Iron deficiency anemia with thrombocytosis on a health checkup

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ABSTRACT

Iron deficiency anemia is reported to have malignant and non-malignant etiologies, including gastro-intestinal bleeding and uterine leiomyoma. Iron deficiency anemia has been associated with secondary thrombocytosis. Furthermore, iron deficiency anemia with thrombocytosis may lead to the development of fatal thrombotic disorders.

Here, we report the case of a 45-year-old asymptomatic woman with severe anemia (Hb 5.9 g/dL) and thrombocytosis ($461.0 \times 10^9/L$) that was detected during a blood test performed as part of a routine health checkup. Based on the findings from the blood test, the patient was clinically diagnosed with iron deficiency anemia with thrombocytosis. Thereafter, computed tomography (CT) revealed uterine leiomyoma which causes chronic anemia. The iron deficiency anemia with thrombocytosis improved following treatment with an oral iron supplement. Furthermore, we discussed the literature review about iron deficiency anemia with thrombocytosis resulting in thrombotic disorders. (HEP. 2020; 47: 516-518.)

Key words iron deficiency anemia, thrombocytosis, thrombotic disorders, health checkup

Introduction

Iron deficiency anemia is reported to have various etiologies including malignancies such as gastric and colon cancer, as well as non-malignant etiologies including gastric and duodenal ulcer and gynecological disorders such as menstrual blood loss with uterine leiomyoma. Of these etiologies, it is essential to rule out asymptomatic cases of malignancy during the early stages based on anemia findings from blood tests performed during health checkups.

Here, we report the case of a woman who presented with severe anemia and thrombocytosis. Furthermore, we discussed the literature review about iron deficiency anemia with thrombocytosis resulting in thrombotic disorders.

Case report

A 45-year-old asymptomatic woman who was a non-smoker underwent an annual health checkup. The medical history of the examinee was documented by nurses using a questionnaire, which was confirmed by a physician. The questionnaire consisted of the chief complaint, medical history, smoking status, medication use, and family history of disease. The examinee had no symptom such as dizziness or any significant medical or family history of disease. The examinee had a body mass index of 25.1 kg/m². Physical examination revealed anemic palpebral conjunctiva. Furthermore, the respiratory sound was clear and heart sound had systolic murmur. Liver and spleen were not palpable.

The laboratory findings on health checkup are shown in **Table 1**. The urinary examination findings were normal. The feces occult blood test was negative. The laboratory finding revealed a decrease of Hb (5.9 g/dL), Hct (23.0%), MCV (57.6 fL), MCH (14.8 pg), and MCHC (25.7 g/dL) and an increase of platelet count ($461.0 \times 10^9/L$). Previous medical records were reviewed to determine the change in anemia, and it was found that the anemia had got worse (**Table 2**). The electrocardiogram showed normal sinus rhythm and flat T wave in lead III, aVF. Chest X-ray revealed cardiomegaly (CTR 58%). Double-contrast upper gastrointestinal barium X-ray radiography was normal.

Accordingly, a referral to the department of Internal Medicine at our institution was made on the same day after health checkup. Further examination revealed that serum iron was 8 µg/dL, total iron binding capacity was 481 µg/dL, whereas ferritin was less than 3 ng/mL. Abdominal CT revealed uterine leiomyoma (4 cm), which causes chronic anemia.

Consequently, a final diagnosis of iron deficiency anemia with thrombocytosis was made. According to the guidelines for the

Table 1 Laboratory findings on health checkup

	2019/10/08		2019/10/08
WBC ($\times 10^9/L$)	6.6	AST (U/L)	17
RBC ($\times 10^6/\mu L$)	3.99	ALT (U/L)	10
Hb (g/dL)	5.9	γ-GTP (U/L)	9
Hct (%)	23.0	ALP (U/L)	138
MCV (fL)	57.6	Cre (mg/dL)	0.48
MCH (pg)	14.8	UA (mg/dL)	3.3
MCHC (g/dL)	25.7	T-cho (mg/dL)	139
Plt ($\times 10^9/L$)	461.0	TG (mg/dL)	46
		HDL-C (mg/dL)	57
		LDL-C (mg/dL)	73
		FBS (mg/dL)	85

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Table 2 The changes in laboratory findings detected on health checkup

	2016 10/27	2017 10/24	2018 11/15	2019 10/8	2019 11/14
	Medical health checkup (pre therapy)			Internal Medicine (post therapy)	
WBC ($\times 10^9/L$)	4.43	7.36	5.43	6.6	5.5
RBC ($\times 10^6/\mu L$)	3.97	4.39	4.14	3.99	4.45
Hb (g/dL)	7.9	7.3	6.4	5.9	8.4
Hct (%)	26.5	27.1	24.4	23.0	31.2
MCV (fL)	n.e.	n.e.	n.e.	57.6	70.1
MCH (pg)	n.e.	n.e.	n.e.	14.8	18.9
MCHC (g/dL)	n.e.	n.e.	n.e.	25.7	26.9
Plt ($\times 10^9/L$)	n.e.	n.e.	n.e.	461.0	417.0

Table 3 Adult cases of thrombosis associated with iron deficiency anemia with thrombosis

Case	Age	Gender	Platelet ($\times 10^9/L$)	The sites of thrombosis/ Thrombotic complications	Complication (HT,DM,dyslipidemia, drinking, smoking, and others)
Case 1 Nagai <i>et al</i> (ref 5)	29	female	1,020	Multiple pulmonary thromboembolism	Not described
Case 2 Keung <i>et al</i> (ref 7)	32	female	865	Extensive infarct of the right middle cerebral artery territory	None
Case 3 Keung <i>et al</i> (ref 7)	48	female	1,139	Transient hemiparesis	None
Case 4 Keung <i>et al</i> 's review (ref 7)	42	male	1,016	Transient hemiparesis	Hemorrhoid
Case 5 Keung <i>et al</i> 's review (ref 7)	42	female	1,736	hemiparesis	Uterine fibroid
Case 6 Keung <i>et al</i> 's review (ref 7)	26	female	850	Thrombosis of middle cerebral artery region	Uterine fibroid
Case 7 Keung <i>et al</i> 's review (ref 7)	30	female	1,050	Right parietooccipital infarct	Uterine fibroid
Case 8 Keung <i>et al</i> 's review (ref 7)	44	female	666	Thrombosis in the bulb of the right internal carotid artery	Menorrhagia
Case 9 Keung <i>et al</i> 's review (ref 7)	20	female	544	Right parietal infarct	Menorrhagia
Case 10 Keung <i>et al</i> 's review (ref 7)	39	female	652	Thrombosis in the left common carotid artery	Uterine fibroid
Case 11 Keung <i>et al</i> 's review (ref 7)	50	female	390	Left eye	Hypermenorrhea
Total	Median 39 (20–50)	Female 10/ Male 1	Median 865 (390–1,736)		

treatment of anemia¹⁾, oral iron supplement was administered immediately.

The patient recovered from anemia and thrombocytosis without development of thrombotic disorders.

Discussion

We described an asymptomatic case presenting with anemia and thrombocytosis on a health checkup that was finally diagnosed as iron deficiency anemia with thrombocytosis after detailed examination.

Iron deficiency anemia has occasionally been complicated by

reactive thrombocytosis in clinical practice. Previous reports regarding iron deficiency anemia with thrombocytosis resulting in thrombotic disorders were summarized in **Table 3**. Dan reviewed the clinical issues of thrombocytosis in iron deficiency anemia in terms of the degree of thrombocytosis (mild-moderate) and the incidence (7%) among 100 consecutive patients with iron deficiency anemia. The cases with severe iron deficiency anemia and marked thrombocytosis were complicated with central retinal vein occlusion²⁻⁶⁾. Furthermore, Keung *et al.* reported two cases of iron deficiency anemia and thrombocytosis, which were peripheral, pulmonary and cerebrovascular thrombosis⁷⁾. Further-

more, Keung *et al.* summarized the data among the adult cases of thrombosis associated with iron deficiency anemia and thrombocytosis (median $865 \times 10^9/L$, range: $390-1,736 \times 10^9/L$)⁷⁾. In **Table 3**, 1 male and 10 females were reported with female predominance, showing that females were reported to be at a higher risk of thrombosis⁷⁾. Regarding as the age distribution, three cases, four cases, one case were reported in twenties, forties and fifties, respectively⁷⁾. Thus, 11 cases were found in all generations (median 39, range: 20–50)⁷⁾. Regarding as platelet counts, one case (case 11), one case (case 9), two cases (case 8 and 10), three cases (case 1, 4, and 7) were $390 \times 10^9/\mu L$, $540 \times 10^9/\mu L$, $600 \times 10^9/\mu L$, over $1,000 \times 10^9/\mu L$, respectively⁷⁾. Thus, the thrombosis cases tended to increase in concordance with the increases of the platelet counts⁷⁾. Furthermore, all cases had not described about complications such as atrial fibrillation, hypertension, dyslipidemia and diabetes mellitus⁷⁾.

In our case, the examinee did not consult a doctor for at least four years according to the previous medical records because she indicated that she had no symptoms. Since iron deficiency anemia may occasionally be complicated by reactive thrombocytosis resulting in fatal thrombotic disorders, it is essential to educate patients with anemia and thrombocytosis to consult a doctor. Moreover, although iron deficiency anemia is a common clinical condition, we should recognize the potential complication of reactive thrombocytosis that may result in fatal thrombotic disorders. Thus, we should consult and refer patients to a specialist to perform additional assessments to identify the underlying cause and implement appropriate treatment.

Compliance and ethics standards

Ethics statement: This case study was conducted in compliance with good clinical practices and the ethics principles of the Declaration of Helsinki.

Informed consent: Informed consent was obtained from the patient for reporting the case details.

The authors state that they have no Conflict of Interest (COI).

REFERENCES

- 1) Goddard AF, James MW, McIntyre AS, Scott BB. British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia 2011; 60(10): 1309-16.
- 2) Dan K. Thrombosis in Iron Deficiency Anemia, Internal Med 2005; 44(10): 1025-6.
- 3) Schloesser LL, Kipp MA, Wenzel FJ. Thrombocytosis in iron-deficiency anemia. J Lab&Clin Med 1965; 66: 107-14.
- 4) Kasper CK, Whissell DY, Wallerstein RO. Clinical aspects of iron deficiency. JAMA 1965; 191: 359-63.
- 5) Nagai T, Komatsu N, Sakata Y, Miura Y, Ozawa K. Iron deficiency anemia with marked thrombocytosis complicated by central retinal vein occlusion. Internal Med 2005; 44: 1090-2.
- 6) Akins PT, Glenn S, Nemeth PM, Derdeyn CP. Carotid artery thrombus associated with severe iron-deficiency anemia and thrombocytosis. Stroke 1996; 27: 1002-5.
- 7) Keung YK, Owen J. Iron deficiency and thrombosis: literature review. Clin Appl Thromb Hemost 2004; 10(4): 387-91.