prescribed corticosteroids and hydrating local treatments were ineffective. The lesion covered approximately 1% of the body surface and infiltrated the scrotum, the left lateral perineal area extending to 2 cm from the anal margin (Figures 1–3). Two smaller satellite infiltrated areas were noted in the left lower inguinal region (Figure 4). The affected skin area was evenly infiltrated and erythematous. Areas of desquamation were present and the eruption borders presented swelling. The lesion was neither tender nor painful and the patient's main complaint was intermittent pruritus. Neither lymphadenopathy nor hepatosplenomegaly was noted. The digital rectal examination and external genitalia inspection were normal.

The histological examination of a punch biopsy specimen showed a typical image of Paget's cells in hematoxylin and eosin coloration (Figure 5A). In immunohistochemistry (IHC) the cells were cytokeratine 7 (CK7) positive (Figure 5B) while S100 (Figure 5C) and Melan A were both negative (Figure 5D).

After the histological confirmation, a comprehensive diagnostic assessment to rule out underlying malignancies was ordered. The whole body CT scan and the urological examination were free of pathological findings.

The gold standard of EMPD treatment being a wide surgical resection a surgical assessment was conducted. Due to the disease extension, the patient's age and the concurrent medical conditions an upfront surgical treatment was deemed not appropriate. Radiotherapy was also ruled out according to the patient's desire. A topical approach with either photodynamic therapy or local immunomodulatory cream application, considered as less invasive, was presented to the patient [12, 13, 15, 16]. None of these treatments are as effective as surgery but promising results are reported in literature, although controversial. The benefit-risk ratio of these approaches being judged favorably by the patient he was addressed to the Lausanne's University Dermatological Hospital. Because of the extent of the lesion, too large to be treated with local immunomodulator application of imiquimod cream 5%, a photodynamic therapy was prescribed. Six months disease's stabilization was observed on this treatment.

DISCUSSION

In this case, the differential diagnosis included several skin conditions (Table 1). The pruritus, as the leading symptom, can be misdiagnosed for eczema. However the extent and characteristics of the eruption, the absence of

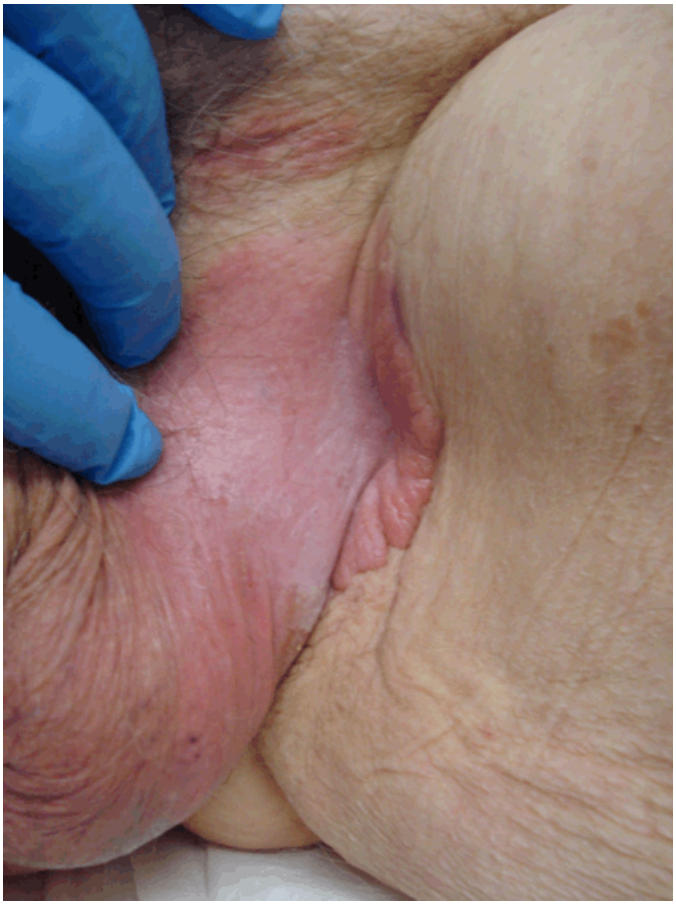

Figure 1: Scrotal eruption.

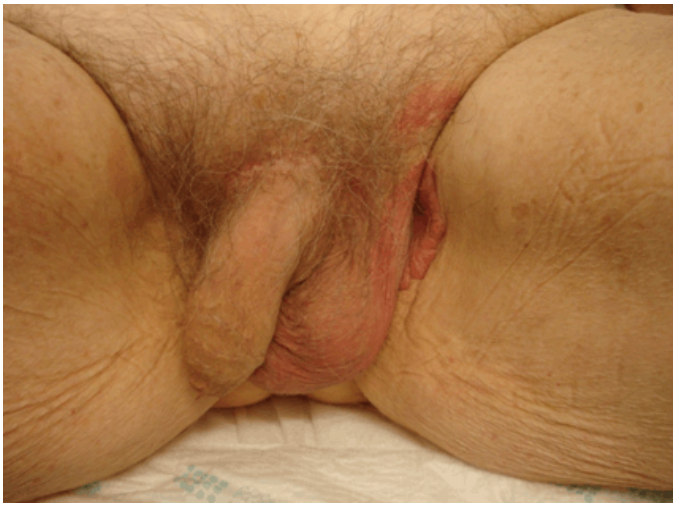

Figure 2: Infiltrated borders.

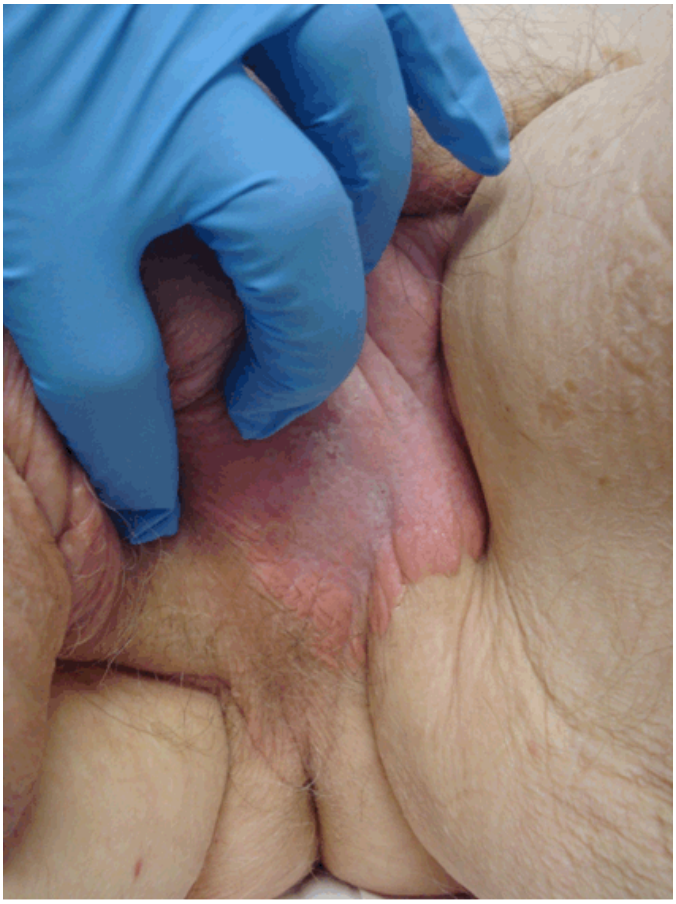

Figure 3: Scrotal extension without anal involvement.

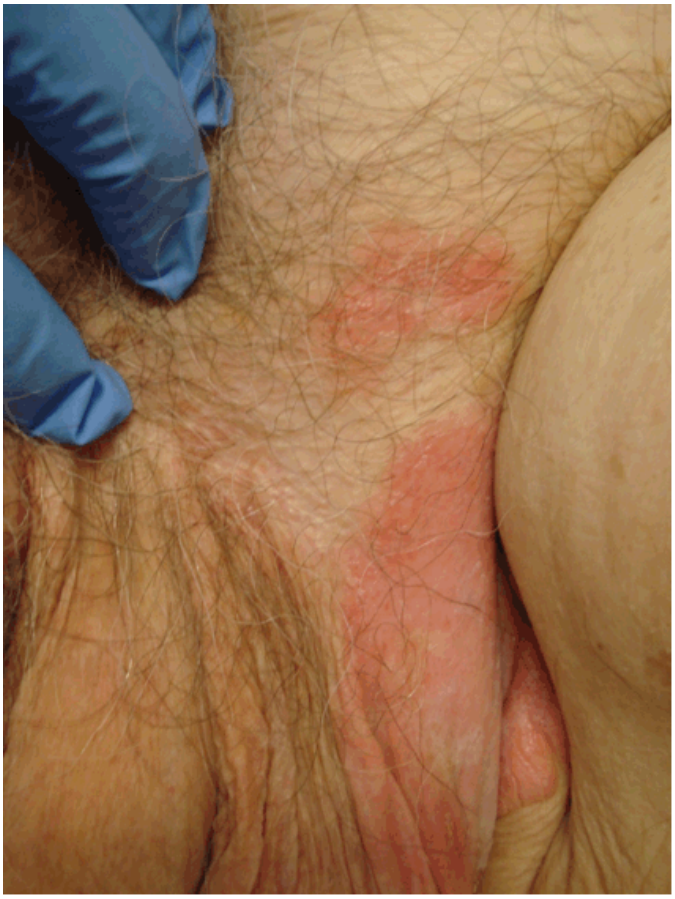

Figure 4: Satellite lesions.

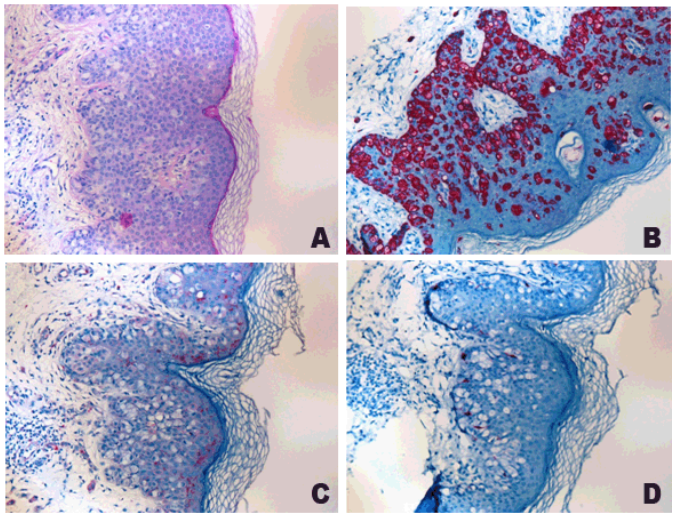

Figure 5: Histological examination of a punch biopsy specimen showed a typical image of Paget's cells (A) H&E staining, (B) CK7 staining, (C) S100 staining, and (D) Melan A staining.

relevant history or clinical findings of atopia and the lack of response to front line eczema treatment suggested an alternative diagnosis.

Inverse psoriasis needs also to be considered as differential diagnosis since it affects intertriginous areas and often appears without the typical scaly lesions.

Fungal infections can grow involving the same anatomical regions as EMPD. Fungal lesions are small sized, but when confluent can merge to larger areas. A skin sample usually provides the diagnosis.

Sexually transmitted diseases (STDs) such as Syphilis needs to be ruled out by screening tests and other serological and bacteriological examinations.

Anogenital warts are often small and asymptomatic but can, if neglected, grow into large exophytic

Table 1: Differential diagnosis of extramammary Paget's disease

Eczema
Inverse psoriasis
Sexually transmitted diseases
Fungal infections
Anogenital warts
Achromic melanoma
Kaposi's sarcoma
Cutaneous squamous cell carcinoma

conglomerates appearing as papilliform masses. A nonspecific test with 5% acetic acid can be useful for the differential diagnosis highlighting wart lesions in white. This was not the patient's case.

Achromic melanoma is a rarity. It presents as a non-pigmented skin lesion and often has a more aggressive natural history with early metastasis, notably, to lymph nodes.

Kaposi's sarcoma involves mostly extremities, exhibits an aggressive behavior and presents with characteristic purple lesions. Nevertheless, due to morphologic variants a biopsy should always be performed.

Another dermato-oncological diagnosis to be ruled out is cutaneous squamous cell carcinoma, an entity that diagnosis exhibits distinct pathological features.

To exclude alternative neoplastic skin disorder a pathological assessment is paramount. The EMPD growth characteristics, including large epithelial cells proliferation- Paget's cells - distributed in small clusters between normal keratinocytes and typical IHC expression is the cornerstone for diagnosis.

The known association of EMPD with underling malignancies mandates a thorough assessment with appropriate laboratory, endoscopic and radiological tests.

Our patient suffered from a primary EMPD since no underlying malignancy was diagnosed on the diagnostic assessment.

The treatment approach was personalized taking into account the medical history, age, expected morbidity and patient's choice. The photodynamic treatment was proved to be an effective therapeutic option with very good local results.

CONCLUSION

Extramammary Paget's disease (EMPD) is a rare neoplasm. The initial presentation can be misleading and easily misdiagnosed. High level of clinical awareness and histological confirmation are essentials in order to obtain correct diagnosis. A comprehensive diagnostic assessment is highly recommended because of the known association of EMPD with underling malignancies. The treatment plan needs to be personalized especially in elderly and frail patients where concomitant health conditions contraindicate extensive surgical management of the disease.

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Author Contributions

Apostolos Sarivalasis – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Cécile Triboulet – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Final approval of the version to be published

Sandro Anchisi – Substantial contributions to conception and design, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Chronic thromboembolic pulmonary hypertension, a disease frequently misdiagnosed

Margita Belicová, Veronika Jankovičová, Marian Mokáň

ABSTRACT

Introduction: Chronic thromboembolic pulmonary hypertension results from incomplete resolution of a pulmonary embolus, leading to pulmonary hypertension and progressive right heart failure and death. Contemporary pharmacological and especially surgical treatment possibilities offer hope for the patient's full recovery, but an early diagnosis is crucial for success. Case Report: A 56-year-old white female, who despite thrombolytic therapy and next appropriate anticoagulation, was re-hospitalized six years after acute pulmonary embolism for severe pulmonary hypertension, due to chronic thromboembolic pulmonary hypertension. Before the diagnosis was established, she underwent lungs biopsy because of suspected interstitial lung disease and a bone marrow aspirate and biopsy because of progressive polycythemia. After chronic thromboembolic pulmonary hypertension was established, she underwent successful pulmonary endarterectomy. Conclusion: Chronic thromboembolic pulmonary hypertension is frequently misdiagnosed in clinical practice. This report aims to increase the awareness of clinicians towards an accurate diagnosis of the disease, which is necessary for the early referral of chronic thromboembolic pulmonary hypertension patients for operability, pulmonary endarterectomy.

Keywords: Chronic thromboembolic pulmonary hypertension, Pulmonary embolism, Pulmonary endarterectomy, Pulmonary hypertension

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INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive potentially fatal disease, in which it is believed that thromboembolic occlusion of pulmonary vessels due to non-resolving but organizing thrombi gradually leads to significant elevation of pulmonary blood pressure, resulting in pressure overload and failure of the right heart. Pulmonary embolism is thought to be the initiating event that despite adequate treatment results only in incomplete resolution. Furthermore, organization of the thromboemboli is associated with

progressive vascular remodeling, relevantly contributing to the severity of pulmonary hypertension and is associated with adverse prognosis [1]. Early diagnosis is crucial to better identify patients who would benefit from a well-established therapeutic strategy, pulmonary endarterectomy (PEA), which is the treatment of choice [2]. The CTEPH is a important disease, because for a long time it may be asymptomatic and its symptoms are nonspecific, therefore it is frequently misdiagnosed.

CASE REPORT

A 56-year-old white female presented without chronic disease, non-smoker, obese with body mass index 32% and with negative family history of venous thromboembolism (VTE). In 2002, she experienced acute pulmonary embolism (PE) treated by systemic thrombolysis (accelerated regimen of alteplase 100 mg over two hours) (Figures 1–4, At this time, she used oral contraceptives for last five years, which were stopped and before discharge from hospital she received oral anticoagulation (vitamin K antagonists, warfarin). After six months of acute PE, she was examined for inherited thrombophilias associated with VTE and elevated levels of factor VIII 240 IU/dl (normal range 60–150 IU/dl) and homocystein 20.9 umol/l (normal range 5–12 umol/l) were revealed. The patient was recommended to continue with warfarin.

One year after pulmonary embolism, exertional dyspnea occurred and the patient was repeatedly examined by pneumologist in 2005 because of its progression. She underwent fibre optics bronchoscopy along with bronchoalveolar lavage and lungs biopsy, because interstitial lung disease was suspected (according to result of high resolution computed tomography) these examinations excluded suspected diagnosis. She underwent a bone marrow aspirate and biopsy because of progressive polycythemia for last two years (before bone marrow aspirate and biopsy hemoglobin was 182 g/l (normal range 120–155 g/l), hematocrit 0.61 (normal range 0.36–0.47), according to results, polycythemia vera was excluded. Despite of progressive dyspnea and only boundary result from pulmonary function tests and negative chest radiograph the patient continued in treatment by a pneumologist as bronchitis chronica.

In the beginning of 2006, the patient experienced sudden chest pain because of which, she was admitted to the hospital as a suspected acute coronary syndrome without ST segment elevation (Figure 5). Next day of hospitalization transthoracic echocardiography (TTE) was performed revealing pulmonary hypertension (PH) with systolic pulmonary artery pressure 105 mmHg and dilatation of right ventricle and atrium (Figure 6). At this time, level of D-dimer was 0.21 mg/L, which was in normal range and apart from high red blood cell count (hemoglobin 18.6 g/dl; normal range 12.0–15.5 g/dl), hematocrit 0.64; normal range 0.36–0.47, leucocytes 8.10x10^9/l; normal range 3.90–10.00x10^9/l; thrombocytes 376x10^9/l; normal range 140–400x10^9/l), other laboratory tests were within the normal values. Subsequently performed computed tomography pulmonary angiogram (CTPA) was negative. Despite negative CTPA, we supposed diagnosis CTEPH, because of which, she underwent ventilation-perfusion (V/Q) lung scintigraphy (Figure 7). At this time, patient was classified in the New York Heart Association (NYHA) functional class III.

After patient consent, she was referred to the highly specialized centre for pulmonary artery hypertension. After additional diagnostic procedures were performed (pulmonary angiography and right heart catheterization) the diagnosis CTEPH was definitely confirmed and she underwent PEA. In the perioperative period, reduction of mean pulmonary artery pressure (57 versus 28 mmHg) was observed. Four months after PEA, patients was in the NYHA functional class I, ECG (Figure 8) shown regress of right ventricle hypertrophy, as well as TTE (Figure 9) shown regress of PH and regress of dilatation right ventricle and atrium. Laboratory investigations revealed normalisation of red blood cell count (hemoglobin 14.6 g/dl; normal range 120–15.5 g/dl, hematocrit 0.43; normal range 0.36–0.47, leucocytes 5.50x10^9/l; normal range 3.90–10.00x10^9/l), thrombocytes 223x10^9/l; normal

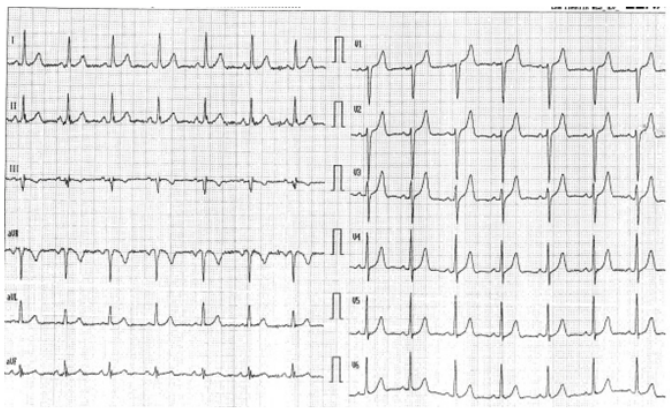

Figure 1: Electrocardiogram before acute pulmonary embolism: sinus rhythm, without pathology.

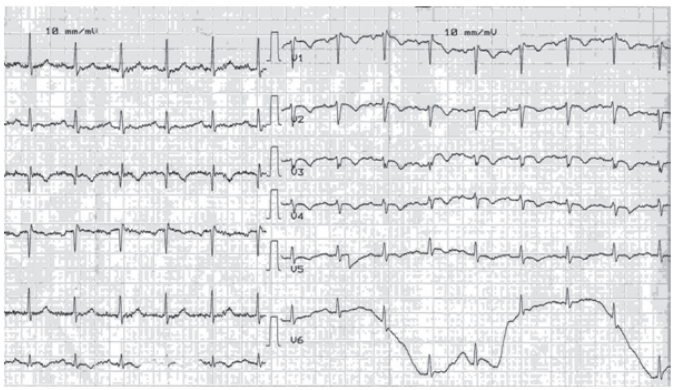

Figure 2: Electrocardiogram at admission to the hospital with acute pulmonary embolism: sinus rhythm, inverted T waves in leads V1–V5.

value 140–400x10^9/l). Presently, the patient is classified in the NYHA functional class I and except warfarin she intakes no other drugs.

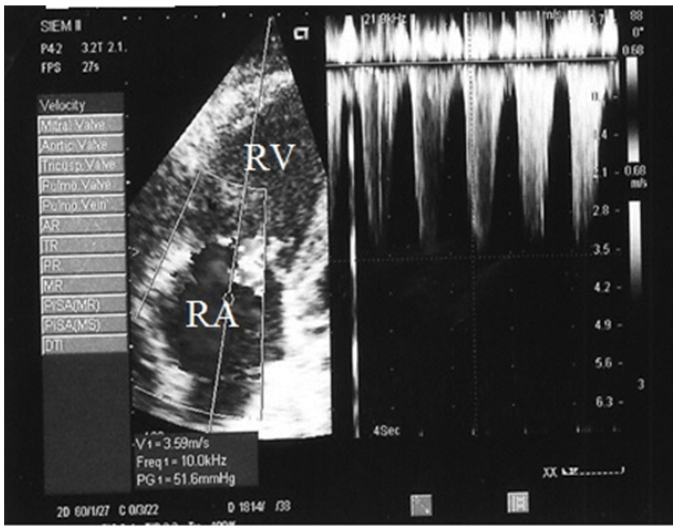

Figure 3: Transthoracic echocardiography before thrombolytic therapy. [RV Right ventricle, RA Right atrium]

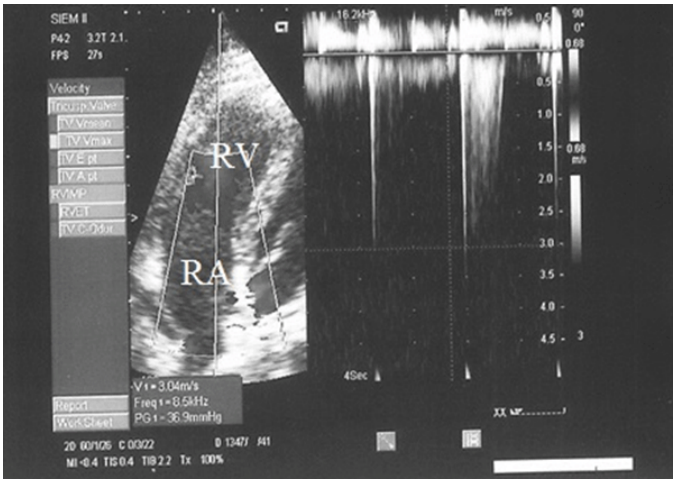

Figure 4: Transthoracic echocardiography 24 hours after thrombolytic therapy. [RV Right ventricle, RA Right atrium]

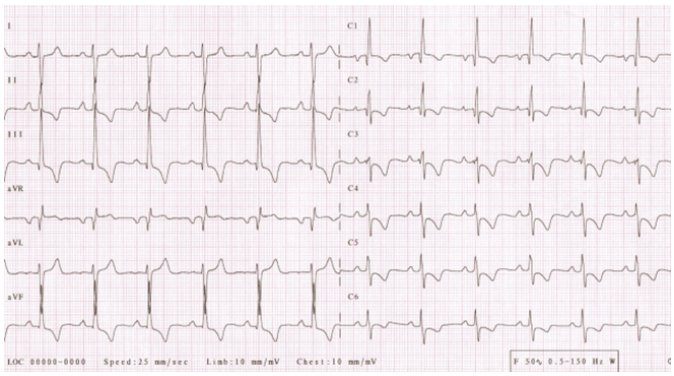

Figure 5: Electrocardiogram before pulmonary endarterectomy: sinus rhythm, right ventricle hypertrophy with strain.

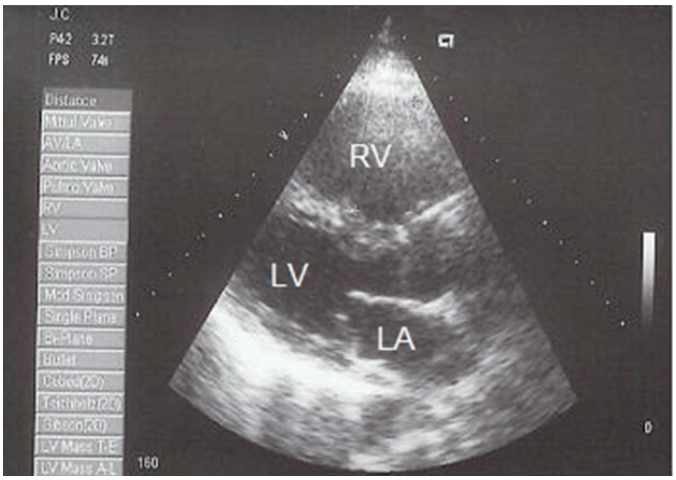

Figure 6: Transthoracic echocardiography before pulmonary endarterectomy: dilated right ventricle. [RV right ventricle, LV left ventricle, LA left atrium]

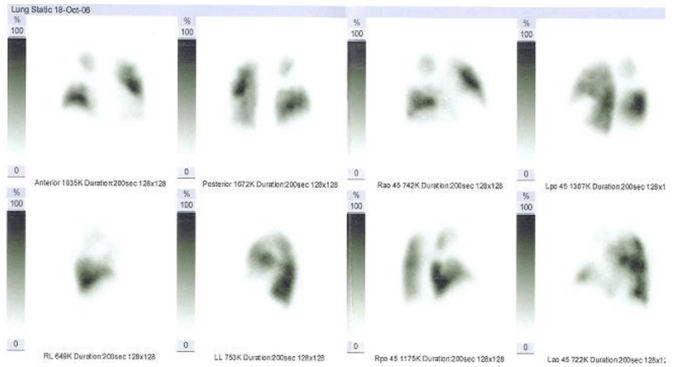

Figure 7: Ventilation-perfusion lung scintigraphy before pulmonary endarterectomy. In this time, computed tomography angiogram of lungs was negative.

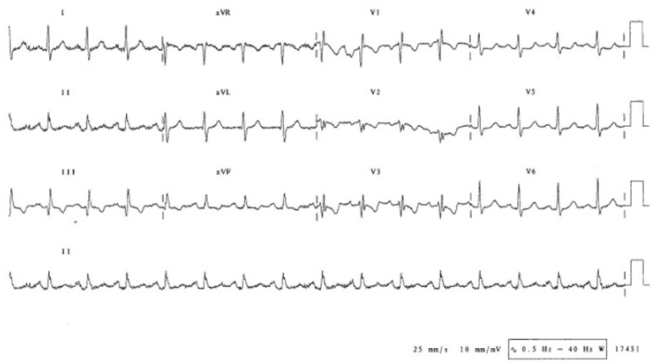

Figure 8: Electrocardiogram four months after pulmonary endarterectomy: sinus rhythm, right ventricle hypertrophy with strain disappeared.

DISCUSSION

Chronic thromboembolic pulmonary hypertension (CTEPH) results from incomplete resolution of a pulmonary embolus predominantly major (central or proximal large) and is listed as distinct subgroup of pulmonary hypertension (group 4) [3, 4]. Chronic

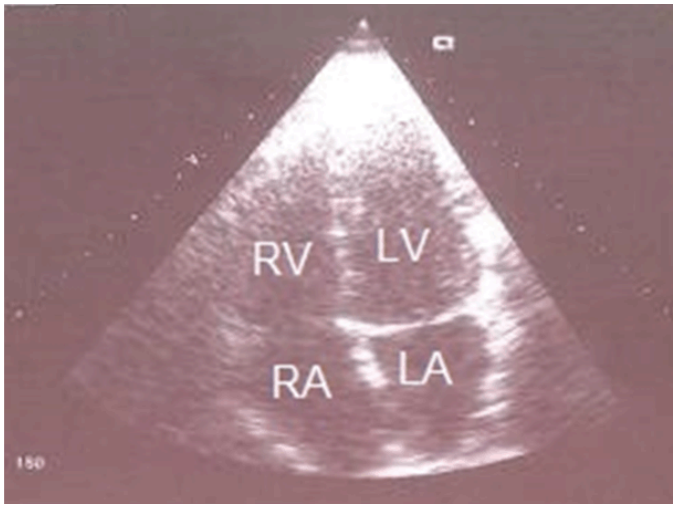

Figure 9: Transthoracic echocardiography four months after pulmonary endarterectomy: dilated right ventricle disappeared. [RV Right ventricle, LV Left ventricle, RA Right atrium, LA Left atrium]

thromboembolic pulmonary hypertension is an underdiagnosed disorder, and the true prevalence is still unclear, the disorder has been demonstrated as late complication of patients who survive an acute PE with a cumulative incidence of 0.1–9.1% within two years of the event [4]. In clinical practice, it is important to differentiate acute PE from an acute episode superimposed on pre-existing CTEPH, because first clinical presentation of CTEPH may mimic acute PE [5]. A significant number of CTEPH cases may originate from asymptomatic VTE (4) or develop in the absence of previous acute PE [6]. The slowly progressive nature of the course of CTEPH allows right ventricle hypertrophy to ensue, which compensates for the increased pulmonary vascular resistance. However, because of progressive thrombosis or vascular changes in the "uninvolved" vascular bed, PH becomes progressive which leads to hypoxaemia [7] and chronic hypoxaemia leads to secondary polycythemia [8].

Patients with CTEPH typically present in either of two scenarios: patients may complain of progressive dyspnea on exertion, hemoptysis, and/or signs of right heart dysfunction including fatigue, palpitations, syncope, or edema after a single episode or recurrent episodes of overt PE. A "honeymoon period" between the acute event and the development of clinical signs of CTEPH is common and may last from a few months to many years [6]. The fibrin derived from patients with CTEPH seems resistant to lysis and D-dimer is not elevated and then to measure of D-dimer is not suitable for diagnosis and prognosis of CTEPH [9, 10], then normal level of D-dimer should exclude CTEPH from acute PE. Chest radiography, pulmonary function tests, ECG and echocardiography are used in the initial assessment of suspected PH.

In general, standard chest radiographs and pulmonary function tests have limited sensitivity and specificity and are insufficient to diagnose CTEPH [7]. Echocardiography at rest remains the best way to estimate elevated pulmonary pressures according to the level of systolic PAP estimated by the tricuspid regurgitant velocity and can reveal an enlarged right ventricle with abnormal contractility [11]. The V/Q lung scintigraphy remains the main first-line imaging modality for CTEPH, as it carries a 96–97% sensitivity and 90–95% specificity for the diagnosis and should be performed in all patients with PH to look for CTEPH, a negative result excludes the diagnosis with almost 100% certainty [12]. While multi-detector computed tomography (MDCT) is the investigation of choice for the diagnosis of acute PE, the investigation may be used as a complementary investigation but does not replace the V/Q lung scintigraphy or traditional pulmonary angiogram [13]. The CTPA alone cannot rule out CTEPH, but may help identify complications of the disease, such as pulmonary artery distension, resulting in left main coronary artery compression [14]. Pulmonary angiography remains a standard diagnostic tool in the assessment of patients with probable or definite CTEPH both to establish the diagnosis and to assess operability. Pulmonary angiography should be performed in conjunction with a diagnostic right heart catheterization, which is an essential diagnostic tool. The comparison of radiographic burden of disease with hemodynamics is a critical exercise in determining operability as well as surgical risk before PEA. Both right heart catheterization and pulmonary angiography should be performed by experienced staff [15]. All patients with established CTEPH should receive life-long oral anticoagulants, unless contraindicated, while no data exist on the efficacy and safety of new direct oral anticoagulants. PEA is the only effective treatment for eliminating the cause of the disease [3]. The effective PEA is associated with the reduced mortality and leads to a permanent improvement in the pulmonary hemodynamics and exercise capacity of patients.

In Europe, in-hospital mortality is currently as low as 4.7% in expert centers [16]. Therefore, all patients with CTEPH should be referred for operability assessment by an experienced CTEPH team to determine if the patient is operable and candidate for PEA. If a patient is deemed non-operable, this patient should be repeatedly referred for operability assessment for a second opinion by an experienced CTEPH team [17, 18]. The highly specialized centre for pulmonary artery hypertension for Slovakia is Cardio Centre of General University Hospital in Prague [19]. For patients deemed non-operable by PEA other treatment options in select cases may include lung transplantation or percutaneous transluminal pulmonary angioplasty [16, 17]. Pharmacological therapy should be considered in patients with inoperable/persistent CTEPH after PEA, who face a poor prognosis. Currently, riociguat (soluble guanylate cyclase stimulator) is the only registered drug [20–22].

CONCLUSION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare complication of acute pulmonary embolims (PE), but it can also occur in patients who do not have a history of acute PE or deep vein thrombosis (DVT) is under-diagnosed and also frequently misdiagnosed in clinical practice. The present report aims to increase the awareness of clinicians towards an accurate diagnosis of the disease. Ventilation-perfusion (V/Q) lung scintigraphy should be the basic and the first diagnostic tool. A negative result virtually excludes the diagnosis with almost 100% certainty. At the same time, the presence of perfusion defects in scintigraphy does not confirm CTEPH. Further diagnostics is necessary, which should involve a number of studies, including right heart catheterization and pulmonary angiography. Each patient diagnosed with CTEPH should be considered for PEA, as it is the only effective treatment method for eliminating the cause of the disease, leading to cure.

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Author Contributions

Margita Belicová – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Veronika Jankovičová – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Marian Mokáň – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Escherichia coli sepsis and pyomyositis following allogeneic stem cell transplant

Folusakin Ayoade, Mohammed Alam, Amy Bozeman, Breanne Peyton-Thomas, Richard Mansour, Nebu Koshy

ABSTRACT

Introduction: Manifestation of infections in hematopoietic stem cell transplant patients tend to be subtle, with subsequent delay in diagnosis and effective therapy. Traditionally, in both normal and immunocompromised hosts, pyomyositis is often attributable to gram positive pathogens such as *Staphylococcus aureus*. Pyomyositis due to *Escherichia coli* is quite rare in the hematopoietic stem cell transplant host, often with uncharacteristic or atypical presentations. Case Report: A 53-year-old male with relapsed acute myelogenous leukemia received allogeneic stem cell transplant. After eight days post-transplantation, he developed fever and other non-specific symptoms, followed by progressive left calf swelling and pain.

The first two ultrasound studies of the affected leg showed no drainable collections despite obvious signs of local infection. The third ultrasound study, done after seven days of onset of symptoms, however, revealed a developing abscess with extensive surrounding cellulitis. Lower extremity computed tomography scan confirmed a 3.4x2.5 cm lesion with a central necrotic portion measuring approximately 1.8x1 cm within the lateral head of the gastrocnemius muscle.

Blood cultures and drained pus from the affected calf muscle grew quinolone-resistant *Escherichia coli* which was sensitive to beta-lactamase antibiotics. Successful treatment was accomplished with three weeks of intravenous meropenem and abscess drainage. Conclusion: This case illustrates the unique peculiarities of infection manifestations in the immunocompromised host, especially recipients of stem cell transplant. The causative pathogen could be atypical, and the clinical and expected imaging findings may be delayed or even absent.

Keywords: Abscess, *Escherichia coli*, Hematopoietic stem cell transplant, Pyomyositis, Quinolone

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INTRODUCTION

Hematopoietic stem cell transplant patients are a unique population and clinical manifestations of infection in this group are often subtle, with subsequent delay in diagnosis and effective therapy. Traditionally, most cases of pyomyositis are attributable to *Staphylococcus aureus* in both normal and immunocompromised hosts [1]. Despite this observation, pyomyositis in the transplant patient and similar immunocompromised hosts often have uncharacteristic presentations and are sometimes associated with the 'unlikely' pathogen [2].

CASE REPORT

A 53-year-old white male with relapsed acute myelogenous leukemia was admitted to our hospital for allogeneic stem cell transplant. Conditioning regimen was fludarabine and melphalan and he received prophylactic levofloxacin 500 mg orally daily starting day-7 post-transplant. On day-8 post-transplant, he developed low grade fever with chills, headache, nausea, vomiting, diarrhea, decreased appetite and myalgia.

The patient's vital signs were temperature 100.6°F (T_{max} 100.9 after 24 hours), heart rate 112 beats/minute, respiratory rate 20 cycles/minute and blood pressure 95/63 mmHg (down from 154/87 mmHg 12 hours earlier).

Physical examination findings at the time of fever including neck, lungs, heart, abdomen and musculoskeletal examinations were all within normal limits. He had a tri-fusion catheter on right chest wall with no evidence of surrounding erythema or tenderness.

Before the onset of fever, he had been severely neutropenic for several days (total white blood cell in blood less than 50 cells per microliter). Other significant laboratory findings include hyperbilirubinemia of 1.6 mg/dl from a baseline of 0.3 mg/dl and INR of 1.77 from a baseline of 1.07. Hepatic aminotransferases were, however, within normal limits. His kidney function showed a slight bump of creatinine from a baseline of 0.7 mg/dl to 1.1 mg/dl. Hemoglobin was 10 g/dl and platelet count 3000/mm^3. Two days later, he complained of mild pain at his left calf with some redness, and over the next few days, the calf became more painful, swollen and indurated. The differential diagnosis at this point included deep vein thrombosis, cellulitis with or without abscess, infected hematoma and deeper infections like pyomyositis or osteomyelitis.

The patient had a total of three ultrasound imaging studies of the affected leg with the first two studies showing no drainable collections despite obvious signs of local infection (Table 1). The third ultrasound study, done after seven days of onset of symptoms revealed 3.2x1.7 cm abscess and extensive surrounding cellulitis. He subsequently had a lower extremity computed tomography (CT) study with intravenous contrast. The CT findings confirmed a 3.4x2.5 cm lesion with thick peripheral enhancement, and a central necrotic portion measuring approximately 1.8x1 cm, located within the lateral head of the gastrocnemius muscle with surrounding edema (Figure 1).

The rationale for multiple ultrasound studies was related to the fact that leg swelling did not improve initially to antibiotic therapy and the treatment team wanted to establish early on the presence of drainable collection.

Blood cultures drawn at the time of fever grew *Escherichia coli* in four of four bottles. Repeat blood cultures (2 sets) drawn two days later were negative. The *Escherichia coli* isolates were all resistant to quinolones but were sensitive to beta-lactamase antibiotics.

The calf abscess was promptly incised, drained and the necrotic wall was excised and sent for pathology.

Abscess culture again grew *Escherichia coli* with antibiotic sensitivities similar to the isolates recovered from the blood culture. Figure 2 illustrates collapse of the abscess cavity after abscess excision.

Pathology of the abscess cavity wall showed striated muscle and connective tissue with suppurative changes and recent hemorrhage but no leukemic infiltrate was identified.

A diagnosis of *E. coli* pyomyositis was made and treatment was provided with intravenous meropenem for three weeks with excellent outcome.

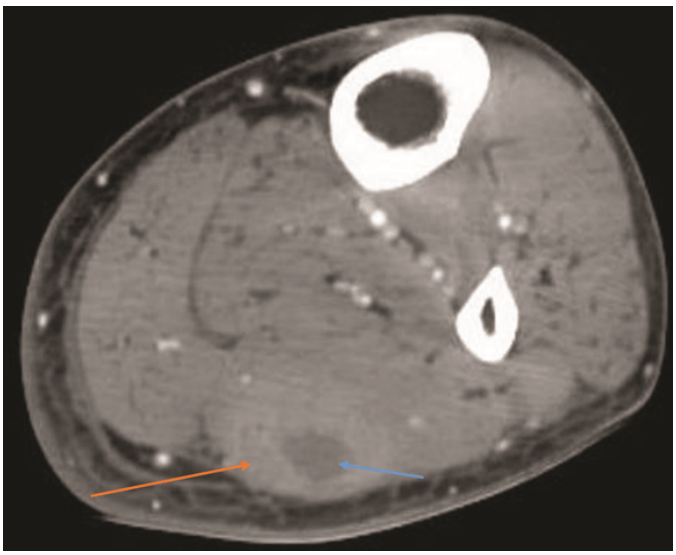

Figure 1: Lower extremity computed tomography scan with intravenous contrast showing 3.4x2.5 cm lesion (orange arrow) and a central necrotic portion measuring approximately 1.8x1 cm (blue arrow) within the lateral head of the gastrocnemius muscle.

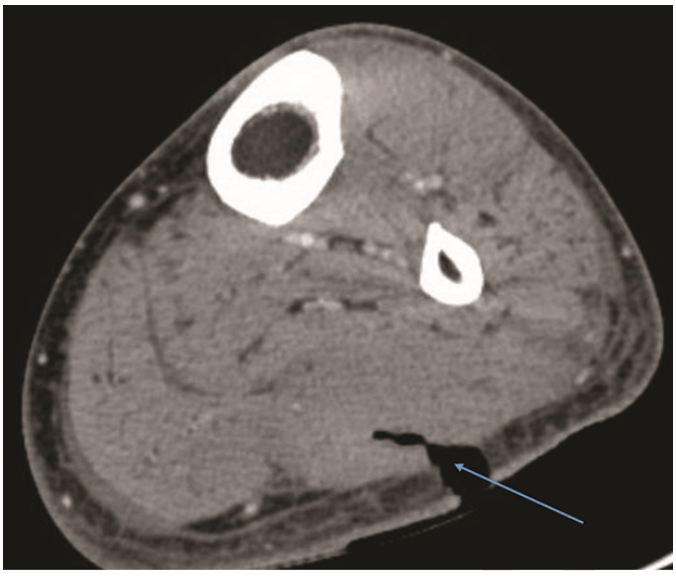

Figure 2: Lower extremity computed tomography scan with intravenous contrast showing collapse of the abscess cavity after incision and drainage.

Table 1: Correlation between clinical features, degree of neutropenia and imaging findings in a 53-year-old immunocompromised patient with *E. coli* pyomyositis

Days	Physical signs and symptoms	WBC in blood (cells/mL)	Ultrasound (USS) imaging study
Day 1	Fever, myalgia	<50	USS not done
Day 3	Calf pain, erythema	240	USS 1: No focal fluid collection, edema or muscle abnormality
Day 4 *	Calf swelling and pain	1060	USS 2: Mild subcutaneous edema of left calf
Day 7	Indurated, erythematous, swollen, warm and tender left calf	1910	USS 3: Extensive cellulitis of left calf with focal area of abscess collection

*Positive *E. coli* bacteremia. Intravenous antibiotic (meropenem) was started on day-1 for febrile neutropenia.

DISCUSSION

Pyomyositis is an infection of skeletal muscle with formation of intramuscular abscesses. The infection occurs predominantly in the tropical regions of the world but to a much lesser extent in the temperate zones where it is often associated with immunocompromised or other serious underlying conditions. Most cases of pyomyositis in both tropical and temperate zones are caused by gram-positive organisms especially Staphylococcus aureus [1–5]. Non staphylococcal pathogens are more typical in temperate regions like in our patient. *Escherichia coli* causing or associated with pyomyositis is a relatively rare occurrence and even rarer is *E. coli* attributed as the main etiologic agent of pyomyositis in patients with hematologic malignancies and immunodeficiency states [2, 3, 6, 7].

The incidence of *E. coli* pyomyositis in the general population is unclear as available data are only from case report or series. In a large population study, the incidence of *E. coli* bacteremia was 30.3/100, 000.

Similarly, the definitive incidence of *E. coli* pyomyositis in the immunocompromised host is unknown as only 15 cases were reported as of August 2011 in eight different case reports or series.

Traditionally, pyomyositis has three stages of evolution as follows:

Stage I is characterized by initial muscle inflammation that is not associated with abscess.

Stage II is associated with early abscess, usually occurring approximately 2 to 3 weeks into illness; and

Stage III is defined by signs of toxicity and systemic infection.

Our patient illustrates a few learning points in the unique hematopoietic stem cell transplant population.

First, the classic signs of localized soft tissue infection: swelling, erythema, induration, tenderness, increased warmth and discoloration are often delayed. This may be attributed to the paucity of inflammatory cells due to the associated profound neutropenia in this patient group [7]. It could be postulated that severe immunosuppression and neutropenia in our patient may explain why abscess formation that one will expect to correspond to the appropriate stage of disease evolution was absent or delayed.

Second, as given in Table 1, even when there are obvious signs and symptoms suggestive of soft tissue inflammation or infection, imaging studies often lag behind and only become obvious when significant neutrophil recovery becomes evident. This observation was also corroborated by Vigil et al. [6] who reported a case series involving six patients, all with hematological malignancies in which half of the patients had demonstrable abscesses only after neutrophilic recovery.

Third, it is not uncommon for pyomyositis caused by *E. coli* to be resistant to quinolones or extended-spectrum beta-lactams (ESBL) especially in patients with hematologic malignancies [2, 6]. At the same time, quinolone susceptibility is not unusual as noted by Sharma et al., who described an isolate with susceptibility to quinolones, with good clinical response to six weeks of oral levofloxacin [7].

Utilization of antibiotic susceptibility results to guide therapy is, therefore, important in providing optimal management.

The patient had pyomyositis involving his left calf muscle. Even though *E. coli* pyomyositis in a hematologic malignancy host seems to favor the calf, as noted in some reports [2, 6], this has not been the case in some other reports with *E. coli* as the sole pathogen [3, 7, 8]. In a report of 44 patients with pyomyositis associated

with hematological malignancies, none of them was attributable to *E. coli* and calf or leg involvement was reported in only six patients (13.6%) [1].

E. coli pyomyositis in the immunocompromised or patients with hematological malignancies has an associated mortality rate up to 33% [1, 4.6]. Even in the general population, *E. coli* sepsis causes approximately 40, 000 deaths yearly in the United states. Notable risk factors for bacteremia or sepsis include extremes of age, hemodialysis, solid organ transplant and neoplasm. *E. coli* pyomyositis with or without sepsis deserves particular attention and aggressive intervention in both immunocompetent and immunocompromised hosts to minimize mortality.

The main limitation of this report is the fact that phylogenetic group determination, polymerase chain reaction analysis and virulence genotyping of the *E. coli* isolates were not available due to inadvertent early discard of the patient's sample by the microbiologic unit of our institution. Previous reports have implicated *E. coli* phylogenetic group B2, from the ST131 subset, which has been linked with virulent, quinolone resistant, ESBL producing, and multi-drug resistant isolates [9, 10]. With our understanding of the increasing antibiotic resistance of ST131 strain and the reported ESBL production in more than 50% in one case series in similar immunocompromised hosts [6], the authors were more comfortable with using a carbapenem such as meropenem rather than a cephalosporin. In addition, the sensitivity of *E. coli* to carbapenems at our institution approaches 100%.

CONCLUSION

Our case illustrates an unusual presentation of pyomyositis in a severely immunocompromised host. Providers caring for patients with stem cell transplant and other hematologic malignancies should include pyomyositis in the differential diagnosis especially in patients with pain and swelling of the extremity, even when classic signs of soft tissue infection are not clearly apparent. Significant infection leading to bacteremia and other complications may occur despite less aggressive clinical findings and 'normal' imaging studies.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

A case report on drug induced pancreatitis due to levofloxacin and methylprednisolone

Balwinder Kaur Rekhi, Srinath Reddy Mannem, H. S. Rekhi, Sushil Kumar Mittal, Sahil Arora, Sathya P., Ravitej Singh, Kaushal Seth

ABSTRACT

Introduction: Acute pancreatitis is the acute inflammation of the pancreatic gland, attributed to a wide range of etiological factors. It is a well-known fact that approximately 80% of the causes are associated with cholelithiasis and alcohol abuse. However, the exact incidence of drug induced pancreatitis is difficult to determine due to the rare presentation, it requires larger, case-controlled studies to determine its incidence and prevalence. Up to 2% cases may be caused by drug. Case Report: This is a case report focusing on a 26-year-old female patient who developed acute pancreatitis following administration of levofloxacin and methylprednisolone for treatment of pneumonitis in intensive care unit. Both the drugs appear to be responsible for pancreatitis because of temporal relationship between the administration of drug, onset of symptoms and improvement of clinical symptoms when drugs were stopped. Conclusion: Levofloxacin and methylprednisolone appears to be responsible for pancreatitis because of the temporal relationship between the administration of drug, onset and improvement of clinical symptoms when drugs were stopped.

Keywords: Acute pancreatitis, Drug induced pancreatitis. Levofloxacin, Methylprednisolone

How to cite this article

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INTRODUCTION

Acute pancreatitis is the acute inflammation of the pancreatic gland associated with varying involvement of the surrounding regional tissues or remote organ system. It is characterized by deep seated abdominal pain radiating to back, nausea and elevated pancreatic enzymes.

Acute pancreatitis has been attributed to a wide range of etiological factors. Approximately, 80% of the cases are associated with cholelithiasis or alcohol abuse [1]. Approximately, 1% develop pancreatitis following endoscopic retrograde cholangiopancreatography (ERCP). Several drugs are casually related to pancreatitis particularly corticosteroids, thiazide diuretics, estrogens, azathioprine, and furosemide. Furthermore, in about

10% of cases, no cause can be identified. Pancreatic toxicity of drugs is of relatively recent knowledge through the publication of isolated cases or small series. Up to 2% of cases may be caused by drugs [2].

We report a case of acute pancreatitis in a young female receiving levofloxacin and methylprednisolone.

CASE REPORT

A 26-year-old female was admitted in intensive care unit as a case of pneumonitis. She presented with history of respiratory distress, cough for seven days and with fever for three days. There is no family history of pancreatic diseases. There is neither any history of alcohol abuse nor drug abuse. On examination, respiratory rate was 30 per min, pulse 128 per min, blood pressure was 118/82 mmHg. Chest examination showed bilateral diffuse crepts and ronchi with the use of accessory muscles. SpO_2 of 92% with venturi fiO_2 40%. After routine hematological and radiological investigations, she was diagnosed as pneumonitis and put on

- Injection ceftriaxone and sulbactum 1.5 g i.v bd
- Injection azithromycin 500 mg i.v od
- Injection omeprazole i.v od
- Nebulization with salbutamol and budesonide

The patient's general condition did not improve and further deteriorated, saturation dropped to spO_2 of 82% with oxygen and there after patient was shifted to ICU put on volume controlled mechanical ventilation and was put on

- Injection ceftriaxone and sulbactum 1.5 g i.v bd
- Injection levofloxacin 500 mg i.v od,
- Injection solumedrol 50 mg iv od.
- Injection omeprazole i.v od
- Nebulization with salbutamol and budesonide

After two days of treatment, the patient started responding to treatment, was weaned off from ventilator and put on venture mask. On the third day patient developed acute abdominal pain which is radiating to back and loose stools, for which ultrasonography was done which showed free fluid in the upper peritoneal recess and in between gut loops with left sided pleural effusion. Surgery call was sent and patient was diagnosed as a case of acute pancreatitis clinically, we advised serum amylase and lipase apart from routine investigations. Serum amylase was 346 U/L and serum lipase was 1432 U/L. Patient was advised contrast CT scan of abdomen which showed acute pancreatitis with modified CTSI of 6/10. Total leucocyte count raised from 11,600/mm^3 to 20,400/mm^3 on same day, the next day it increased to 52,000/mm^3 and then to 70,300/mm^3. The initial antibiotics were stopped and patient was put on

- injection meropenem 1 g i.v tds,
- injection metronidazole 100 ml iv tds

After three days patient responded well, serum amylase and lipase levels came back to normal range with normal ultrasonographic findings. Patient was later discharged and advised for follow-up.

DISCUSSION

Drug induced pancreatitis is relatively a less known concept in acute pancreatitis, as it is a relatively rare occurrence considering the small number of patients who develop pancreatitis compared to the large number of patients who receive potentially toxic drugs. Its incidence varies among different studies between 0.1% and 5.3% of all acute pancreatitis cases [3]. The clinical presentation and mechanisms of injury to the pancreas are not well understood and are controversial. The diagnosis of drug induced pancreatitis remains possible or probable in many patients. The resolution of pancreatitis after discontinuation of drug, could improve the diagnosis of drug induced pancreatitis. However, it is difficult to establish the direct correlation between resolution of symptoms and drug withdrawal sometimes.

Pancreatic toxicity of drugs is of relatively recent knowledge through the publication of isolated cases. According to pancréatox file prepared by the Paris Regional Centre - Saint-Antoine, the number of offending drugs reached 261, representing potentially 1–2% of acute pancreatitis [4]. More than 500 different drugs are listed in the World Health Organization (WHO) database suspected to cause acute pancreatitis as a side effect. Many of them are widely used to treat highly prevalent diseases [5].

Levofloxacin belongs to the new fluoroquinolones group. The most commonly reported adverse reactions are minor digestive disorders and elevated liver transaminases [6].

Mennecier et al. [7] suggest a possible pancreatic toxicity of levofloxacin used alone or with steroids and therefore, encourages us to recommend pancreatic biological tests before the onset of abdominal pain during treatment with levofloxacin. They also stated that there is temporal relationship between the drug intake and development of acute pancreatitis as well as resolution of acute pancreatitis upon discontinuation of drugs in a short interval.

In our case, the time criteria are based on the evolving profile of acute pancreatitis according to the administration and medication discontinuation.

Re-administration of drug has not been made. The temporal relationship between drug intake and the occurrence of pancreatitis is suggestive because the time between the administration of treatment and the occurrence of acute pancreatitis is short. Upon discontinuation of treatment, resolution of acute pancreatitis is suggestive as the clinical and laboratory abnormalities decreased within hours. The problem here is, what is the offending drug? Several cases of acute pancreatitis have been reported with methylprednisolone is a well-established fact [8]. In acute pancreatitis secondary to taking methylprednisolone, the time frame is 3 days to 22 weeks with a dose-dependent mechanism assumed. The mechanism of corticosteroid-induced pancreatitis is complex and currently unknown [9]. In

a case report of Seneviratne et al. [9], the pancreatitis started after eight days of high-dose (250 mg) steroid treatment. In our patient, we started 50 mg dose of methylprednisolone. In our observation, the speed of the onset of acute pancreatitis can argue more in favor of an immunological mechanism. This suggests that the already incriminated levofloxacin in elevated pancreatic enzymes can cause acute pancreatitis. However, further observations are needed to confirm this hypothesis.

CONCLUSION

In this case reported, levofloxacin and methylprednisolone appears to be responsible for pancreatitis because of temporal relationship between the administration of drug, onset of symptoms and improvement of clinical symptoms when drugs were stopped.

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Author Contributions

Balwinder Kaur Rekhi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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H. S. Rekhi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Kaushal Seth – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Myxoedema: A rare cause of massive ascites

Rabab Fouad, Mohamed B. Hashem, Mohamed Said, Marwa Khairy, Mahmoud Abouelkhair, A. A. Helmy

ABSTRACT

Myxoedema ascites is a rare condition with a known incidence of 4% which makes it in the bottom of the list of causes of ascites, that is why diagnosis is often delayed and physicians usually do not put it in the preliminary differential diagnosis of a case of ascites. We here report a case of Ascites due to hypothyroidism which markedly improved after thyroxin therapy. To our knowledge, this makes it the first case reported in Egypt with myxoedema ascites. Myxoedema ascites is characterized by the dramatic response to replacement therapy. The message to be taken is that myxoedema is a rare cause of massive ascites but should be evaluated if suspected since the condition is easily controlled by medical treatment.

Keywords: Massive ascites, Myxoedema, Serum ascites albumin gradient (SAAG)

How to cite this article

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INTRODUCTION

Portal hypertension secondary to liver cirrhosis is the leading cause of ascites (more than 80% of cases) and peritoneal involvement in patients with malignant diseases is the second at about 10% [1]. However, some cases maybe due to other rare diseases including hypothyroidism which is characterized by a marvelous response to treatment. Patients with ascites due to portal hypertension and nephrotic syndrome usually respond to diuretic therapy while patients with ascites due to other disorders whether biliary, pancreatic, myxoedema etc. respond to treatment of the underlying cause. That is why it is essential to search for the underlying etiology of ascites carefully.

CASE REPORT

A 48-year-old female was presented with one year history of progressive abdominal distension, bilateral lower limb edema and chronic constipation. On admission, her blood pressure was 120/70 mmHg, pulse rate was 70 bpm and BMI was 26 kg/m^2. General examination as well as cardio-respiratory examination were free apart from bilateral partially pitting lower limb edema reaching the thighs, with overlying slightly rough skin.

The abdomen was markedly distended, with tight skin and liver was mildly enlarged. There was also shifting dullness detected by percussion.

Urine analysis was normal with no evidence of proteinuria, complete blood count showed mild normocytic normochromic anemia with hemoglobin

of 10.3 g/dL while leukocyte and platelet counts were normal. Regarding liver biochemical profile, albumin was 2.9 (normal range 3.5–5.5), total proteins 6.2 (normal range 6.5–8.5), total bilirubin 0.3 (normal range 0.2–1.2), ALT 23 (normal range 12–37), AST 30 (normal range 25–65), ALP 70 (normal range 50–130), GGT 26 (normal range up to 42), PC 88% (normal range 70–130), INR 1.07. Renal functions, electrolytes, HBsAg and HCV Ab were all negative.

Ascitic fluid analysis was done next showing clear sample containing total leukocyte count of 200 cells of mixed cellularity and negative for malignant cells. Total proteins were 4.2 and serum-albumin ascitic gradient (SAAG) was 0.9. Gram staining, bacterial, fungal and MGIT culture (Mycobacterial growth indicator tube) cultures were all negative.

Echocardiography was done which ruled out congestive heart failure as a cardiogenic causes of Ascites showing dilated left atrium, dilated left ventricle, left ventricular grade I diastolic dysfunction with an ejection fraction of 42%.

We performed imaging studies to evaluate the possible cause of the ascites, Ultrasonography (Figure 1A–B) and computed tomography (CT) scan (Figure 2) of the abdomen revealed bright hepatomegaly, massive ascites, parietal and visceral peritoneal thickening as well as an echogenic omental thickening seen in the mid line raising the possibility of local peritoneal disease.

The findings yielded from the imaging studies, we decided to rule out the possible causes of peritoneal diseases including peritoneal malignancies and tuberculosis so tuberculin skin test, chest X-ray and tumor markers were done showing no abnormalities. The next crucial step was to perform ultrasound guided biopsy of the thickened heterogeneous omentum where the specimen revealed moderate inflammatory reaction with possible fat necrosis, no granulomas and no malignancy encountered.

At this stage, we started evaluation of other unusual causes of high protein content with low SAAG ascites so complete thyroid profile was done showing TSH 25.40 ulU/ml (normal range 0.4–4 ulU/ml), T3 < 0.3 pg/ml (normal range 2–4.4 pg/ml) and T4 0.1 ng/dl (normal range 0.8–1.9 ng/dl). Thyroid ultrasound was done next showing no abnormality in both lobes.

Thyroxin was started with gradually increasing doses of levothyroxine, from 0.05 mg to 0.12 mg daily to treat the patient's hypothyroidism. However, after one month of treatment there was no improvement in her condition despite being euthyroid. This forced us to re-evaluate the diagnosis since the incidence of ascites in myxoedema is rare (4%). Also, there was omental and peritoneal thickening which are strongly suggestive of the presence of local peritoneal diseases. Furthermore, there was no accepted improvement in the amount of ascites after one month of treatment.

A laparoscopy was done showing omental, visceral and parietal peritoneal thickening which were biopsied and their histopathological examination showed fibro fatty tissue infiltrated by chronic inflammatory cells with fat necrosis. That was consistent with the previous biopsy taken under ultrasound guidance so the patient was discharged after increasing the dose of levothyroxine to 0.15 mg and followed-up over the next three months where follow-up showed dramatic improvement in her condition; the ascites resolved completely and did not recur and thyroid function tests were maintained. The latest thyroid profile showed TSH 3.0 ulU/ml, T3 3.6 pg/ml and T4 2.1 ng/dl.

DISCUSSION

Most patients with ascites usually suffer from liver cirrhosis [2]. In about 15% of patients with ascites, there is a non-hepatic cause of fluid retention. Successful treatment is dependent on an accurate diagnosis of the cause of ascites; e.g., peritoneal carcinomatosis does not respond to diuretic therapy. Patients with ascites should be questioned about risk factors for liver disease [3]. Past history of cancer, heart failure, renal disease, thyroid

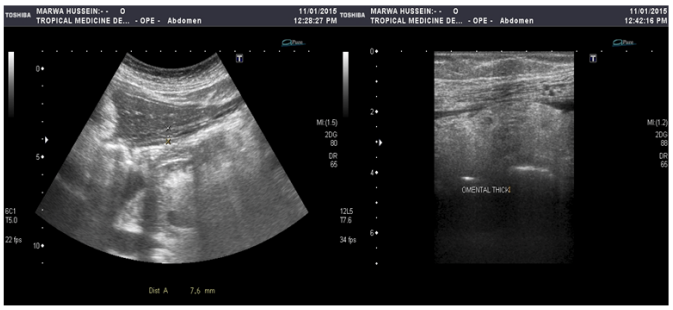

Figure 1: Ultrasound showing omental thickening.

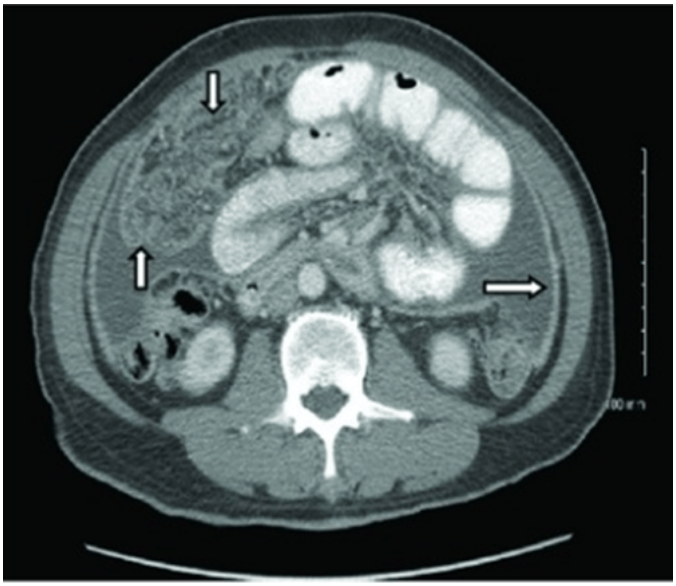

Figure 2: Computed tomography scan of abdomen showing moderate amount of abdominal and pelvic ascites with diffuse thickening of peritoneal surfaces. Diffuse thickening also is seen throughout the omentum.

disease or tuberculosis is also relevant. Hemophagocytic syndrome can masquerade as cirrhosis with ascites. These patients have fever, jaundice, and hepatosplenomegaly, usually in the setting of lymphoma or leukemia [4].

The serum ascites albumin gradient (SAAG) is formula used to assist in determining the etiology of ascites. The SAAG is the best single test for classifying ascites into portal hypertensive (SAAG >1.1 g/dL) and non-portal hypertensive (SAAG < 1.1 g/dL) causes. Calculated by subtracting the ascitic fluid albumin value from the serum albumin value, it correlates directly with portal pressure. The specimens should be obtained relatively simultaneously. The accuracy of the SAAG results is approximately 97% in classifying ascites. The terms high-albumin gradient and low-albumin gradient should replace the terms transudative and exudative in the description of ascites.

Hypothyroidism though being relatively common condition yet, it manifests with ascites in a minority of patients [5]. The SAAG is usually low in cases of ascites caused by myxoedema [6]. The mechanisms by which a patient with myxoedema develops ascites is unknown. There have, however, been several hypotheses proposed. One of them suggested that ascites occurs due to the extravasation of plasma proteins as a result of abnormal capillary permeability. Another theory showed that accumulation of hyaluronic acid under the skin of patients with myxoedema may lead to ascites by a direct hygroscopic effect.

CONCLUSION

To conclude, the message to be delivered here is that myxoedema though being a rare cause of ascites, should be excluded early especially in cases with vague presentation since it carries an excellent prognosis with adequate replacement therapy.

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Rabab Fouad – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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CASE REPORT PEER REVIEWED | OPEN ACCESS

Erythema ab igne in patients with dementia: Implications for caregivers

Zijian Zheng, Sid Danesh

ABSTRACT

Introduction: Erythema ab igne is a benign, asymptomatic skin condition caused by heat exposure. It is an uncommon condition, making it challenging for physicians and healthcare providers to diagnose and follow-up for potential progression to malignancy, especially in patients with dementia. Case Report: Herein, we present a case of erythema ab igne in a 70-year-old male with dementia, in whom careful history taking from family was required to elicit the cause (a warming blanket) and diagnosis. Conclusion: Erythema ab igne can be recognized and prevented if physicians have a high index of suspicion and are aware of the history and signs. Patients with dementia require particularly close clinical follow-up.

Keywords: Dementia, Erythema ab igne, Squamous cell carcinoma

How to cite this article

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INTRODUCTION

Erythema ab igne is a benign cutaneous disease caused by prolonged heat exposure [1]. Although uncommon, dementia patients are particularly susceptible due to lack of self-care and cognitive impairment. Furthermore, they find the skin condition difficult to monitor, particularly for secondary malignant transformation. Here we report a case of erythema ab igne in an elderly male with dementia to illustrate that a high index of suspicion, close observation, and prompt treatment are required in this vulnerable population.

CASE REPORT

A primary care physician (PCP) referred a 70-year-old Asian male with a history of dementia, chronic heart failure, and back pain to the dermatology clinic due to a three-month history of unexplained leg rash.

Most history was obtained via family members due to the patient's dementia, who reported multiple scaly rounds to oval shaped blisters on the lower limbs. On examination, the patient was alert and not in distress. He was oriented in person, time, and place and vital signs were stable and within normal range. The patient had general dry and loose skin due to aging with multiple verrucous, hyperkeratotic lesions. There were multiple varicose veins on the posterior lower legs and benign nevi on the face, upper trunk, and abdomen.

The lesion of interest was a non-tender violaceous, macular rash resembling livedo reticularis on the right

lower lateral thigh and upper lateral leg (Figure 1). The lesion blanched with alternating red pigmentation and normal skin. Healing wounds and hyperkeratotic scars were also present. There were no joint effusions or warmth in the lower extremity joints, which had a full range of both active and passive movement. Motor and sensory examinations were normal. Although the patient had difficulty distinguishing present and past events, he reported no pruritus, pain, or bleeding. His family reported no history of bleeding disorders, anticoagulant use, or similar past events. Apart from 81 mg aspirin every other day, he was not on any other prescribed antiplatelet or anticoagulant therapy.

The patient's PCP had recently performed a well adult check that revealed normal hematological and biochemical parameters. Further direct questioning of the patient and family revealed that patient had lower back pain and that he was reluctant to take pain medication. He had instead been using an electrical warming blanket to alleviate his back pain. His family often found him forgetting to turn it off and sleeping with it in place. The patient lay on his left side at sleep.

Given the history and findings, erythema ab igne was diagnosed. The patient was given triamcinolone cream and the lesions had resolved by the next visit. Instructions on prevention of similar symptoms were given to patient and the caregiver.

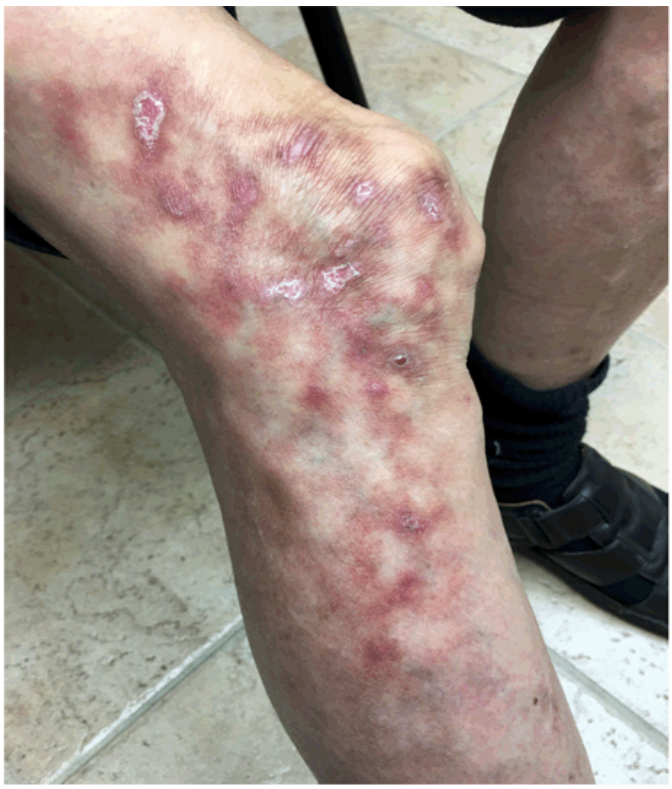

Figure 1: Right leg showing erythematous, violaceous maculopapular rashes.

DISCUSSION

Erythema ab igne describes persistent, blanching erythematous areas that gradually develop into reticulated pigmentation and focal epidermal atrophy due to excessive or long-term heat exposure. The heat is not usually hot enough to cause overt burning in most cases. Hemostasis cause by the heat leads to a mottled appearance and subsequent pigmentation. The pigmentation can be erythematous, violaceous, pink, gold or dark brown. Various heat sources have been reported to cause erythema ab igne including heating pads, heating pans, and even laptops [2]. In our patient, a heating blanket led to his symptoms and signs. In most cases, after removal of the heating source, pigmentation gradually resolves but permanent pigmentation is possible [3].

A skin biopsy should be obtained to rule out other etiologies rather than to confirm the clinical diagnosis of erythema ab igne, which has non-specific histopathologic findings [4]; indeed, the biopsy taken in this case showed only a sparse perivascular infiltrate and non-specific findings. In early disease, epidermal atrophy, lymphocytic infiltrates, and epithelial atypia may be seen with dermal elastin deposition seen in late disease. Epithelial atypia can progress into squamous cell carcinoma, which is preventable with 5-fluorouracil or imiquimod. The use of steroid cream may help to reduce the pigmentation [5].

Livedo reticularis and other vasculitides should form part of the differential diagnosis, but our patient's recent normal laboratory results helped us to rule out any systemic vasculitis. Further, the patient did not have other symptoms such as fever or weight loss.

Close follow-up of patients with erythema ab igne is crucial, not only due to a risk of malignancy but also because it is hard for patients to monitor skin changes on the lower back and at other difficult to see locations. Ulceration and worsening of the lesion warrant biopsy to rule out squamous cell and Merkel cell carcinomas, both of which have been described in association with the condition [6]. Dementia patients in particular need close follow-up since they are less likely to self-monitor and may continue to apply heat. Physicians and other healthcare providers managing dementia patients need to pay close attention to the use of heating sources, and make sure that they are properly used, and need to be aware of the cutaneous manifestations of benign and malignant diseases arising from heat exposure to ensure prompt diagnosis and management.

CONCLUSION

Erythema ab igne can be recognized and prevented if physicians have a high index of suspicion and are aware of the history and signs. Patients with dementia require particularly close clinical follow-up.

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Author Contributions

Zijian Zheng – Substantial contribution to the concept and design, Drafting the article, Final approval of the version to be published
Sid Danesh – Substantial contribution to the concept and design, Drafting the article, Final approval of the version to be published

Guarantor

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Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

A fever of unknown origin as a presenting symptom in toxoplasmosis: Back to earth

Jill F. Mentink, Michiel van Rijn, Adriaan Dees

ABSTRACT

Introduction: Fever of unknown origin (FUO) and weakness in the upper legs are among the presenting symptoms in acute toxoplasmosis, which can occur in immune-competent individuals. Case Report: A 76-year-old Caucasian male presented at the hospital with relapsing fever and weakness in both upper legs. A neurological examination confirmed weakness in the quadriceps muscles, which appeared to be atypical for any neurological substrate. An extensive work-up did not lead to a diagnosis. After two weeks of clinical investigations and persistent fever, we re-examined our patient to look for anamnestic signs. We again asked about (recent) vacations, hobbies and potential exposures. Ultimately, the patient told us he performed charity work at a care farm for more than ten years. He had contact with sheep and soil, which occurred while working in the garden without wearing gloves. A diagnosis of a primo toxoplasmosis infecton was made and the patient was treated with daraprim and clindamycin. Within two days his temperature normalized and the strength in his legs improved gradually. He achieved a complete recovery within three months. Afterwards his wife mentioned that her husband was afraid of losing his volunteer job, when telling his doctors about his work with disabled people. Conclusion: In patients presenting with FUO, clinicians in search of a diagnosis must struggle through a long list of possible diagnosis. Diagnostic delay can be shortened by considering the potential clues in the patient's history.

Keywords: Diagnostic delay, Fever of unknown origin (FUO), *Toxoplasma gondii*

How to cite this article

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INTRODUCTION

Fever of unknown origin (FUO) and weakness in the upper legs are among the presenting symptoms in acute toxoplasmosis, which can occur in immune-competent individuals.

The prevalence of the obligate, intracellular protozoan *Toxoplasma gondii* varies worldwide, but it is generally assumed that the global infection rate is 25–30%. Some healthy individuals who are infected become

symptomatic. Immunocompromised patients are at risk of reactivation of a primo infection and developing a severe and complicated illness.

In patients presenting with FUO, clinicians in search of a diagnosis must struggle through a long list of possible diagnosis. In this modern era of sophisticated imaging techniques, the temptation to fully rely upon laboratory tests results and scans should be resisted [1, 2]. This diagnostic delay can be shortened by considering the potentially diagnostic clues in the patient's history.

CASE REPORT

A 76-year-old male was admitted to hospital with relapsing fever along with weakness and pain in his upper legs. He said told that the weakness, which had a progressive course, had begun several weeks earlier and had progressively worsened. His medical history included diabetes mellitus type 2, hypertension, uncomplicated coronary angiographic bypass graft and laparoscopically performed cholecystectomy. Moreover, 24 years earlier, he had undergone allogeneic bone marrow transplantation because of paroxysmal nocturnal hemoglobinuria (PNH). His daily medication regime included metformin, enalapril, fluvastatin and acetylsalicylic acid.

On admission the patient was in a poor condition. He had lost 4 kg, was anorectic and had a temperature of 39.0°C. On physical examination, his heart and lungs were normal. Neurologic examination: the patient was alert, febrile, Glasgow Coma Scale E4M6V5. Investigation of the lower extremities: the patient was unable to lift his feet, the sensibility was normal. Mild weakness was observed. Knee and Achilles reflexes were 0/0 and -4/-2 respectively.

Laboratory tests on admission: leucocytosis of $15.9x10^9$/L, sedimentation rate in the first hour of 90 and C-reactive protein of 386 mg/L. Blood and urine samples were obtained for cultures, full blood count and chemistry, along with serological tests for underlying infectious causes and rheumatic diseases. A chest X-ray and abdominal ultrasound were performed. A presumptive diagnosis of infection was made and because of the lack of focus we decided not to start antibiotics but wait for the results of the cultures. A neurologist was consulted, but found no central or peripheral abnormalities, apart from painful quadriceps muscles, that might explain the clinical picture. We did not perform a muscle biopsy at that moment. During his stay in the hospital, a relapsing fever was observed, that met the criteria of FUO, also known as febris e causa ignota (Figure 1). Cultures of blood and urine remained negative. Autoimmune serology and ANCA's were absent. Based on serology hepatitis, HIV, *Borrelia*, influenza, syphilis, *Coxiella burnetii* (Q-fever) and brucellosis were ruled out. The serological tests for Epstein—Barr and cytomegalic virus were positive for past infections. Withdrawal of fluvastatin did not result in any improvement. A thoracic and abdominal computer tomography (CT) scan did not reveal solid masses, abscesses, lymphadenopathy or any sign of malignancy, except for a benign cyst in the liver. A whole body (18) F-fluorodeoxyglucose ((18)F-FDG) position emission tomography (PET)-CT scan showed some, perhaps physiological uptake in the kidneys and bowel. Bone marrow aspiration and immunology analyses revealed normal cell lines following the previous transplantation, without signs of leukaemia or myeloproliferative disease. Throughout this diagnostic process, we failed to arrive at a definite diagnosis. The patient remained febrile and his condition progressively worsened in a couple of days. We decided to return to the patient to seek out potentially diagnostic clues that we had previously neglected. Subsequently, the patient mentioned that he had travelled to Brazil several years ago, but was not sure whether he had received all the proper vaccinations. Thereafter, a thick blood smear was performed to exclude malaria parasites, as well as tests for schistosomiasis and Q-fever. Eventually, the patient told us that he had worked as a charity worker for more than ten years at a care farm for disabled people. He had contact with sheep and also maintained the gardens without wearing gloves while working with soil. Afterwards his wife told us that he had been very afraid to lose his volunteer job, as a consequence of telling his doctors this information.

Finally, we found that toxoplasmosis serology for IgM and IgG were positive with a rather low avidity of 0.548, which fit the diagnosis of acute infection. We considered this a primo infection in an immunocompetent host.

We started our patient on daraprim (pyrimethamine) and clindamycin. Daraprim is a folic acid antagonist that is highly effective against toxoplasma especially when used in combination with sulphonamide. We preferred the combination with clindamycin because of less symptoms and similar effectiveness. We started with one dose of 100 mg Daraprim and continued with 50 mg once daily in combination with clindamycin 600 mg four times daily for two weeks.

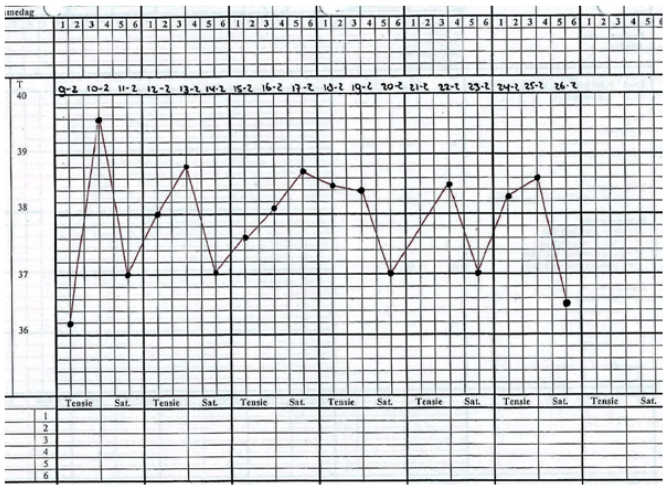

Figure 1: Temperature curve.

The patient was regularly seen at outpatient clinic after his discharge from hospital,. His condition gradually improved, without a return of complaints or fever. The patient remained seropositive (IgM and IgG) during six months of follow-up.

DISCUSSION

This report illustrates the pitfalls in the diagnostic route of a patient, who may present with a fever of unknown origin. During the ward grand rounds we discussed the immune status of this patient. He was known to have diabetes type two. He exhibited no previous signs of recurrent infections. He had undergone bone marrow transplantation because of a benign disease more than 20 years ago. However, after we made the diagnosis, we wondered whether our initial assumption was right. Very few healthy individuals who have been infected with *Toxoplasma gondii* become symptomatic, although fever and myalgia have been described as presenting symptoms, even in immunocompetent individuals [3, 4].

The IgG and IgM antibodies were positive at presentation, with a low avidity of 0.548 for IgG. The IgM antibodies usually present within the first week of presentation, peak in one month, but may persist for a year or more. The IgG titer helps to distinguish an acute infection from a past infection [5]. A low avidity is associated with an acute infection, a high avidity makes an past infection or re-activation more likely.

Toxoplasma gondii is an obligate intracellular protozoan. The prevalence of this single cell parasite differs worldwide, but is generally assumed that that the infection rate of the global population is 25–30% [6]. A high prevalence infection occurs in tropical Africa and Latin America. A total of three major genotypes have been identified, among which type I is the most virulent. Cats facilitate the sexual parasitic cycle and spreading of oocysts though faeces. Humans can acquire *Toxoplasma* by eating undercooked meat, drinking contaminated water, swallowing parasites after contact with cat feces (via contaminated soil or cleaning a cat litter box) or they are infected by receiving an infected organ transplant or donor blood. Some infected individuals experience non-specific flu-like symptoms. By contrast, immunocompromised patients are at risk of developing severe toxoplasmosis infections after primary infection or re-activation that may result in myocarditis, pneumonitis, polymyositis, meningoencephalitis or other conditions. Morbidity is even higher after infection with a type one or atypical strain. Afterwards we asked the transplantation centre that had previously treated the patient, whether his toxoplasmosis serology had been noted in the charts prior to transplantation. This information could not be located.

The role of the FDG-PET/CT scan may be questioned. This nuclear imaging test has shown its utility in patients with FUO, along with reasonable performance [7].

In the patient presented here, the diagnostic yield of CT and PET was unclear. In contrast to the imaging techniques, our search for specific diseases based on clinical reasoning and serology was more successful [8].

CONCLUSION

The case demonstrates that FUO and weakness in the upper legs can be the presenting symptoms in toxoplasmosis and that this might present in immune-competent individuals. Unravelling the patient history can shorten the diagnostic delay. The diagnostic clue in this case turned out to be the patient's previous social work on a charity farm. The clinical course of the patient suggested an acute infection, however a reactivation from a prior infection, in case of a transplantation history, could not be excluded definitely.

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Author Contributions

Jill F. Mentink – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Michiel van Rijn – Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Adriaan Dees – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

A case of abnormal uterine bleeding of unknown origin

Jianping Zheng, Cunjian Yi, Qing Huang

ABSTRACT

Introduction: Abnormal uterine bleeding is a common but complicated clinical presentation that impairs the quality of life in women. Case Report: A reproductive-aged woman presented abnormal uterine bleeding of unknown reason with a heavy bleeding intermenstrual period. By physical examination, laboratory and imaging tests, pregnancy, iatrogenic cause, systemic condition and genital tract pathology were excluded. After high doses of estrogen with oxytocin and intrauterine balloon pipe treatment, the bleeding gradually reduced and stopped. Conclusion: Abnormal uterine bleeding is one of the most common reasons that reproductive-aged women seek health care. In rare complicated cases, however, the causes are difficult to identify which will lead to a delay in treatment and significant loss of the blood.

Keywords: Abnormal uterine bleeding, Hemostasis, Reproductive-aged women

How to cite this article

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INTRODUCTION

Abnormal uterine bleeding is a common but complicated clinical presentation that impairs the quality of life in women. The causes of abnormal uterine bleeding are varied, depending largely on the age and life stage of the women. The common causes in women of reproductive age include pregnancy and pregnancy-related disorders, medications, iatrogenic causes, systemic conditions, genital tract pathology, and dysfunctional uterine bleeding (anovulatory or ovulatory). The rare ones are genital cancers [1]. In this report, we reported a case of abnormal uterine bleeding of unknown reason in a reproductive-aged woman who presented a heavy bleeding after the normal last menstrual period.

CASE REPORT

A 32-year-old female had the normal last menstrual period from October 1, 2014 to October 8, 2014. Since October 17, 2014, she had a heavy bleeding form virginal without any significant incentives. Taking a three-day hemostatic drug treatment was not effective. Therefore, the diagnostic uterine curettage was taken at the clinic. She visited a local hospital on October 26, 2014 because of the constant bleeding after operation, and her blood results were as follows: hemoglobin 7.5 g/dL, beta-human chorionic gonadotropin (β-hCG) < 1.2 mIu/ml. Transvaginal ultrasound showed that the thickness of endometrial was about 2 mm, with uterine cavity effusion and pelvic cavity effusion in small quantities.

The hysteroscopy was performed on November 3, 2014 the depth of uterine was 7.5 cm, the cervical showed no obvious placeholder lesions and special-shaped vessels and no aliens vascular and space-occupying lesions, and the openings of bilateral fallopian tube were clear. Blood hemoglobin was 5.5 g/dL, after blood transfusion hemoglobin increased to 7.7 g/dL. Marvelon (3 pills daily) was given after the hysteroscopy, and then the bleeding gradually reduced.

The patient was sent to our hospital by ambulance with heavy bleeding again on November 15, 2014. She was pale with cold clammy skin and her blood pressure was 106/72 mmHg. Speculum examination showed moderate bleeding coming through the cervical os with around 150 mL of clots. Bimanual examination revealed a softer uterus in normal size. Her abdomen was soft and non-tender and no mass was palpable. The patient denied the use of medications and had no significant past medical history. Her blood results were as follows: urine pregnancy test was negative, hemoglobin was 8.8 g/dL, thrombin time was 21.8 s/20 s. Transvaginal ultrasound showed endometrial cavity fluid (60x35 mm) most likely hematometra, but no obvious adnexal mass. Progynova (12 mg daily) was administrated for three days, but was ineffective. Hemoglobin was 5.06 g/dL on November 18, 2014 then blood transfusion was performed and the dose of progynova was increased to 16 mg daily. In addition, oxytocin and intrauterine balloon pipe were added in the treatment. As the cause of bleeding could not be determined from any coagulation disorder or observed from a scar site, we performed pelvic magnetic resonance imaging and uterus CTA and the results were normal. The bleeding gradually reduced and stopped on November 23, 2014. Transvaginal ultrasound was performed on December 3, 2014 and the results showed that the thickness of endometrial was about 6 mm and no obvious adnexal mass was observed.

DISCUSSION

Abnormal uterine bleeding in reproductive-aged women is a manifestation of a number of disorders or pathologic entities. In the clinical, women of reproductive age with heavy bleeding should be given immediate intervention to prevent further blood loss [2, 3]. The follow-up is largely dependent on whether they require investigation and ongoing care for some underlying diseases. Thus it is important to find the cause of bleeding.

The cause of abnormal uterine bleeding in reproductive-aged women may be organic or non-organic. Blood test, vaginal examination, endometrial curettage, ultrasound, and hysterogram are helpful in the diagnosis and differential diagnosis [4]. For cases not responding to conservative treatment, pelvic angiogram and magnetic resonance imaging scan, even hysteroscopy may be performed to detect the lesions in the uterus.

In our case, we performed the sequential steps of the differential diagnosis as described previously [1]. By physical examination, laboratory and imaging tests, the pregnancy, iatrogenic cause, systemic condition and genital tract pathology were excluded. Then we suspected a dysfunctional uterine bleeding [1]. However, haemostatic and hormones, even the curettage could not stop the heavy bleeding [5, 6]. The biopsy of endometrial showed secretory phase in accordance with the patient's menstrual cycle (the 21st day of menstrual cycle) (Figure 1). By bimanual examination, the uterus was found softer than normal, and the bleeding gradually stopped only after oxytocin and intrauterine balloon pipe treatment in addition to high doses of estrogen. Therefore, the cause of bleeding cannot be attributed to dysfunctional uterine bleeding. The unexplained uterine contractions fatigue and some unknown factors may be the causes of abnormal uterine bleeding in this case.

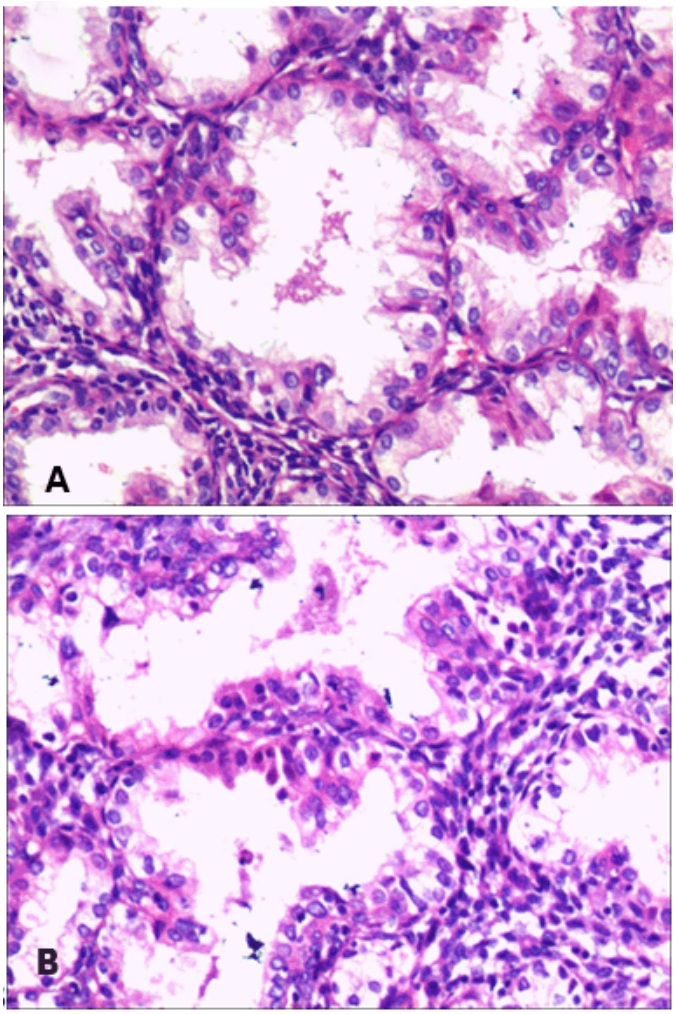

Figure 1: (A, B) Glandular epithelium showed apocrine change (H&E stain, x400).

CONCLUSION

Abnormal uterine bleeding is one of the most common reasons that reproductive-aged women seek health care. Medical history, physical examination, and laboratory

evaluation help the physician find the causes and give suitable therapy. In rare complicated cases, however, the causes cannot be identified which will lead to a delay in treatment and significant loss of blood.

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Author Contributions

Jianping Zheng – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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CASE REPORT PEER REVIEWED | OPEN ACCESS

Nodular fasciitis: A pseudomalignant clonal neoplasm characterized by USP gene rearrangements and spontaneous regression

Jennifer Hennebry, Douglas Mulholland, Nairi Tchrakian, Charles Martin Gillham, Peter Julian Beddy, Dearbhaile Mai O'Donnell, Máirín McMenamin

ABSTRACT

Introduction: Nodular fasciitis (NF) is a rapidly growing, self-limited, myofibroblastic neoplasm that typically arises in subcutaneous tissues of young adults and regresses spontaneously. Nodular fasciitis mimics sarcoma on clinical, radiological, and histological grounds and is usually, diagnosed following excision. Case Report: A 26-year-old female presented at surveillance computed tomography (CT) scan one year post-treatment for stage 1c ovarian dysgerminoma with a 4 cm axillary soft tissue mass, radiologically suspicious for metastasis with subclavian vein invasion. Histopathology of core biopsies favored NF, confirmed by detection of USP6 gene rearrangements by FISH analysis. This case describes an unusual relatively deep NF, suspicious for metastasis on CT scan with confirmed spontaneous regression over two years. Conclusion: Nodular fasciitis should be considered in the differential diagnosis of rapidly growing enhancing soft tissue masses. Molecular cytogenetic testing of USP6 gene rearrangements allows definitive diagnosis on core biopsies in challenging cases, permitting a conservative approach and avoiding potentially radical and unnecessary surgery.

Keywords: Nodular fasciitis, Intravascular fasciitis, resolution, USP6, FISH

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INTRODUCTION

Nodular fasciitis (NF) is a self-limited mass-forming myofibroblastic proliferation, which typically presents with sudden appearance and rapid growth and is generally less than 3 cm in size [1, 2], first described as 'pseudosarcomatous fibromatosis' in 1955 [3]. Nodular

fasciitis usually presents between second and fourth decade of life with no gender predilection. Recurrence is rare, unless excision is subtotal in the active growing phase [2]. Spontaneous involution has been described [1, 2, 4, 5] and is probably the natural course in NF. However, the majority are excised due to clinical concern for malignancy and histological difficulty in making a definitive diagnosis on core biopsy. A minority of cases (10–15%) are associated with recent prior trauma [1].

Typical sites of presentation include the upper limb, trunk, and head and neck. Nodular fasciitis is usually subcutaneous, but can be intramuscular or fascial based, can rarely arise in an intradermal or intra-articular location and can be entirely or partly intravascular [2].

Radiologic and histologic features can be highly variable [2, 6], and in the clinical setting of a rapidly growing mass, distinction from sarcoma can be difficult. Diagnosis is usually confirmed on an excision specimen. Histologic appearances can vary depending on the area sampled and the duration/phase of the lesion. Early lesions comprise a haphazard or short fascicular arrangement of cellular spindle cell proliferations with brisk mitotic rate. Lesions can show a feathery or loose discohesive appearance mimicking granulation tissue with microcysts. Red cell extravasation and scattered lymphocytes, macrophages and osteoclast-like giant cells are often present. Older lesions are more paucicellular with hyalinized collagen, scattered apoptotic cells and macrophages and may show central cystic degeneration [2]. Immunohistochemical staining profile is not specific [7]. Smooth muscle actin is positive but this does not distinguish it from other myofibroblastic lesions such as cellular scars, fibrous histiocytomas, desmoid-type fibromatosis or desmin negative leiomyosarcomas. CD34, desmin and cytokeratin are negative. Detection of USP6 gene rearrangement by fluorescence in situ hybridization (FISH) has emerged as a very helpful tool in confirming the diagnosis of NF [5, 8, 9] and is of particular use in cases where there is limited tissue for diagnosis, or when histological, radiological, or clinical appearances are atypical.

CASE REPORT

A 25-year-old female presented with a pelvic mass, which was surgically resected and diagnosed as a stage 1c ovarian dysgerminoma. The patient received adjuvant chemotherapy and a CT scan performed six months following treatment confirmed complete radiological remission. Four months post-chemotherapy, she developed bronchiolitis obliterans/organizing pneumonia as a complication of bleomycin chemotherapy. Following oral steroid therapy for several months, symptoms and radiological changes resolved and pulmonary function tests improved. Thirteen months post-chemotherapy, a CT scan showed a soft tissue mass, measuring 4x4x3 cm, deep to the pectoralis major muscle and abutting the chest wall without rib invasion. This was detectable on clinical examination as a sub-clavicular anterior chest wall asymmetry. Radiological impression was of confluent pathologic adenopathy with central necrosis representing metastases from the patient's prior ovarian dysgerminoma. A soft tissue sarcoma was in the differential diagnosis. Contrast enhanced MRI scan showed central necrosis or degeneration within the mass with close proximity to the right subclavian artery and vein (Figure 1) and features suspicious for subclavian vein invasion and thrombosis. PET-CT scan demonstrated intense tracer uptake within the mass with an SUV of 9.6. (Figure 2).

Ultrasound confirmed that the mass was partly intravascular. Core needle biopsy yielded a cellular spindle-cell proliferation with some short fascicles (Figure 3). Elsewhere there was a haphazard arrangement of cells with a loose discohesive feathery appearance with scattered chronic inflammatory cells (Figure 4). Cytonuclear atypia was not conspicuous and there was no necrosis. Mitoses numbered up to 3 per 10 40x fields (Figure 5).

Immunohistochemical stains showed that lesional spindle cells were positive for smooth muscle actin (SMA) (Figure 6) and negative for desmin, cytokeratin and S100. CD68 stained lesional macrophages. The MIB1 proliferative index was <10%. Histological features favored NF but sampling of a bland area of a sarcoma could not be excluded. Due to the worrying clinical presentation and the lack of definitive tissue diagnosis, an MRI scan was performed with a view to planning surgical excision. Repeat core needle biopsy again favored NF. Given the histologic appearances and the proximity to major vessels, a 'watch and wait' approach was adopted with repeat MR scans scheduled at three-monthly intervals. However, over the next three-week period, the patient developed swelling of the right arm with skin mottling, worrisome for vascular compromise. The case was referred to the London sarcoma service for advice on further management. The FISH analysis using custom-made break-apart BAC probes detected USP6 gene rearrangement, confirming the diagnosis of NF (Figure 7). The FISH was performed by Dr. Fernanda Amary's group at the Royal National Orthopedic Hospital NHS Trust. This news coincided with spontaneous improvement in clinical symptoms. In the two years following detection of the mass, it has undergone spontaneous and complete resolution on MRI and the patient remains symptom-free.

DISCUSSION

Nodular fasciitis (NF) is a self-limited myofibroblastic proliferation, which is usually subcutaneous in location and rarely presents as multiple lesions [10]. Due to its typical clinical presentation as a rapidly growing mass and its variable radiological and histological features, NF

can be misdiagnosed as a sarcoma [1, 2, 6]. In this case, a female with a history of treated ovarian dysgerminoma, a relatively deep-seated axillary NF was identified on surveillance imaging. Nodular fasciitis was in the active growing phase and showed concerning clinical and radiological features simulating metastatic tumor or sarcoma, including enhancement, central degeneration and vascular involvement.

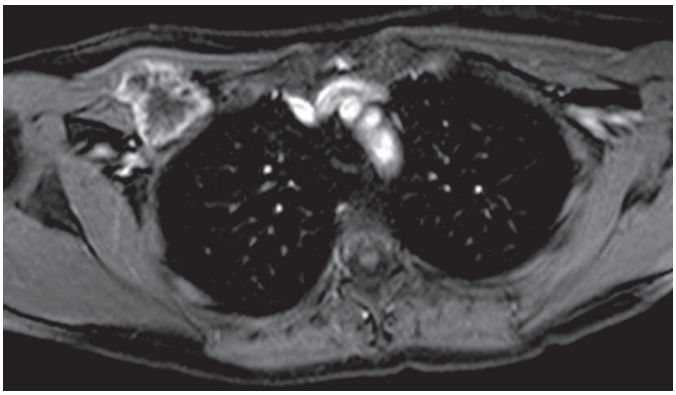

Figure 1: Axial post-contrast T1 fat suppressed MRI, demonstrating peripheral enhancement of a centrally necrotic mass in the right axilla in proximity to subclavian vessels.

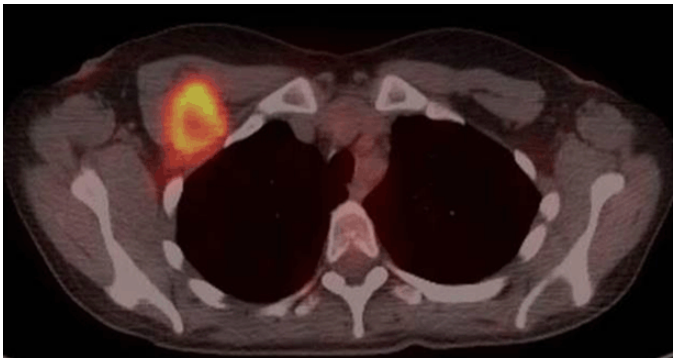

Figure 2: Axial PET-CT showing intense radio tracer uptake (SUV 9.6) within the mass.

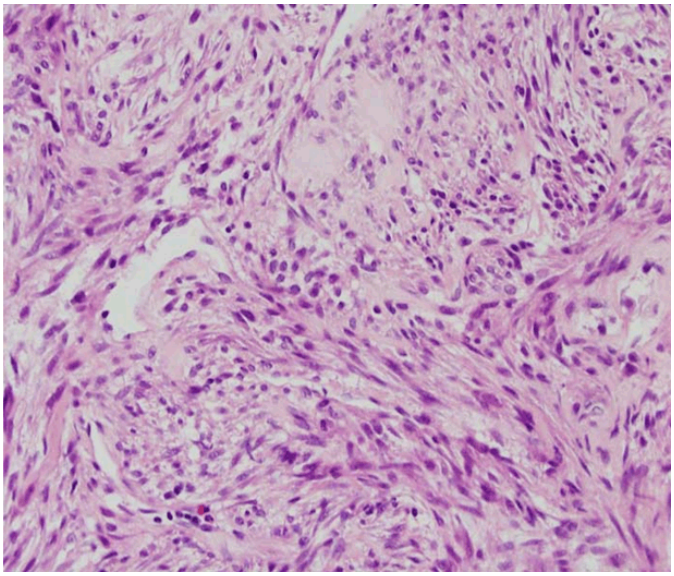

Figure 3: Core biopsy showing cellular spindle cell proliferation with short fascicular arrangement of cells (H&E stain, x100).

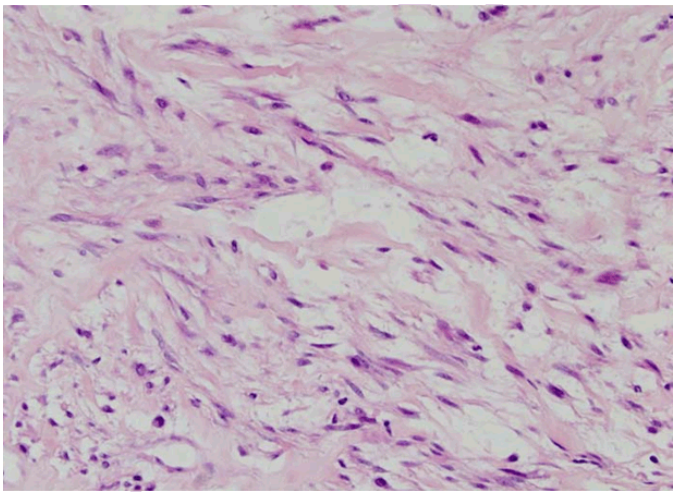

Figure 4: Bland spindle cells with haphazard discohesive feathery appearance (H&E stain, x100).

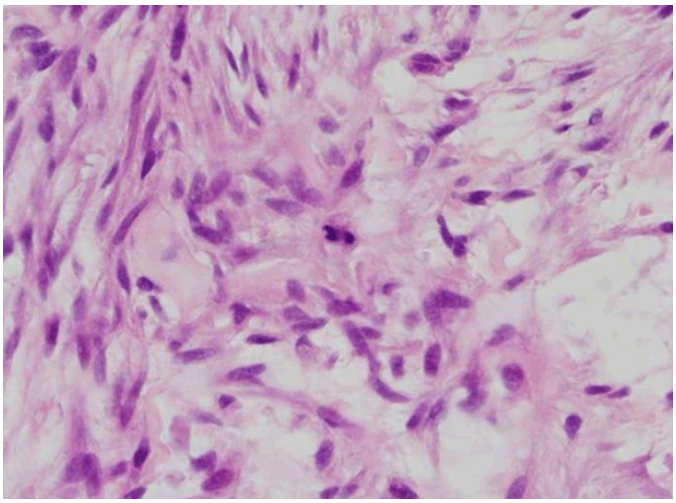

Figure 5: A mitotic figure is present in the center of the image (H&E stain, x200).

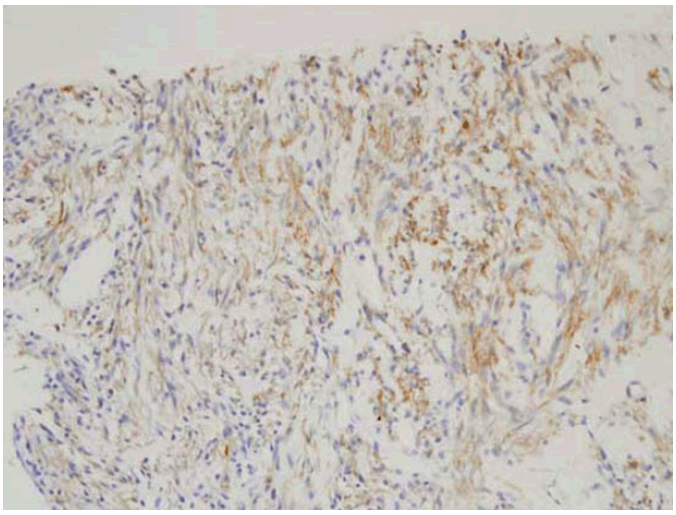

Figure 6: Lesional spindle cells are positive for smooth muscle actin immunostain [Cell Marque anti actin, smooth muscle (IA4)].

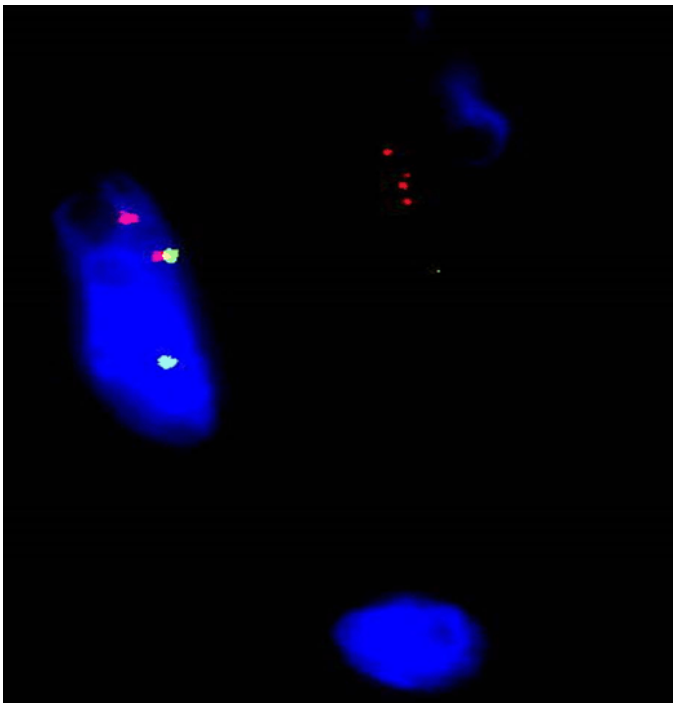

Figure 7: Rearrangements of USP6 gene (splitting of red and green signal) by fluorescence in situ hybridization using custom made break-apart probes. [Positive result: ≥15% cells harbored break-apart signal]. Image courtesy of Dr. Fernanda Amary, Histopathology Department, Royal National Orthopedic Hospital NHS Trust, UK.

The differential diagnosis of nodular fasciitis on MRI scan is broad, spanning benign and malignant lesions, including neurofibroma, extra-abdominal desmoid fibromatosis, fibrous histiocytoma, early myositis ossificans and sarcoma [6]. MRI scan imaging is helpful for defining the intrinsic signal characteristics, size and compartmental extensions of these lesions. Depending on the distribution of the myxoid or fibrous components, nodular fasciitis is usually isointense to skeletal muscle on T1 sequence and hyperintense to fat on T2 sequence. Lesions with predominantly cellular content or myxoid degeneration appear hyperintense on T2-weighted sequence and those with mostly collagenous contents appear hypointense [4, 6]. Contrast enhancement pattern is most commonly diffuse but it may also be peripheral in lesions with cystic degeneration, as in this case. Histological examination is essential for the diagnosis of NF as radiological appearances are not specific.

Nodular fasciitis is typically circumscribed, but may display an infiltrative growth pattern, especially those that are fascial based [2]. The cut surface of a macroscopic lesion varies from myxoid to fibrous, sometimes with central cystic change [1]. The lesion is typically composed of spindled fibroblast-like cells with a haphazard, 'tissue culture'-type architecture resembling granulation tissue with cellular areas and looser areas and scattered inflammatory cells [2]. Cellular areas can show a fascicular arrangement of cells. The looser areas have a discohesive arrangement of cells with a feathery appearance and can show microcystic change. Mitotic figures are usually readily identified, but atypical forms are not generally present. Other microscopic features of NF include extravasated red blood cells and osteoclast-like giant cells [2] but they were not seen in this case. Older lesions show more hyalinized collagen. It is easier to make a histological diagnosis on an excision specimen as the architectural pattern is evident. It can be difficult to make a definitive diagnosis on core biopsy, when limited features are available. Immunohistochemistry is not specific— smooth muscle actin and muscle-specific actin are typically positive, supporting a myofibroblastic phenotype [2, 7]. CD68 stains lesional macrophages, osteoclast-like giant cells and occasionally weakly stains the spindle cells [1].

Until recently, no specific or consistent cytogenetic abnormality was observed in NF and diagnosis was based on histological features. Furthermore, due to its rapid growth, low risk of recurrence, spontaneous resolution and the fact that it has not been associated with malignant transformation, NF has traditionally been considered reactive in nature. In 2011, Erickson-Johnson et al. reported genomic rearrangements of the USP6 locus on chromosome 17 in 92% of NF, the majority of which resulted in the formation of the fusion gene MYH9-USP6 [8] and have proposed that the identification of a recurrent somatic fusion gene event in NF is supportive of a clonal transient neoplasm. This suggestion challenges the traditional paradigm that nonrandom fusion gene formation is associated solely with sustained autonomous neoplasms. This molecular diagnostic approach is a tremendous advance in the diagnosis of NF [5, 8, 9]. Spontaneous resolution is likely by cellular apoptosis but to date the mechanism has not been elucidated.

Opinions have varied on the optimal treatment of NF. Most have advocated for simple excision [2]. Following a confirmed biopsy diagnosis, a conservative 'watch and wait' approach with repeat imaging and anticipated spontaneous involution is preferable particularly in surgically challenging sites [4, 5]. The FISH is cost effective, especially if challenging surgery can be avoided. The price of USP FISH can be obtained from referral centers. Current price is approximately 300 GBP.

CONCLUSION

We present an unusual nodular fasciitis (NF) in a young woman that was discovered on follow-up for previous ovarian dysgerminoma. As the NF was in the active growing phase, clinical and radiological features were suspicious for malignancy with progressive subclavian vein involvement and compromise. The suspected histopathological diagnosis of NF was confirmed by detection of USP6 gene rearrangements and permitted a conservative approach, sparing this patient unnecessary surgery and potential morbidity. There was spontaneous resolution over two years, confirmed radiologically.

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Author Contributions
Jennifer Hennebry – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of version to be published
Douglas Mulholland – Acquisition of data, interpretation of data, Drafting the article, Final approval of version to be published
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Dearbhaile Mai O'Donnell – Substantial contribution to conception and design, acquisition of data, Revising it critically for important intellectual content, Final approval of version to be published
Máirín Eibhlín McMenamin – Substantial contribution to conception and design, acquisition of data, Revising it critically for important intellectual content, Final approval of version to be published

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Authors declare no conflict of interest.

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CLINICAL IMAGES PEER REVIEWED | OPEN ACCESS

Inferior vena cava agenesis with exuberant collateral circulation

Ana Vaz Cristino, Renata Silva, Carmen Pais, José Presa

CASE REPORT

We present a case of 55-year-old female with a history of past alcohol consumption (75 g/day for ten years), with no other relevant medical history, who was referred to our hepatology unit. She presented with leukopenia and thrombocytopenia, normal mean corpuscular volume, mildly elevated total bilirubin (1.8 mg/dL), alkaline phosphatase (192 U/L) and gamma-glutamyl transferase (127 U/L), with normal aminotransferases, albumin and coagulation. Physical examination revealed exuberant collateral circulation of the abdominal wall (Figure 1). The esophagoduodenoscopy revealed grade III esophageal varices, and the abdominal ultrasonography showed hypertrophy of the caudate lobe and heterogeneous echotexture, and splenomegaly with collateral circulation of the splenic hilum. The autoimmune study, hepatitis serologies and iron studies were normal, and the transient elastography was 48 Kpa, consistent with liver cirrhosis. A computed tomography (CT) scan of the abdomen (Figure 2A) revealed exuberant retrocrural collateral circulation, with varices in the azygos and hemiazygos systems, hepatorenal and splenorenal spaces, with lack of permeability in the inferior vena cava, between the renal and the suprahepatic veins. The magnetic resonance angiography (Figure 2B) confirmed inferior vena cava agenesis.

Due to beta-blocker intolerance, the esophageal varices were obliterated with endoscopic variceal ligation. She remains in follow-up after three years.

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DISCUSSION

In this case, a history of alcohol consumption had been assumed as cause for liver cirrhosis and evidence of portal hypertension. The exuberance of collateral circulation prompted further image studies, with the diagnosis of inferior vena cava agenesis [1, 2].

Although considered a rare condition, the number of diagnosed cases is increasing, and it is thought that this condition may be underdiagnosed, mainly because most patients are asymptomatic [3].

The best methods for imagiological evaluation are computed tomography scan and magnetic resonance angiography [4].

These individuals generally develop extensive collateral circulation, and it is associated with diverse manifestations, such as deep venous thrombosis [2], lumbosacral radiculopathy and myelopathy due to

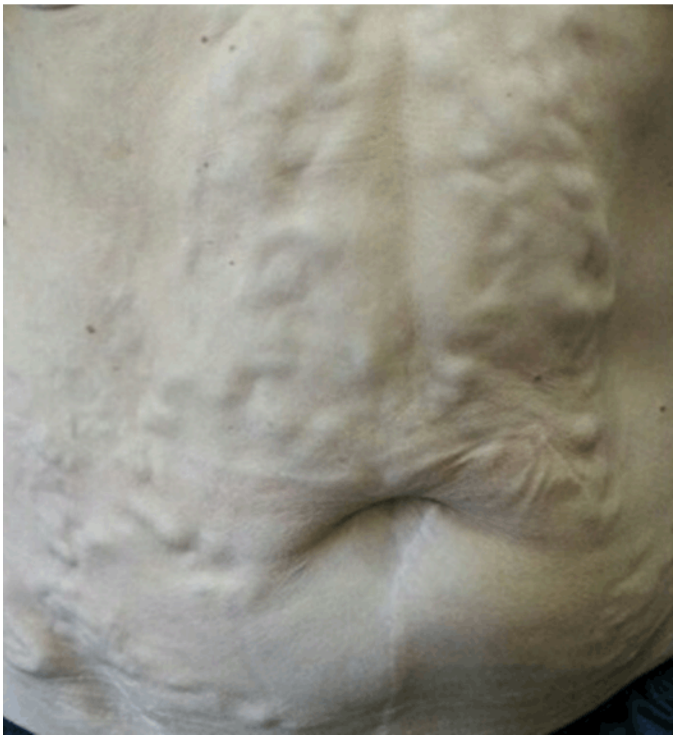

Figure 1: Abdominal wall with exuberant collateral circulation.

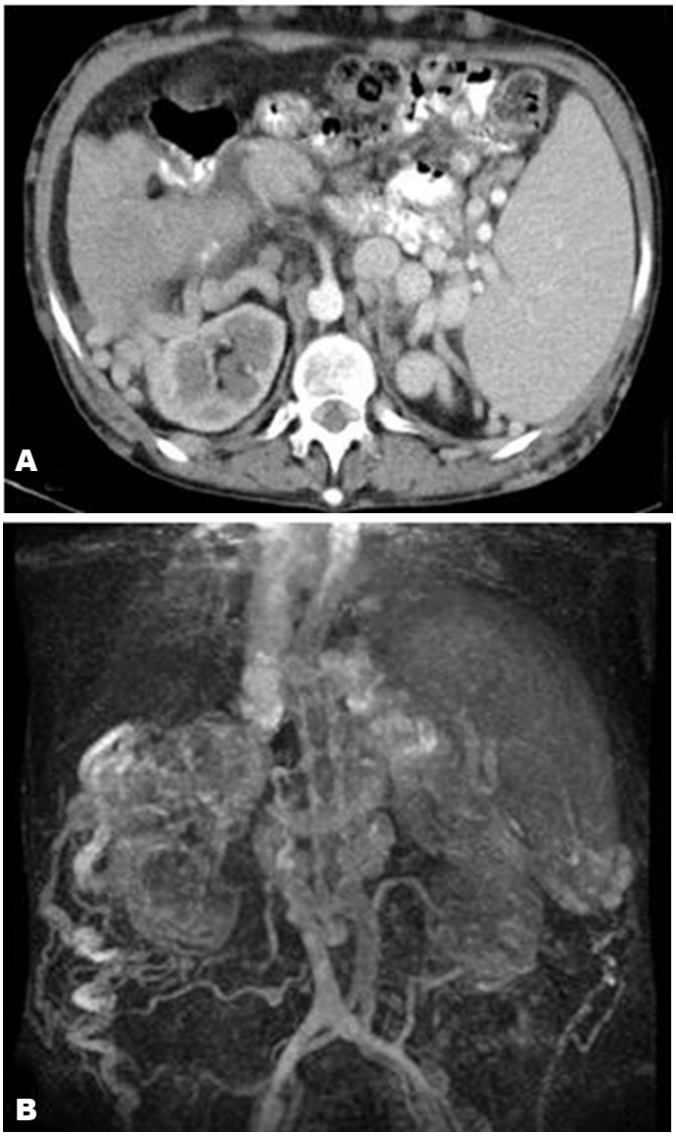

Figure 2 (A, B): Contrast computed tomography scan showing exuberant retrocrural collateral circulation and varices, and abdominal magnetic resonance imaging scan confirming inferior vena cava agenesis.

venous congestion [5], congenital heart disease, splenic abnormalities and liver disease due to inadequate portal flow, with portal hypertension, development of nodal nodular hyperplasia and hepatic tumors. Portal hypertension and hepatic encephalopathy are uncommon before adulthood [4].

The management of inferior vena cava agenesis depends on the anatomical alterations and clinical manifestations of the disease, in a case-by-case basis [4]. High thrombotic risk and presence of liver tumors are important factors to have in mind in patients with this condition.

CONCLUSION

Inferior vena cava agenesis is a rare condition, but recent evidence shows that it may be underdiagnosed, and can be simply detected with current image methods. Diagnosing inferior vena cava has potential implications on patient management, but it can be challenging due to lack of symptoms.

Keywords: Collateral circulation, Inferior vena cava agenesis

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Ana Vaz Cristino – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Renata Silva – Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Carmen Pais – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
José Presa – Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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CLINICAL IMAGES PEER REVIEWED | OPEN ACCESS

Visible effect of immunomodulatory drugs on rib tumor in multiple myeloma

Kenji Shinohara

CASE REPORT

A 76-years-old female was diagnosed with multiple myeloma, immunoglobulin G (Ig-G), λ type. There was not involvement of the rib at the time of initial presentation. She was initially treated with bortezomib, 1.3 mg/m^2 once weekly, for five months, with the effect of lowering IgG. However, it was stopped due to peripheral neuropathy. Anemia, bone pain including pain at the rib tumor (Figure 1), renal impairment, and an increase in IgG appeared nine months later (Table 1). She was treated with lenalidomide and dexamethasone (DXA) for two weeks, which were stopped due to skin eruption, and subsequently with pomalidomide and DXA for two months, and a visible therapeutic effect of a tumor size decrease (Figure 2), as well as markedly lowering IgG and bone marrow plasma cells (Table 1), were observed.

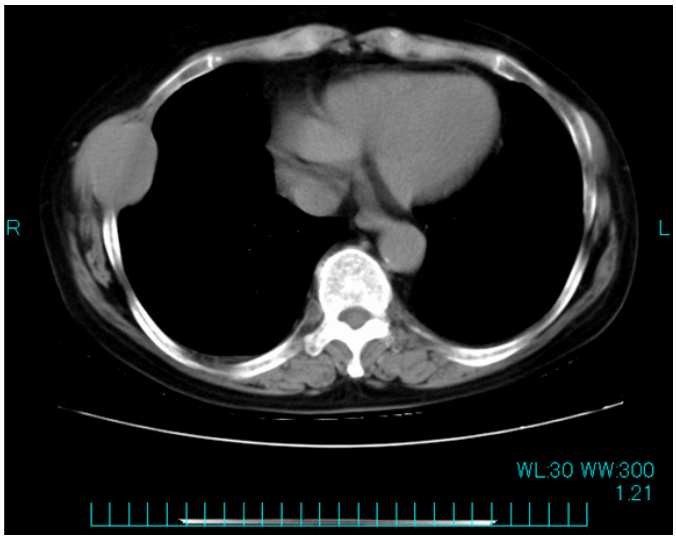

Figure 1: A rib tumor, 5.9x4.1 cm, demonstrated by computed tomography scan.

DISCUSSION

Plasmacytoma of the rib is observed as solitary or a tumor after progression of multiple myeloma. It was hitherto treated with surgical resection, radiation, systemic chemotherapy before or after surgical resection including alkylating agents, anthracyclines, vinca alkaloids, steroids, and bone marrow transplantation [1–3]. In last decade, the treatment of multiple myeloma has greatly improved by the introduction of novel agents, including proteasome inhibitors (PI) and immunomodulatory drugs (IMiDs) [4]. In the present

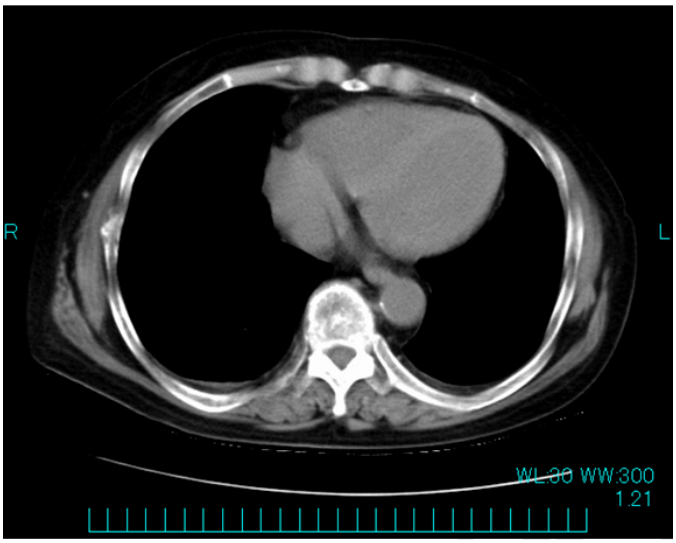

Figure 2: The rib tumor disappeared, almost 0 cm, after the administration of immunomodulatory drugs (IMiDs), including lenalidomide and subsequently pomalidomide with dexamethasone.

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Table 1: Laboratory data before and after administration of immunomodulatory drugs

	Before	After
Total protein (g/dl)	10. 4	6.0
Alb (g/dl)	2.2	3.4
Glb (g/dl)	8.2	2.6
γ-Glb (%)	53.2	
IgG (mg/dl)	6355	1138
Bone Marrow		
Plasma Cell (%)	50	10
BM FCM		
CD38 (%)	41	
CD 38 gating		
cy k-ch (%)	85.3	
CD 33 (%)	9.5	
CD 45 (%)	41.2	
CD 49e (%)	10.0	
CD 54 (%)	94.6	
CD 56 (%)	97.3	
CD 138 (%)	17.1	
MPC-1 (%)	10.1	

patient remarkable effect on rib tumor was observed after administration of IMiDs. These novel treatments should be tried before surgical resection.

CONCLUSION

A visible effect on a rib tumor in multiple myeloma was observed on administration of the recently developed immunomodulatory drugs.

Keywords: Immunomodulatory drugs (IMiDs), Multiple myeloma, Rib tumor

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Author Contributions

Kenji Shinohara – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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