

Clinical and Occasional Notes

TORULA HISTOLYTICA MENINGO-ENCEPHALITIS*

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Summaries of the knowledge concerning infections in man caused by *Torula histolytica* have been made from time to time since Stoddard and Cutler's¹ monograph was published; the most recent reports are those by Shapiro and Neal,² and by Rappaport and Kaplan.³ In 1925, Shapiro and Neal, mentioned thirteen reports then recorded. They added another case and included a personal communication from Sheppe, thus making the total number of reported cases at that time fifteen, of which thirteen were infections of the central nervous system, one of the lungs and one of the muscles of the back. Rappaport and Kaplan reported a systemic torulosis and McKendree and Cornwall⁴ in the same year reported an infection of the brain and meninges. An account by Hansmann⁵ in 1924 of a case of meningitis and encephalitis caused by *Torula* is not mentioned by these investigators. Lynch and Rose⁶ reported another case of *Torula* meningitis, and McGehee and Michelson⁷ reported the case of a negress with a left inguinal abscess which contained *Torula histolytica*.

The purpose in this account is to record another case of *Torula* infection of the brain and meninges, with a statement of the clinical symptoms, the bacteriologic observations and the results of the postmortem examination. *Torula histolytica*, according to the present classification, is a yeastlike organism which reproduces by budding in tissues and in cultures, but which differs from the true yeasts by not fermenting sugars.

REPORT OF CASE

G. S., a white man, aged 33, married, entered St. Luke's Hospital, Chicago, on Nov. 4, 1926, complaining of severe headache of three weeks' duration,

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1. Stoddard, J. L., and Cutler, E. C.: Monograph of Rockefeller Institute for Medical Research, Jan. 31, 1916, no. 6.

2. Shapiro, L. L., and Neal, J. B.: *Torula* Meningitis, Arch. Neurol. & Psychiat. **13**:174 (May 23) 1925.

3. Rappaport, B. Z., and Kaplan, Bertha: Generalized *Torula* Mycosis, Arch. Path. **1**:720 (April) 1926.

4. McKendree, C. A., and Cornwall, L. H.: Meningo-Encephalitis Due to *Torula*, Arch. Neurol. & Psychiat. **16**:167 (Aug.) 1926.

5. Hansmann, G. H.: *Torula* Infection in Man, Boston M. & S. J. **190**:917 (May) 1924.

6. Lynch, F. B., and Rose, E.: *Torula* Meningitis, Ann. Clin. Med. **4**:755 (March) 1926.

7. McGehee, J., and Michelson, T.: *Torula* Infection in Man, Surg. Gynec. Obst. **42**:803 (June) 1926.

tingling of the fingers for the same length of time and pain behind the eyes for twenty-four hours. He had consulted a physician just before the onset of the headache because of pain in the left arm and shoulder. He had received four injections of serum, and on the day following the last injection he complained of headache. This, he said, was constant and it seemed as though the head was compressed in a vise. He was unable to sleep because of the headache, except when relieved by acetyl salicylic acid or tablets for migraine. He had some difficulty in walking and vomited once. The personal and family histories did not contain anything noteworthy. As a child he had had measles. He used tobacco moderately, alcohol very seldom and he usually drank three or four cups of coffee daily. For the past few years, his time had been spent as a boy scout leader.

Clinical Findings.—The results of an examination of the eyes, by Dr. E. K. Findley, on Nov. 6, 1926, were reported as follows: "The pupils are moderately dilated, both optic disks are slightly edematous, and the vessels around them are tortuous. The edema of the optic disks is greater on the right side and measures about 1 diopter. It is not possible to determine whether there is a toxic neuritis or a slight papilledema from intracranial pressure." On this day, the patient complained of a sensation of pressure behind the right eye and a generalized headache. Diplopia, other cranial nerve paralyses, nystagmus, ataxia and paralysis of the upper extremities were not present. The results of tests for various reflexes were as follows: abdominal reflex, sluggish; left knee jerk, slight; achilles' reflex, active on both sides; Babinski and Oppenheim signs, absent; ankle clonus, absent; Kernig sign, on both sides doubtful.

On Nov. 7, 1926, there were: pain over the left eye; increased papilledema on both sides, that of the right disk measuring 2 diopters, that of the left less than 1; bilateral Kernig sign; soreness of the muscles of the neck, with anterior flexion. The leukocytes of the blood numbered 14,040 per cubic millimeter. A culture of the blood did not contain bacteria. On November 8, the edema of both optic disks had increased, and on November 9, there was choked disk on the right and a beginning choked disk on the left. The leukocyte count was 9,640; the blood pressure was systolic 118, diastolic 70; the temperature was 97.6 F.; the pulse rate 56 per minute, and rate of respiration 18. An exudate was expressed from each tonsil. Transillumination of the ethmoidal and maxillary sinuses, by Dr. L. Thompson, did not disclose any changes. Examination of the frontal sinuses was unsatisfactory.

Diagnosis.—An abscess of the brain, some form of meningitis, and possibly a brain tumor were considered as a clinical diagnosis. Because of the rapidly developing papilledema in the optic disks, decompression of the brain was regarded as a safer procedure than drainage by spinal puncture.

Operation.—On November 9, a right subtemporal decompression of the brain was made. When the dura was opened, a large quantity of cerebrospinal fluid escaped. No tumor or abscess was found by probing the brain with a dull needle.

Course.—November 10, there was ptosis of the right eyelid, and both optic disks were edematous. The next day there were: jacksonian twitching of the right arm, face, and leg; paresis of the left side of the body, and a positive Babinski sign on the left side. By this time, cultures of the cerebrospinal fluid, removed during the decompression operation, revealed opaque white colonies containing yeast organisms and the diagnosis of *Torula meningitis* was made.

The spinal fluid pressure, on November 12, was 300 mm.; on November 13, it was 340 mm. and after withdrawal of about 30 cc., the pressure fell to 120 mm. The patient became irrational on November 14; the face and chest were cyanotic and breathing was stertorous. The right arm and leg were in constant motion. The temperature rose to 103.6 F., and death occurred in the evening of Nov. 14, 1926.

Autopsy.—The postmortem examination was made on the morning of Nov. 15, 1926. The tissues of the trunk, head, and spinal canal were examined.

Anatomic Diagnosis.—The diagnosis was: acute *Torula* meningitis, marked edema of the cerebrum and of the meninges, multiple subpial hemorrhages of the brain, marked hyperemia of the leptomeninges of the brain and spinal cord,

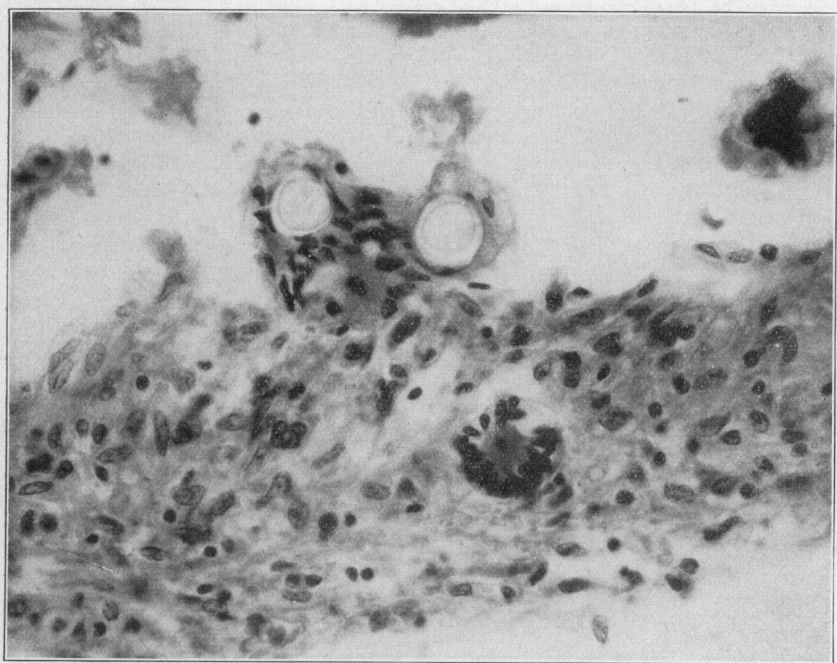


Fig. 1.—The tissue of the left gasserian ganglion containing torula organisms; \times 375.

acute internal hydrocephalus, acute bilateral bronchopneumonia, bilateral fibrinous pleuritis, purulent tracheitis and bronchitis, recent unhealed trephine wound of the cranium, recent right subtemporal decompression wound, marked herniation of the cerebrum through the trephine hole of the cranium, passive hyperemia of the lungs and kidneys, cloudy swelling of the myocardium and parenchymatous organs, hyperplasia of the biliary and peribronchial lymph nodes, fatty changes of the liver, etc.

The brain (unfixed) with the top half of the dura weighed 1,460 Gm. There was marked distention of the leptomeninges by a faintly turbid, limpid and colorless fluid. In the pia-arachnoid were scattered thin, gray opacities from 2 to 3 mm. in diameter. Under the pia-arachnoid, in the brain substance,

were scattered hemorrhages, 1 cm. in their greatest diameter.⁸ Gross changes in the middle ears, the sinuses of the dura and the cranium or in the gasserian ganglia were not noted.

Histologic Examination.—Sections from different parts of both lungs, chiefly the consolidated portions, contained regions of bronchopneumonia. Careful examination of many sections revealed no yeastlike structures. The dilated sinusoids of the lymph nodes in the hilum of each lung and the regional tissues contained masses of large mononuclear cells and leukocytes, but no yeastlike organisms. Other lymph nodes were without noteworthy changes. In the spleen were large recent hemorrhages and hyperplasia of the reticular cells. Slight fatty changes and passive hyperemia were the only changes of note

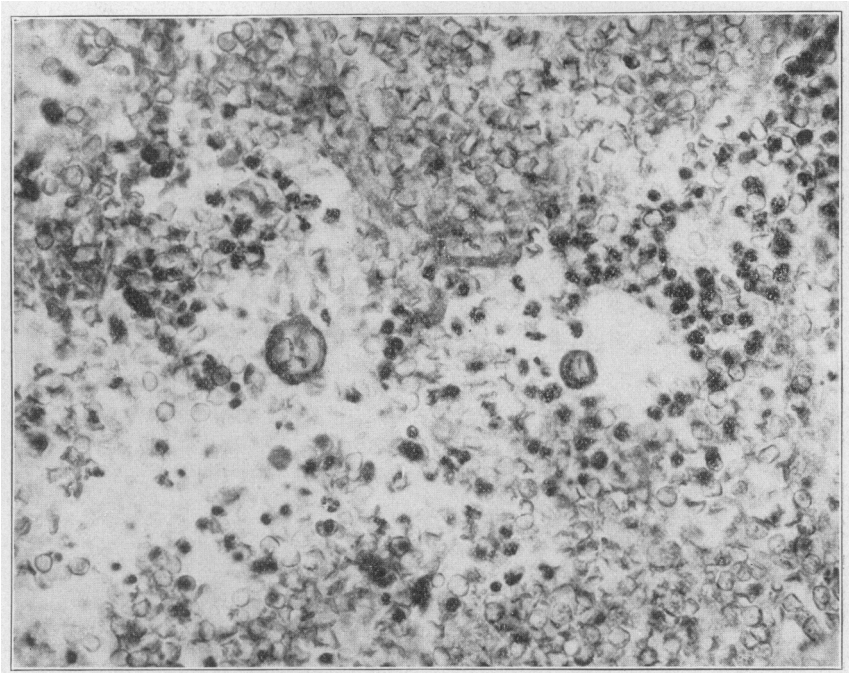


Fig. 2.—The torula organisms in traumatized brain tissue removed during the decompression operation; $\times 375$.

in the liver. Tissues from the kidneys, aorta, urinary bladder, gallbladder, prostate, seminal vesicles, testes, vasa deferentia, suprarenal glands, and muscle of the heart were without noteworthy alterations.

Sections from each gasserian ganglion contained ganglion cells and nerve fibers, between which were ingrown bands of a loose fibrous connective tissue with many lymphocytes, practically no polymorphonuclear leukocytes, and with many yeastlike inclusions that varied in size between 10 and 19 microns. These organisms had been present sufficiently long to stimulate the fibrous and chronic granulation tissue reaction. Foreign-body giant cells occurred in the left gasserian ganglion. The hypophysis did not present any noteworthy changes, but in the adherent meninges were small masses of chronic granulation tissue containing yeastlike organisms.

8. A complete study of the brain and spinal cord is being made.

Bacteriologic Results.—Cultures of the cerebrospinal fluid taken during the decompression operation on Nov. 9, 1926, presented, after seventy-two hours in the aerobic containers, a heavy growth of round, slightly friable, cream-white, raised colonies with sharp edges. These, in stained preparations, were composed of yeast cells. Stains of the spinal fluid demonstrated the presence of yeast organisms. Cultures were made of the spinal fluid removed on Nov. 13, 1926, and twice on Nov. 14, 1926; they were examined in the same way, with identical results. A culture from the nose and throat made on Nov. 13, 1926, did not contain *Torula* organisms, nor were there organisms in cultures of the blood made on November 8 and 9. On March 20, 1927, cultures were made of spinal fluid removed on Nov. 14, 1926, and kept in the icebox; an abundant growth of *Torula* organisms was obtained.

Cultures of the fluids and tissues obtained at the postmortem examination were made with the following results: left lung, *Torula* not isolated; right lung, *Torula* not isolated; tracheal exudate, *Torula* not isolated; pericardial fluid, sterile; heart blood, pure culture of *Torula*; spleen, pure culture of *Torula*; spinal fluid, *Torula* isolated with *Streptococcus salivarius*.

Histologic examination of a small piece of tissue from the brain removed during the decompression operation contained torn substance of the cerebral

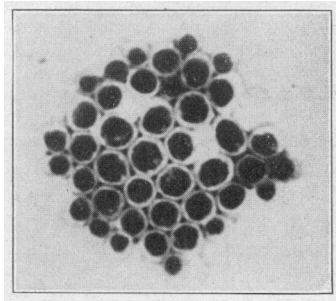


Fig. 3.—The torula organisms in cultures; $\times 1200$.

cortex in which were yeastlike structures. Three strains of *Torula histolytica* obtained from: (1) spinal fluid during life, (2) heart blood (postmortem), and (3) spinal fluid (postmortem) did not ferment lactose, mannite, raffinose, salicin, levulose, maltose, xylose or adenite. Acid was formed slowly by the growth of these strains in dextrose and saccharose mediums.

COMMENT

Although reports of patients with *Torula* meningitis are relatively few, persistent severe headache is mentioned as a symptom in many of the accounts. Türk's⁹ patient complained of severe headache and vomiting and had symptoms at first considered to be due to tuberculous meningitis. Evans,¹⁰ Freeman and Weidmann,¹¹ Bettin,¹² Hansmann,⁵ Shapiro and Neal,² McKendree and

9. Türk, Wilhelm: Deutsches Arch. f. klin. Med. **90**:335, 1907.

10. Evans, Newton: *Torula* Infection, California State J. Med. **20**:383 (Nov.) 1922.

11. Freeman, W., and Weidmann, F.: Cystic Blastomycosis of Cerebral Gray Matter Caused by *Torula Histolytica*, Arch. Neurol. & Psychiat. **9**:589 (May) 1923.

12. Bettin, Mona E.: *Torula* Infection, California & West. Med. **22**:98 (March 3) 1924.

Cornwall,⁴ Rappaport and Kaplan,³ and Lynch and Rose¹¹ mentioned this symptom in their reports. Other symptoms mentioned in these accounts include disturbances in vision, dizziness, ptosis of the eyelids and stiffness of the neck. All of these symptoms accompany meningitis, but, because of their chronicity and insidious onset, they resemble those caused by a tumor of the brain. The diagnosis of *Torula histolytica* meningitis is established by demonstrating *Torula* organisms in the spinal fluid.

How the organisms reach the meninges has not been determined. In the lungs of our patient, regions of chronic infection could not be considered the primary focus, and in microscopic preparations of these tissues, as well as in cultures, *Torula* organisms were not found. It seems, therefore, that the infection of the meninges in our patient came through the nasopharynx.

FRACTURE INTO THE FRONTAL SINUSES WITH DISCHARGE OF CEREBROSPINAL FLUID FOR OVER A YEAR

Report of a Case with Death from Pneumococcus Meningitis

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Spontaneous discharge of cerebrospinal fluid through the nose without traumatic cause has been reported frequently.¹ An altogether different group comprises those cases of persistent flow of cerebrospinal fluid following fractures or operative procedures on the skull. In view of the frequency of fractures of the base of the skull and of the common textbook formula that cerebrospinal fluid may escape through such fractures, it seems remarkable that its occurrence is mentioned so infrequently in the copious literature on this subject describing specific cases. No doubt in many cases of fracture with a discharge of cerebrospinal fluid, the blood or secretions concealed it until death, or healing of the dural opening occurred promptly. Rawling,² in his Hunterian lecture on basal fractures of the skull, stated that in his cases 70 per cent of these fractures involved the sphenoidal sinus, and in many of these a probe could be passed through the nose into the cranial cavity. He also discussed in detail the various complications of fractures into the frontal sinuses and petrous bone, yet he referred to the outflow of the cerebrospinal fluid as a rare occurrence. In that lecture he stated that in 1840, Blaudin was the first to describe a case of flow of the subarachnoid fluid from the nose after a fracture. He refers to Goucard's and Malgaigne's cases of flow through the eustachian tube after fracture into the middle ear; also to the early case

1. Thomson, St. C.: Nasal Hydrorrhea, *J. Laryngol.* **13**:500, 1898. Glynn, T. R., and Glynn, E. E.: A Case Simulating Intracranial Tumour in Which Recovery was Associated with Persistent Cerebrospinal Rhinorrhea, *Brit. M. J.* **1**:871, 1905. McDougall, J. E.: Case of Idiopathic Cerebrospinal Rhinorrhea, *Liverpool M. Chir. J.* **30**:391, 1910. Locke, C. E., Jr.: Spontaneous Escape of Cerebrospinal Fluid Through the Nose; Its Occurrence with Brain Tumor, *Arch. Neurol. & Psychiat.* **15**:309 (March) 1926.

2. Rawling, L. B.: On Fracture of the Skull, *Lancet* **1**:973, 1034 and 1097, 1904.