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Perspective

Differential diagnosis between iron deficiency anemia and thalassemia trait-induced anemia

Andy Sun [a,b†], Julia Yu-Fong Chang [a,b†], Ying-Tai Jin [c,d**], Chun-Pin Chiang [a,b,e*]

[a] *Department of Dentistry, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan*
[b] *Graduate Institute of Oral Biology, School of Dentistry, National Taiwan University, Taipei, Taiwan*
[c] *Department of Pathology, Taiwan Adventist Hospital, Taipei, Taiwan*
[d] *Department of Pathology, National Cheng Kung University Hospital, Tainan, Taiwan*
[e] *Department of Dentistry, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan*

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According to the World Health Organization (WHO) criteria, the anemia is defined as having a blood hemoglobin (Hb) concentration <13 g/dL in a male patient and <12 g/dL in a female patient. The anemia is mainly caused by reduced production of Hb, which is essential for oxygen transport in the red blood cell (RBC). Hb is a tetramer that is composed of two α-globin chains and two β-globin chains. Moreover, each α-globin or β-globin polypeptide chain contains a heme molecule that consists of a protoporphyrin IX and an iron ion. Therefore, the globin, iron, and protoporphyrin IX are structural components of a Hb. A deficiency of any one or two of the Hb structural components may result in Hb deficiency or anemia.

Iron deficiency anemia (IDA) is caused by insufficient iron levels in the body, leading to reduced production of Hb or the anemic condition. The etiologies of iron deficiency

* Corresponding author. Department of Dentistry, Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, No. 707, Section 3, Chung-Yang Road, Hualien 970, Taiwan.
** Corresponding author. Department of Pathology, Taiwan Adventist Hospital, No. 424, Section 2, Bade Road, Taipei 10556, Taiwan.
E-mail addresses: yingtaijin@gmail.com (Y.-T. Jin), cpchiang@ntu.edu.tw (C.-P. Chiang).
† These two authors contributed equally to this work.

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Table 1 Differential diagnosis between iron deficiency anemia (IDA) and thalassemia trait-induced anemia (TTIA).

Microcytic anemia	IDA	TTIA
Hemoglobin concentration	Men <13 g/dL Women <12 g/dL	Men <13 g/dL Women <12 g/dL
Red blood cell (RBC) number	<4 M/μL	>5 M/μL usually
Mean corpuscular volume (MCV)	<80 fL	<74 fL
Mentzer index (MCV/RBC)	>16	<13
Serum iron level	<60 μg/dL	Normal
RBC distribution width - coefficient of variation (RDW-CV)	>15%	>15%

include a decreased intake of iron (during infancy and old-age stage), a reduced absorption of iron in the gastrointestinal tract (in patients with partial or total gastrectomy or celiac sprue), an increased demand for RBC production (during childhood growth spurts and during pregnancy), and chronic blood loss (women with excessive menstrual flow or patients with peptic ulcer, diverticulosis, or malignancies).[1] The typical blood profile of a patient with IDA is shown in Table 1. Thus, an IDA patient usually has a reduced RBC number (<4 M/μL), a lower mean corpuscular volume (MCV <80 fL, so-called microcytic RBC), a higher Mentzer index [> 16, the Mentzer index is calculated by MCV/RBC, for example, if a patient has a MCV of 70 fL and a RBC number of 3.8 million/μL, then the Mentzer index is 18.4 (70/3.8)], a lower serum iron level (<60 μg/dL, by the WHO criterion), and a higher RBC distribution width - coefficient of variation (RDW-CV > 15%) (Table 1).[1]

Thalassemia is an autosomal recessive blood disorder in which the body makes an abnormal form of α-globin or β-globin polypeptide chains usually due to gene mutations.[2–4] The α-globin polypeptide chains are encoded by two closely linked genes on chromosome 16 and the β-globin polypeptide chains are encoded by a single gene on chromosome 11. There are two main types of thalassemia: α-thalassemia and β-thalassemia. The majority of the mutations that cause α-thalassemia are deletional, whereas those that cause β-thalassemia are generally point mutations.[3] Both α- and β-thalassemias include the following forms: thalassemia major (with the defective genes from both parents) and thalassemia minor (with the defective gene from only one parent).[2] A genetic test such as DNA analysis can identify specific mutations in the genes responsible for α-thalassemia or β-thalassemia.[4]

The patients with thalassemia major may be fatal or often develop severe anemia in the early childhood. The patients with the minor form of α- or β-thalassemia may have no apparent anemia in the young-age stage, but they may develop mild or moderate hypochromic and microcytic anemia in the middle-age or old-age stage depending on the degree of α-globin or β-globin chain deficiency. The patients with a typical thalassemia trait-induced anemia (TTIA) usually have a higher RBC number (>5 M/μL usually), a lower MCV (<74 fL), a lower Mentzer index (<13), a normal serum iron level, and a higher RDW-CV (>15%) (Table 1).[2]

Therefore, both IDA and TTIA share some similar features: both are microcytic anemia and have a higher RDW-CV. The IDA patients often have a reduced RBC number (<4 M/μL), but the TTIA patients usually have a higher RBC number (>5 M/μL usually), probably due to bone marrow compensation to make a great number of microcytic RBCs. The Mentzer index is a good biomarker for clinical diagnosis of a typical IDA (the Mentzer index >16) and for clinical diagnosis of a typical TTIA (the Mentzer index <13) (Table 1). For a simple differential diagnosis between IDA and TTIA, a complete blood count (CBC) and serum iron and ferritin (an iron storage protein) level examinations are usually enough for providing the blood data for the clinical diagnosis (Table 1). The TTIA patients often have a family history of thalassemia, but the IDA patients usually have no significant family history unless they have underlying genetic defects affecting iron absorption or metabolism. The IDA patients usually demonstrate a good response to iron supplement therapy, with a significant increase in the Hb level after a few weeks or months of treatment. The TTIA patients does not improve with iron supplement therapy unless they have iron deficiency simultaneously. However, the TTIA patients with severe anemia may need blood transfusion.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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