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Iron deficiency anemia in monoclonal gammopathy of undetermined significance

Kenji Shinohara

ABSTRACT

Introduction: Anemia in plasma cell in multiple myeloma (MM) is found in 60–90 % of the patients, and is usually noromocytic and normochromic. Rarely, iron deficiency anemia (IDA) occurs with microcytic and hypochromic red blood cells, however the pathogenesis remains unknown. Case Report: A 75-year-old male with monoclonal gammopathy of undetermined significance (MGUS) had iron deficiency anemia (IDA) with microcytic and hypochromic red blood cells. The serum levels of erythropoietin (EPO), interleukin-6(IL-6) and hepcidin-25 were normal. The administration of oral iron ameliorated IDA. Conclusion: The cause of IDA in the present patient was unknown. The administration of oral iron improved IDA.

Keywords: Hepcidin, Iron deficiency anemia, Monoclonal gammopathy

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INTRODUCTION

Anemia in plasma cell neoplasma, multiple myeloma (MM) and macroglobulinemia, is found in 60-90 % of the patients, and is usually noromocytic and normochromic [1, 2]. Several causes of anemia have been implicated; anemia of chronic disorder (ACD) with inadequate production of red blood cells due to either erythropoietin (EPO) deficiency from accompanying renal failure, pronounced marrow replacement by myeloma cells or cytokine-mediated marrow suppression [1, 2].

Rarely, iron deficiency anemia (IDA) with microcytic and hypochromic red blood cells was observed. However, the pathogenesis remains unknown [3–5].

We report a case of iron deficiency anemia in monoclonal gammopathy of undetermined significance (MGUS), a part of the patients ultimately progress to MM and macroglobulinemia, and the study of pathogenesis and treatment of IDA.

CASE REPORT

A 75-year-old male was diagnosed with monoclonal gammopathy of undetermined significance (MGUS) in Sep. 2013. The laboratory data is presented in Table 1. The serum level of immunoglobulin(Ig)G was increased, and was monoclonal (Figure 1). The bone marrow aspirate smear from iliac bone demonstrated increase of atypical plasma cells to 8% (Figure 2). The patient was diagnosed with monoclonal gammopathy of undetermined significance (MGUS). He was followed up at the out-patient clinic without treatment and no change of clinical manifestation was observed.

Table 1: Laboratory data of the patient

Status	A	B	C
Complete blood count			
Red blood cells(x10^{12}/l, 4.0–5.0)	3,92	3,56	3,94
Hb(g/dl,12.0–18.0)	12.2	9.1	12.1
Ht(%, 37.0–55.0)	37.1	29.9	37.1
MCV(fl,84–100)	95	84	94
MCH(pg, 28–35)	31	26	31
MCHC(% 33–36)	33	30	33
White blood cells (x10^{9}/l, 4.0–7.0)	5,1	4,0	4,5
Platelets (x10^{9}/l, 100–320)	269	283	285
Iron status			
Seum iron (µg/dl, 80–199)	87	27	63
Ferritin (ng/ml, 38–465)	100	11	66
UIBC (µg/dl, 81–351)		359	193
TIBC (µg/dl, 237–458)		332	256
Hepcidin-25 (ng/ml, 7.8±7.0)		3	
Epo (mIU/mL, 4.2–23.7)		24.3	
IL-6 (pg/mL,<4.0)		2.4	
Chemistry			
Total protein (g/dl, 6.8–8.0)	8.3	7.9	
Albumin (g/dl, 3.8–5.1)	4.4	3.9	
γ– Globulin (%, 10.9–21.7)	25.5	26.5	
IgG (mg/d, 870–1700)	2399	2247	
Bone marrow			
Plasma cells (%)	8		

A: diagnosis of MGUS, B: IDA, C: Amelioration of IDA. ( ): unit, normal range

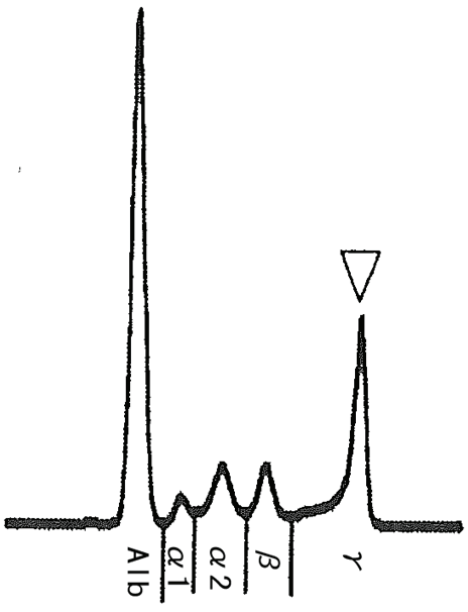

Figure 1: Monoclonal increase of γ-globulin in serum indicated by arrow.

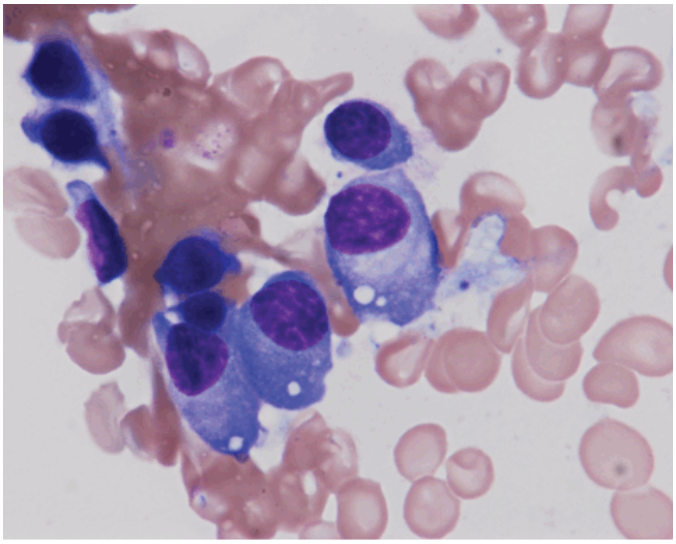

Figure 2: A cluster of atypical large plasma cells in the bone marrow aspiration smear (x100).

The patient complained of exertional palpitation and the hematological examination demonstrated microcytic and hypochromic anemia, with low values of mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) of red blood cells, in March 2017. Serum levels of iron and ferritin were decreased, and those of unsaturated iron binding capacity (UIBC) and total iron binding capacity (TIBC) were increased. The patient was diagnosed with iron deficiency anemia (IDA). Serum IgG level was unchanged.

Endoscopic examination of the upper gastrointestinal tract (GI) and colon did not reveal any pathological lesions. The examination of helicobactor pylori by urea breath test (UBT) was negative. The serum concentrations of erythropoietin (EPO) and interleukin-6(IL-6) were not significantly increased. The serum level of hepcidin-25 was measured by liquid chromatography and mass spectrometry, and it was found to be normal.

Administration of oral iron agent, sodium ferrous citrate, 100mg/day, was started. The progressive increase of hemoglobin and amelioration of symptom of anemia were observed after three months.

The clinical course of MGUS was unchanged.

DISCUSSION

Iron is essential for erythropoiesis and immune system, as well as is a crucial element for many pathogens. Upregulation of hepcidin in coordination with ferroportin, hepcidin-ferroportin axis, which impairs the absorption of iron from the intestine and the release of stored iron in the reticuloendothelial cells into circulation, causes anemia of inflammation (AI) or anemia of chronic disorder (ACD) [6]. In the present patient, the serum levels of EPO and the inflammatory cytokine, IL-6, were

found to be normal. The serum levels of hepcidin-25 are elevated in iron overload, inflammation, bone marrow suppression, and are usually low in normal, and iron deficiency [6].

In Mayo clinic review of more than 1,000 patients with multiple myeloma, 1% had MCV of lower than 80fl; and some of these patients had a low serum iron value [2].

Increased serum concentrations of hepcidin-25 and IL-6 with low levels of hemoglobin and iron, and increased ferritin, TIBC and transferrin, were observed in the patients of multiple myeloma [7].

Gastric Helicobacter pylori infection is a common cause of IDA of unknown origin in adult patients. It was negative in the present patient.

The treatment of IDA is administration of oral or parenteral iron administration. While AI/ACD, are dependent on the serum level of hepcidin-25, as iron is not absorbed from the gastrointestinal tract, if level of hepcidin-25 in serum increases and oral iron agent is administered. In the present patient, it could be predicted that oral iron administration might be effective for the treatment of IDA since the serum level of hepcidin-25 was normal. In the other instance, parenteral iron administration with or without EPO is considered, however EPO is expensive and is not approved by medical insurance in Japan. The adverse effect of parenteral administration of iron should also be considered. In the Europe and United States, the effective and safe preparation, ferric carboxymaltose, for parenteral iron administration in a single bolus dose, especially for chronic kidney disease and heart failure, are available [8]. However, it is not yet approved in Japan.

The mechanism of iron deficiency anemia in the present patient is still unknown. However, the studies in the present patient prompted the need for the study for the mechanism of IDA in MGUS.

CONCLUSION

The cause of IDA in the present patient studied including the measurement of serum level of hepcidin-25. However, it remained still unknown. Oral Iron supplement helped to improve IDA.

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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 of Submission
The corresponding author is the guarantor of submission.

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Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest
Author declares no conflict of interest.