The co-existence of autoimmune hemolytic anemia and iron deficiency anemia: a case report

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Abstract:
Background: Autoimmune hemolytic anemia (AIHA) is a rare acquired hemolytic disease due to the autoantibody against the antigen upon the own red blood cells whereas the iron deficiency anemia is resulted from the inadequate production of red blood cells due to lack of the iron. Their basic pathogeneses are totally different, so it is hardly to see both entities co-exist. This study is aimed to describe the co-existence of AIHA and IDA simultaneously in a Thai woman. Case Presentation: A 33-year-old Thai woman presented progressive fatigue for a few weeks without blood loss. The physical examination revealed only pallor without jaundice, no hepatosplenomegaly. The blood tests were: Hb 9.0 g%, WBC 4,050/mm³, platelet 238,000/mm³, MCV 90.8 fl, MCH 30.6 pg, reticulocyte 1.72 %, ferritin 8.57 ng/ml and the direct anti-globulin test-weakly positive. The urine hemosiderin was negative. The diagnosis was the co-existence of AIHA and IDA. The treatment was started with oral prednisolone, folic acid and the oral iron tablets. And she responded well to therapy, Hb 11.7 g%, MCV 95.3 fl within 8 weeks. Conclusion: The co-existence of AIHA and IDA is very unusual but they are not mutually exclusive. Its diagnosis is not simple because the microcytosis or hypochromia, the significant clues of IDA, are all masked. Likewise, the jaundice and reticulocytes, the clues of hemolysis with the increased erythropoietic compensation, are not recognized in this co-existence.

Key words: Autoimmune hemolytic anemia, Iron deficiency anemia
Introduction

An autoimmune hemolytic anemia (AIHA) is a rare acquired hemolytic disease due to the autoantibody against the antigen upon the surface of the own red blood cells. The RBC coated with the autoantibody will be mainly destroyed by the reticulo-endothelial cells. AIHA may be classified as idiopathic if it occurs spontaneously and associated with other diseases including an autoimmune disease, malignancy, infection or drugs. The onset of symptom may be insidious or rapid and the clinical course may be chronic or acute fatal hemolytic normocytic anemia. Besides the signs of hemolysis, the direct anti-globulin test is mostly positive.

As other extravascular hemolytic diseases, serum ferritin in AIHA is moderately higher than the normal control. Therefore, it is very unusual to find a case of iron deficiency anemia in the patients with AIHA.
So far only one case of AIHA with megaloblastic disease was reported in one woman who used to have the iron deficiency anemia\(^5\). Herein, we reported a case of the co-existence of AIHA and iron deficiency in a Thai woman.

**Case Report**

A 33-year-old Thai woman complained of gradually progressive fatigue without fever for a few weeks. She had no frank blood loss and no weight loss. The physical examination revealed only pallor but no jaundice, and no hepatosplenomegaly.

The initial blood tests included: Hb 9.0 g%, Hct 26.7 %, WBC 4,050/mm\(^3\), N 64.9%, L 22.7%, platelet 238,000/mm\(^3\), MCV 90.8 fl, MCH 30.6 pg, MCHC 33.7 g%, RDW 12.4 %, reticulocyte 1.72 %, ferritin 8.57 ng/ml, direct anti-globulin test-weakly positive, indirect anti-globulin test-negative, ANA-positive, fine speckled nuclear titer 1:160, anti-double stranded DNA-negative, C3 complement 0.92 g/l (normal 0.9-1.8), C4 complement 0.22 g/l (normal 0.12-0.75), cold agglutinin-negative, Hb analysis using the high performance liquid chromatography method: Hb \(\text{A}_2\), HbA\(_2\) 3.4 %, Hb F 0.3 %.

Creatinine 0.68 mg%, eGFR 115.3 ml/min/1.73 m\(^2\), TSH 0.733 uIU/ml, FT\(_3\) 2.41 pg/ml

The urinalysis showed no protein, no sugar, no white blood cell, red blood cell 50-100/HPF, negative for urine hemosiderin.

She was diagnosed as having an idiopathic autoimmune hemolytic anemia (AIHA) and iron deficiency anemia (IDA) and promptly treated as an outpatient with oral prednisolone 60 mg, folic acid and one iron tablet a day for every day.

Within eight weeks of continuous treatment, she became well and her blood was tested again, Hb 11.7 g%, Hct 34.9 %, WBC 5600/mm\(^3\), platelet 219,000/mm\(^3\), MCV 95.3 fl, MCH 31.8 pg, MCHC 33.3 g%, RDW 15.2 %, ferritin 28.9 ng/ml. The direct anti-globulin test was repeated and found negative. The dose of prednisolone was gradually decreased while the iron therapy was continued for six months. An urologist was consulted for the microscopic hematuria but no opaque stone was found. She did not accept any endoscopy for identifying the source of iron loss.

**Discussion**

The diagnosis of AIHA was based on the positive direct anti-globulin test although she did not have reticulocytosis\(^1\) whereas the iron deficiency anemia was diagnosed solely based on the serum ferritin less than 30 ng/ml in anemic patient\(^6\).

Because her initial red blood cell indices, MCV 90.8 fl and MCH 30.6 pg were the normocytic anemia and her reticulocyte was 1.72 % that was not more than 2 %, she was firstly supposed to have the anemia of chronic disease (ACD), the most common cause of the normocytic anemia which is characterized by the increased ferritin, decreased serum iron and decreased TIBC\(^7\). But her initial serum ferritin was very low (8.57 ng/ml) that was opposed to those of ACD and it preferably represented the depletion of iron storage or even more the iron deficiency anemia. So iron study should not be neglected even in cases of normocytic anemia. In fact, up to 40 % of patients with iron deficiency anemia can have normal MCV\(^8\).

To differentiate the anemia in this patient, the kinetic approach\(^9\) could not be applied because AIHA is basically a hemolytic disease or the increased RBC destruction with increased erythropoietic com-
pensation whereas the IDA is resulted from the inadequate production of RBC. The clinical manifestations in this patient were equivocal, viz., due to the lack of jaundice, hepatosplenomegaly and reticulocytosis, it did not signify the hemolysis\(^\text{10}\). On the other hand, because of lack of the microcytosis and hypochromia, it did not suggest IDA. The diagnosis of IDA was accidentally made in this case based on the iron study to confirm the diagnosis of ACD whereas the direct anti-globulin test was requested because of the problem of cross-matching test.

Because the iron study including the serum ferritin, serum iron and iron binding capacity (TIBC) is essential for making the diagnosis of ACD\(^\text{11}\), IDA co-existing with AIHA could not be missed. In contrast, AIHA might be simply overlooked because of absolute lack of clinical and laboratory clues of hemolytic anemia\(^\text{12}\).

The co-existence of AIHA and IDA is very unusual and difficult to be diagnosed because both can mask the manifestations of each other, the low MCV and low MCH, the prominent characteristic of IDA\(^\text{6}\) was absent probably due to being masked by the polychromasia of hemolysis\(^\text{13}\) whereas the reticulocytosis of AIHA was not prominent due to the iron storage depletion\(^\text{14}\).

**Conclusion**

A 33-year-old Thai woman had progressive anemia that was finally found to have the co-existence of an autoimmune hemolytic anemia and iron deficiency anemia. Both entities can mask the important manifestations of each other, viz. no microcytosis of iron deficiency and no reticulocytosis of hemolysis with increased erythropoietic compensation.

**References**

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