Pancytopenia with Iron Depletion and Subclinical Primary Hypothyroidism

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Abstract: Although normochromic normocytic anemia is commonly found in primary hypothyroidism both subclinical and overt, pancytopenia as in our case has been still rarely reported. She was a 24-year-old Thai patient who was referred to the hematologists because of the pancytopenia and gradual onset of fatigue for a month without fever. The physical examination revealed nothing abnormal, except for the obvious pallor. The blood tests showed Hb 5.3 g%, WBC 3,800/mm^3, platelet 58,000/mm^3, MCV 55.6 fL, MCH 15.8 pg, ferritin 14.4 ng/mL, serum iron 31.0 mcg/dL, TIBC 381 mcg/dL, Hb electrophoresis: Hb A_2 2.2 %, Hb F 2.0 %,TSH 21.04 uIU/mL, FT3 3.0 pg/mL, FT4 0.6 ng/dL, ANA-positive, fine speckled cytoplasmic titer 1:80, anti-microsomal antibody 739.4 IU/mL, anti-thyroperoxidase antibody 1,168.8 IU/mL. The flow cytometry for PNH clone was not found. The diagnosis of pancytopenia with iron depletion and subclinical primary hypothyroidism was establishedand she was treated with the iron tablet without the thyroid hormone replacement. The pancytopenia was much improved within 3 months, Hb 12.8 g%, Hct 39.4 %, WBC 10,900/mm^3, platelet 111,000/mm^3, MCV 83.3 fL, MCH 27.0 pg. The pancytopenia in our case is presumed to be associated with both the iron deficiency anemia and the autoimmune process which leads to subclinical hypothyroidism because anemia and leukopenia completely recover after only iron therapy while theplatelet is still lowered. However the thrombocytopenia is not severe enough to be treated with the immunosuppressants.

Key words: Pancytopenia, Iron deficiency, Subclinical hypothyroidism

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บทคัดย่อ: **แพนไซโตพีเนียร่วมกับการขาดธาตุเหล็ก ในผู้ป่วยไธรอยด์ต่ำปฐมภูมิที่ไม่มีอาการ**

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แม้ว่า normochromic normocytic anemia จะเป็นภาวะที่พบได้บ่อยในผู้ป่วยฮอร์โมนไธรอยด์ต่ำปฐมภูมิ ไม่ว่าจะมีอาการทางคลินิกร่วมด้วยหรือไม่ก็ตาม แต่ pancytopenia แบบในผู้ป่วยต่อไปนี้ นับว่ายังพบน้อยมาก ผู้ป่วยเป็นหญิงไทยอายุเพียง 24 ปี ถูกส่งตัวมาพบโลหิตแพทย์เนื่องจากมี pancytopenia และอาการค่อย ๆ อ่อนเพลียเป็นเวลา 1 เดือน โดยไม่มีไข้ ตรวจร่างกายไม่พบความผิดปกติชัดเจน ยกเว้นความซีดที่เห็นอย่างเด่นชัด ตรวจเลือดก็พบว่า Hb 5.3 กรัม%, WBC 3,800/มม^3, platelet 58,000/มม^3, MCV 55.6 เฟมโตลิตร, MCH 15.8 พิโครกรัม, ferritin 14.4 นาโนกรัม/มล, serum iron 31 ไมโครกรัม/ดล, TIBC 381 ไมโครกรัม/ดล, ตรวจแยกชนิดของฮีโมโกลบิน พบ Hb A_2 2.2 %, Hb F 2.0 %, TSH 21.04 uIU/mL, FT3 3.0 พิโครกรัม/มล, FT4 0.6 นาโนกรัม/ดล, ANA-ให้ผลบวกชนิด fine speckled cytoplasmic titer 1:80, anti-microsomal antibody 739.4 หน่วยสากล/มล, anti-thyro-peroxidase antibody 1,168.8 หน่วยสากล/มล, ตรวจไม่พบโคลนของ PNH ให้การวินิจฉัยว่าเป็น pancytopenia ร่วมกับการขาดธาตุเหล็ก และฮอร์โมนไธรอยด์ต่ำแบบไม่มีอาการ และให้การรักษาด้วยยาเข้าธาตุเหล็ก โดยที่ยังไม่ได้ให้ฮอร์โมนไธรอยด์ชดเชย pancytopenia ก็ดีขึ้นภายใน 3 เดือน ผลตรวจเลือดพบ Hb 12.8 กรัม%, Hct 39.4 %, WBC 10,900/มม^3, platelet 111,000/มม^3, MCV 83.3 เฟมโตลิตร, MCH 27.0 พิโครกรัม ภาวะ pancytopenia ในผู้ป่วยรายนี้ อาจจะเกี่ยวข้องกับทั้งโลหิตจางจากการขาดธาตุเหล็กโดยตรง และเกี่ยวกับภาวะ autoimmune process ที่ทำให้ฮอร์โมนไธรอยด์ต่ำ แต่ยังไม่ต่ำพอที่จะเกิดอาการของโรคไธรอยด์ต่ำก็ได้ เพราะเมื่อได้รับการรักษาด้วยยาเข้าธาตุเหล็กเพียงอย่างเดียว ผู้ป่วยหายจากภาวะซีดและเม็ดเลือดขาวต่ำ แต่ระดับเกล็ดเลือดยังคงต่ำอยู่ แม้จะยังไม่ต่ำพอที่จะต้องให้รับยากดภูมิคุ้มกันก็ตาม

คำสำคัญ: Pancytopenia, การขาดธาตุเหล็ก, ฮอร์โมนไธรอยด์ต่ำแบบไม่มีอาการ

Introduction

Anemia is the common hematologic complication in hypothyroidismbecause the thyroid hormone usually enhances the erythropoiesis via the erythropoietin activity[1]. It is found in 43% of patients with the overt hypothyroidism and 39% of patients with the subclinical hypothyroidism, as compared with 26% found in the normal control group ($p < 0.05$). And the most common form is the anemia of chronic disease, viz., normochromic normocytic anemia, Hb levela-round 8.5-10.0 g% or more, low serum iron and low TIBC[2]. Because of its high prevalence, the authors suggest the investigation for hypothyroidism when the patients with anemia with uncertain etiology are encountered[3]. Among 60 anemic adult patients with primary hypothyroidism, all three morphologic anemias are found, the most common morphology is normocytic, normochromic anemia that is present in 31 patients (51.6 %) followed by microcytic anemia in 26 patients (43.3 %). Six patients (10 %) have megaloblastic anemia with vitamin B_{12} deficiency

including 3 cases of pernicious anemia. Two patients have combined the deficiencies of the iron and vitamin B_{12} whereas 12 (20 %) have severe anemia (Hb< 8 g%)[4]. However, peripheral pancytopenia found in caseswith hypothyroidism has been rarely reported[5,6], and herein, we report one young woman who was found tohave the pancytopenia as well as subclinical hypothyroidism and iron depletion.

Case Report

A 24-year-old woman was referred to the hematologistsby the general practitioner because ofthe gradual onset of fatigue, dizziness and pancytopenia for a month, no blood loss, no fever. The physical examination revealed unremarkable, except for frank pallor, BP 107/73 mmHg, pulse 98/min.

The blood tests included: Hb 5.3 g%, Hct 18.5%, WBC 3,800/mm^3, platelet 58,000/mm^3, MCV 55.6 fL, MCH 15.8 pg, MCHC 28.4 g%, RDW 22.2 %, N 58.3 %, L 35.1 %, reticulocyte 1.2 %, ferritin 14.4 ng/mL, serum iron 31 mcg/dL (normal 35-165), TIBC 381 mcg/dL (normal 259-388)

Hb electrophoresis: HbA_2 2.2 %, HbF 2.0 %, PCR for alpha thalassemia-1-negative for Southeast Asian deletion and Thai deletion,

BUN 6.4 mg%, creatinine 0.86 mg%, GFR 95 mL/min/1.73 m^2, direct bilirubin 0.2 mg%, total bilirubin 1.0 mg%, AST 15 U/L, ALT 12 U/L, alkaline phosphatase 88 U/L, albumin 4.5 g%, globulin 4.1 g%, cholesterol 117 mg% HBsAg, anti-HCV, anti-HIV were all negative, VDRL-positive, 1:1 but TPHA was negative.

TSH 21.040 uIU/mL (normal 0.3-5.0), FT3 3.0 pg/mL (normal 2.39-6.79), FT4 0.6 ng/dL (normal 0.6-1.6), anti-microsomal antibody 739 IU/mL (normal 0-34), anti-thyroperoxidase antibody 1,168.8 IU/mL (normal 0-115), ANA-positive, fine speckled cytoplasmic titer 1:80

Urine hemosiderin-negative, flow cytometry for paroxysmal nocturnal hemoglobinuria (PNH) clone was negative.

The bone marrow study was not allowed.

The ultrasonography of the upper abdomen showed the fatty liver and mild splenomegaly.

She was diagnosed as having pancytopenia with iron deficiency anemia with subclinical primary hypothyroidism and she was treated with ferrous sulfate tablet without the thyroid hormone repla-cement for a few months, and her final CBC were demonstrated to be: Hb 12.8 g%, Hct 39.4%, WBC 10,900/mm^3, platelet 111,000/mm^3, MCV 83.3 fL, MCH 27.0 pg, ferritin 32.4 ng/mL.

Discussion

Pancytopenia used to be reported in onecase of Hashimoto's thyroiditis combined with primary adrenal insufficiency and it completely recovered after the treatment of hypothyroidism and hypoadrenalism[5] and in one case with panhypopituitarism after chemotherapy who also recovered after thyroid hormone replacement[7]. Likewise, pancytopenia used to be occasionally reported in cases of iron deficiency anemia and it would be improved after the iron treatment with the initial deterioration of the white blood cell and platelet[8,9]. Our case is proved to have iron deficiency anemia based on the combination of the microcytic hypochromic anemia, the low serum ferritin and the low percentage of transferrin saturation and all these parameters become normal after the adequate iron therapy. Furthermore, by the flow cytometry, she

was proved to be free from PNH clone which can be present as the IDA with pancytopenia[10].

If the patient has only iron deficiency anemia with subclinical hypothyroidism, the anemia can be effectively corrected with the combination of oral iron and levothyroxine[11]. It is different from our case who has not only iron deficiency anemia but also has leucopenia and thrombocytopenia and only erythroid and myeloid series respond well to iron therapy.

The anti-thyroglobulin and the anti-microsomal antibodies are found with high levels in our case whereas the thyroid function test shows only the high TSH level with the normal level of FT3 and FT4. The clinical diagnosis is subclinical hypothyroidism. Because she does not have an abnormal lipoprotein level, no cardiac symptom, no symptoms relating to hypothyroidism such as fatigue, dry skin, constipation, muscle cramp, etc, the thyroid hormone replacement seems unnecessary[12]. However, the platelet count should be followed because it does not achievethe completely normal level after the adequate iron therapy. It seemsto suggest that the platelet level may be also associated with the underlying autoimmune process that contributesthe subclinical hypothyroidism and it is left to go on its activity. Some authorities recommended to treat the subclinical hypo-thyroidism because they believed it was the mild thyroid failure[13]. However the platelet level in our case was more than 30,000/mm^3 that is beyond the dangerous level[14], so any immunosuppressive therapy is considered unnecessary.

Conclusion

Pancytopenia, iron deficiency anemia and subclinical hypothyroidism were diagnosed in a 24-year-old Thai woman. Her microcytic anemia and leukopenia could be corrected with just only iron therapy while the thrombocytopenia was partially improved. Either the iron deficiency anemia or the underlying autoimmune process of subclinical hypothyroidism or both was presumed to be associated with the pancytopenia.

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