Evans's Syndrome in Hashimoto's Thyroiditis: A Case Report

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Abstract: Hashimoto's thyroiditis or chronic lymphocytic thyroiditis which is one of autoimmune diseases may be found associated with other autoimmune diseases but Evans' syndrome, an autoimmune hemolytic anemia (AIHA) with simultaneous autoimmune thrombocytopenia, has been rarely reported. Herein, we report a 20-year-old Thai woman with Evans' syndrome who simultaneously develops acute AIHA as well as thrombocytopenia after the diagnosis of Hashimoto's thyroiditis because of FT_4 0.1 ng/dl, FT_3 6.70 pg/ml, TSH > 100 IU/ml, anti-thyroglobulin antibody > 4,000 IU/ml, anti-microsomal antibody > 600 IU/ml has been established and well treated with eltroxin for many years. Her blood tests show pancytopenia: Hb 5.9 g%, WBC 3,400/mm^3, platelet 52,000/mm^3, reticulocyte 7.2 %, with strongly positive direct antiglobulin test. No other underlying or precipitating diseases are recognized. In other reports of patients with Hashimoto's thyroiditis, the AIHA always happened few months or years before the occurrence of thrombocytopenia. Our case is additionally diagnosed as Evans' syndrome and treated with oral prednisolone 60 mg a day and intramuscular injection of vitamin B_{12} every week. She responds to therapies well, her CBC becomes normal in two months without blood transfusion. The occurrence of Evans' syndrome in the case of Hashimoto's thyroiditis may signify their association because both conditions have the autoimmune processes as the main basic pathogenesis with the different target organs, viz., the thyroid gland tissue in Hashimoto's thyroiditis but the red blood cells, platelets and possibly white blood cells as in our case in Evans' syndrome.

Key words: Evans's Syndrome, Hashimoto's Thyroiditis

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บทคัดย่อ: **Evans's Syndrome ใน Hashimoto's Thyroiditis: รายงานผู้ป่วย 1 ราย**

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Hashimoto's thyroiditis หรือ chronic lymphocytic thyroiditis ซึ่งเป็นโรคทาง autoimmune จึงอาจจะพบร่วมกับโรคในกลุ่ม autoimmune อื่น ๆ ได้ แต่ที่พบร่วมกับ Evans' syndrome หรือ autoimmune hemolytic anemia (AIHA) กับ autoimmune thrombocytopenia ในผู้ป่วยคนเดียวกัน ยังมีรายงานน้อยมาก การศึกษานี้เป็นรายงานผู้ป่วย Evans' syndrome หญิงอายุ 20 ปี ที่แสดงอาการ AIHA พร้อมกับภาวะเกล็ดเลือดต่ำอย่างเฉียบพลัน หลังจากที่ได้รับการวินิจฉัยว่าเป็น Hashimoto's thyroiditis เพราะ FT_4 0.1 นาโนกรัม/ดล, FT_3 6.70 พิโครกรัม/มล, TSH >100 IU/มล, anti-thyroglobulin antibody >4,000 IU/มล, anti-microsomal antibody >600 IU/มล. และได้รับการรักษาด้วย eltroxin ประจำเป็นเวลาหลายปี ผลการตรวจเลือดพบว่าผู้ป่วยมี pancytopenia คือ Hb 5.9 กรัม%, WBC 3,400/มม^3, platelet 52,000/มม^3, reticulocyte 7.2 %, และให้ผลบวกกับ direct antiglobulin test อย่างชัดเจน ไม่พบว่ามีโรคอื่น ๆ ร่วมด้วย ทั้งโรคที่นำมาก่อนและโรคที่มากระตุ้นในรายงานผู้ป่วยรายอื่น ๆ ที่พบ Evans' syndrome ในผู้ป่วย Hashimoto's thyroiditis มักพบว่าผู้ป่วยมักจะแสดงอาการของ AIHA นำมาก่อนเป็นเดือนหรือเป็นปี ก่อนที่จะเกิดภาวะเกล็ดเลือดต่ำผู้ป่วยได้รับการวินิจฉัยเพิ่มเติมว่าเป็น Evans' syndrome และให้การรักษาด้วยการให้รับประทาน prednisolone 60 มก. ต่อวันร่วมกับการฉีด vitamin B_{12} เข้ากล้ามทุกสัปดาห์ ผู้ป่วยตอบสนองดีต่อการรักษา ตรวจ CBC พบว่าเป็นปกติใน 2 เดือน โดยไม่จำเป็นต้องเพิ่มเลือด การพบ Evans' syndrome ในผู้ป่วย Hashimoto's thyroiditis บ่งบอกว่าทั้งสองภาวะอาจจะมีความสัมพันธ์กันก็ได้ เพราะต่างก็มีพยาธิกำเนิดหลัก ๆ จากขบวนการ autoimmune ทั้งคู่ เพียงแต่อวัยวะเป้าหมายในการทำลายต่างกันเท่านั้น นั่นคือในโรค Hashimoto's thyroiditis เป้าหมายคือเนื้อเยื่อของต่อมไธรอยด์ส่วน Evans' syndrome เป้าหมายหลักคือเม็ดเลือดแดงและเกล็ดเลือดอาจจะรวมทั้งเม็ดเลือดขาวแบบที่พบในผู้ป่วยรายนี้ด้วย

Introduction

Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is the inflammatory disease of the thyroid gland mainly from organ specific T cell mediated autoimmune pathogenesis. Its clinical manifestation may be asymptomatic or overt hypothyroidism. Two autoantibodies which are commonly seen in Hashimoto's thyroiditis are the antibodies against the primary thyroid-specific antigens, thyroglobulin (Tg), and the thyroid peroxidase (TPO). Hashimoto's thyroiditis can be often found to coexist with other autoimmune diseases such as type 1 diabetes mellitus, rheumatoid arthritis, multiple sclerosis, vitiligo, SLE, pernicious anemia due to autoantibody against the intrinsic factor[(1)] and an autoimmune polyendocrine syndrome type 2 which is usually defined by the occurrence of two or more of the followings: Addison's disease, autoimmune thyroid disease and/or type 1 DM[(2)].

Evans's syndrome is the autoimmune disease

which produces the antibody destroying his/her own red blood cells (RBC), neutrophils and platelets, resulting in autoimmune hemolytic anemia (AIHA), neutropenia and thrombocytopenia[3]. The clinical severity may vary from asymptomatic to the life threatening anemia. It can be found associated with some diseases such as SLE, lymphoproliferative disorder. However Evans's syndrome has been rarely reported in cases with Hashimoto's thyroiditis[4] while the most common cause of anemia in the case of primary hypothyroidism who have 100 % positive anti-TPO antibody, is the anemia of chronic disease[5], other occasionally mentioned anemia including aplastic anemia[6], coexistence of megaloblastic anemia and iron deficiency anemia[7] and autoimmune hemolytic anemia[8]. Herein we report a case of Evans' syndrome with the underlying Hashimoto's thyroiditis in a Thai woman.

Case Report

A 20-year-old woman was referred by the general practitioner to the hematologist due to acute severe hemolytic anemia for a few days. Her underlying disease was Hashimoto's thyroiditis which had been diagnosed depending on the combination of FT_4 0.1 (normal 0.6-1.6 ng/dL), FT_3 6.70 (normal 2.39-6.79 pg/mL) TSH >100 (normal 0.3-5.0 IU/mL), anti-thyroglobulin antibody >4,000 IU /mL (normal 0-115), anti-microsomal antibody >600 IU/mL (normal 0-34), and she had been well controlled with Eltroxin 150 mcg a daywhile the thyroid function tests were within normal limit for many years, FT_4 1.5, FT_3 3.4, TSH 1.276.

Her physical examination revealed marked pallor with mild jaundice, no exophthalmos, no hepatosplenomegaly, mildly diffuse enlargement of thyroid gland, no petechial hemorrhage.

CBC: Hb 5.9 g%, Hct 18.1%, MCV 116.5 fL, MCH 37.8 pg, MCHC 32.4 g%, RDW 23.0 %, WBC 3,400/mm^3, platelet 52,000/mm^3, reticulocyte 7.2 %, N 50%, L 45%, M 1%, E 3%, B 1%. Direct antiglobulin test 3+, indirect antiglobulin test 1+, Hb electrophoresis showed normal findings, positive ANA, nuclear pattern 1:160, negative anti-dS DNA, negative urine hemosiderin, normal urinalysis, ferritin 99.1-213.4 ng/mL, creatinine 0.8 mg%.

She was additionally diagnosed as having Evans' syndrome and she was treated with oral prednisolone 60 mg a day and weekly intra-muscular injection of vitamin B_{12} 1,000 mcg. She responded well to therapies without blood transfusion. Within 2 months, her CBC became normal, Hb 11.2 g%, Hct 33.9 %, MCV 112.5 fL, MCH 37.1 pg, MCHC 33.0 g%, RDW 19.0 %, WBC 8,800/mm^3, platelet 163,000/mm^3 whereas eltroxin therapy was still continued and no flare up of hypothyroidism was recognized.

Discussion

Among the various types of anemia found in 60 patients with the primary hypothyroidism, with 58.3% of them having positive anti-TPO antibody, normocytic normochromic anemia is present in 31 patients (51.6%) followed by microcytic hypochromic 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 deficiency of iron and vitamin B_{12}[9]. Evans's syndrome or AIHA with thrombocytopenia in the absence of the known etiologies[10] is still very rare in Hashimoto's thyroiditis.

AIHA and thrombocytopenia are simultaneously found in our case after Hashimoto's thyroiditis has been well controlled with eltroxin for many years. It is not similar to other studies in which most cases sequentially develop the AIHA few months[4,11] or years[12] before the occurrence of thrombocytopenia. It seems to suggest that although the hypothyroid state can be corrected by the thyroid hormones butthe autoimmune process is still going on.

Basically both Hashimoto's thyroiditis and Evans' syndrome have the autoimmune processes as the main basic pathogenesis in common but each disease has its own autoantibodies. In Hashimoto's thyroiditis, nearly all patients have antibodies against thyroid gland tissues such as anti-Tg or anti-TPO although the apoptotic destruction of the thyroid cells is mainly the role of the activating cytotoxic T cells[13]. On the other hand, in AIHA, there is mainly IgG with or without the third complement component which reacts with the protein antigen on the RBC surface leading to the agglutination or the destruction of the RBCs[14].

Our case has macrocytosis (MCV >100 fL) which is presumed to be due to the increase of the reticulocyte (7.2%), responding to any hemolytic anemia that is actually larger than the mature RBCs[15], and the megaloblastic anemia, particularly pernicious anemia due to anti-intrinsic factor antibody. But the blood tests for vitamin B_{12} and folic acid are not available in our hospital, the patient is decided to receive the therapeutic trial with oral folic acid and intramuscular injection of vitamin B_{12} for possible B_{12} deficiency. And she responds well to this combination therapy, the pancytopenia becomes nearly normal within two months although the MCV is still high probably due to the active reticulocytosis.

Conclusion

A 20-year-old woman is diagnosed as Evans' syndrome based on the combination of acute hemolytic anemia, pancytopenia with the strongly positive direct antiglobulin test. Her underlying disease is Hashimoto's thyroiditis in which the hypothyroidism has been well overcome with the thyroid hormone for many years. Both of them are supposed to have some association because their basic pathogenesis is similarly the autoimmune process.

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