Generalized Lymphadenopathiesand Pancytopenia in Primary Hypothyroidism

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Abstract: Anemia is a very common manifestation in hypothyroidism but pancytopenia withgeneralized lymphadenopathy has rarely been mentioned. Herein we report a 51-year old Thai woman who presents with the generalized purpura, weight loss, progressive enlargement of generalized lymphadenopathies without fever for a few weeks. The physical examination revealed the diffuse enlargement of the thyroid glandand generalized lymphadenopathies 1.5-2 cm. The blood tests show pancytopenia, Hb 8.1 g%, WBC 1,700/mm^3, platelet 4,000/mm^3, absolute neutrophil count 510/mm^3. Other blood tests include TSH>100 uIU/mL, FT3 1.15 pg/dL, FT4 0.2 ng/dL, anti-thyroglobulinand anti-thyroperoxidaseantibodies are positive. The bone marrow biopsy shows normal trilineage with the absence of iron storage whereas the lymph node microscopic pathology is only reactive hyperplasia. Finally she is diagnosed as having primary hypothyroidism due to autoimmune process. After treatment with L-thyroxine 100 mcg a day, without corticosteroid, for a few months, the generalized lymphadenopathy gradually diminishesand the pancytopenia becomes normal. Although the direct association between lymphadenopathy and hypothyroidism cannot be concluded, it may besupposedly related via the autoimmune processes as the basicpathogenesis in common.

Key words: Generalized Lymphadenopathy, Pancytopenia, Primary Hypothyroidism

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บทคัดย่อ: **ต่อมน้ำเหลืองโตทั่วตัวและเม็ดเลือดต่ำโดยรวมในภาวะไธรอยด์ต่ำปฐมภูมิ**

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ภาวะโลหิตจางในผู้ป่วยที่มีภาวะฮอร์โมนไธรอยด์ต่ำ เป็นเรื่องที่พบได้บ่อย แต่การที่จะพบภาวะเม็ดเลือดต่ำทั้งสามอย่างร่วมกัน (pancytopenia) และมีต่อมน้ำเหลืองโตทั่วไปนั้น นับว่าหาได้ยากมากจึงได้เขียนรายงานผู้ป่วยรายนี้ขึ้นผู้ป่วยเป็นหญิงไทย อายุได้ 51 ปี มาพบแพทย์ด้วยการมีจ้ำเลือดทั่ว ๆ ไป ร่วมกับอาการน้ำหนักลด และต่อมน้ำเหลืองโตทั่ว ๆ ไป โดยไม่มีไข้ ภายในระยะเวลาเพียง 2-3 สัปดาห์ ตรวจร่างกายก็พบว่าต่อมไธรอยด์โตสม่ำเสมอทั่ว ๆ และมีต่อมน้ำเหลืองโตขนาด 1.5-2 เซนติเมตร ทั่วร่างกายจากการตรวจเลือดก็พบว่าเซลล์เม็ดเลือดต่ำทั้งสามชนิด จนเหลือ Hb 8.1 g%, WBC 1,700/mm^3, platelet 4,000/mm^3, absolute neutrophil count 510/mm^3, TSH >100 uIU/mL, FT3 1.15 pg/dL, FT4 0.2 ng/dL, ทดสอบหา anti-thyroglobulin และ anti-thyroperoxidase antibodies ต่างให้ผลบวก ตรวจชิ้นเนื้อไขกระดูกพบว่าปกติทั้งสามอนุกรม แต่ไม่มีเหล็กสะสมเลยส่วนผลชิ้นเนื้อจากต่อมน้ำเหลืองพบเพียง reactive hyperplasia เท่านั้น ในที่สุดจึงให้การวินิจฉัยว่าเป็นโรคไธรอยด์ต่ำปฐมภูมิ เนื่องจากระบบภูมิคุ้มกันต่อต้านตนเอง และหลังจากรักษาด้วย L-thyroxine 100 mcg ต่อวัน โดยไม่ต้องใช้ corticosteroid เลยภายใน 2-3 เดือน ต่อมน้ำเหลือง ทั้งหลายเริ่มเล็กลง และภาวะเม็ดเลือดต่ำทั้งสามอย่างร่วมกัน ก็กลับเป็นปกติได้แม้ว่าความสัมพันธ์โดยตรงระหว่างภาวะต่อมน้ำเหลืองโตทั่วไป กับภาวะฮอร์โมนไธรอยด์ต่ำปฐมภูมิ จะยังไม่สามารถชี้ชัดได้ก็ตามแต่ทั้งสองภาวะอาจจะมีพยาธิกำเนิดแบบภูมิคุ้มกันต่อต้านตนเองร่วมกันก็ได้

คำสำคัญ: ต่อมน้ำเหลืองโตทั่วไป, เม็ดเลือดต่ำโดยรวม, ภาวะฮอร์โมนไธรอยด์ต่ำปฐมภูมิ

Introduction

Primary hypothyroidism is characterized by the decreased function of the thyroid gland due to the pathology of the thyroid gland itself. One of its common pathogenesis is the autoimmune disease of the thyroid glandin which thesingle or multiplelymphadenopathiesmay be foundupto 23% and most of them are pathologically demonstrated to be reactive lymphoid hyperplasia[1]. However, there is no correlation between lymphadenopathy, age, thyroid volume and nodularity, or autoantibody levels. And during follow-up, the lymphadenopathies remain stable in the majority of cases while theyspontaneously decrease in size in the rest[2]. Besides the reactive lymphoid hyperplasia, malignant diseases of the enlarged lymph nodes such ascentroblastic lympho-mamay also be occasionally found.

Various kinds of anemia are commonly found in the patients with hypothyroidism, in one study of 60 cases with anemia in hypothyroidism from India, normocytic, normochromic anemia is present in 31 patients (51.6%) followed by microcytic anemia in 26 patients (43.3%). Six (10%) havemegaloblastic anemia with vitamin B12 deficiency including 3 cases of pernicious anemia. Two have combined deficiency

of iron and vitamin B12 anemia[3]. Anemia is found even in cases of subclinical hypothyroidism with the frequency as in the overt hypothyroidism. Therefore, suspicion of hypothyroidism should be considered in cases with anemia with uncertain etiology[4].

Pancytopenia is rarely seen in hypothyroidism[5], furthermore the pancytopenia in combination with generalized lymphadenopathy in primary hypothyroidism has not been mentioned. Herein, we report such as case.

Case Report

A 53-year-old Thai woman presented with generalized purpurawith a significant weight lossfor a few weeks, no fever. BP 140/90, heart rate 90/min, BT 36.9 degree Celsius. The physical examination confirmed petechiae and ecchymoseswith gum oozing and pallor. The enlarged lymphadenopathies 1.5-2.0 cm in size, firm consistency, no tenderness, were found at bilaterally cervical and axillary regions. She had no goiter or no hepatosplenomegaly.

Investigations included: Hb 9.1 g%, Hct 27.4%, WBC 1,600/mm^3, platelet 6,000/mm^3, N 47.6 %, L 39.2 %, MCV 78.4 fL, MCH 26.0 pg, MCHC 33.1 g%, RDW 16.0%, BUN 9.0 mg%, creatinine 1.08 mg%, albumin 3.4 g%, globulin 5.3 g%, cholesterol 128 mg%, direct bilirubin 0.3 mg%, total bilirubin 1.2 mg%, AST 36 U/L, ALT 24 U/L, alkaline phosphatase 245 U/L, triglyceride 198 mg%, Na 135.2 mEq/L, K 3.5 mEq/L, Cl10 2.2 mEq/L, HCO3 22.0 mEq/L, FBS 72 mg%, LDH 774 U/L

FT_4 0.2ng/dL (normal 0.93-1.7), FT_3 1.15 pg/mL (normal 2.39-6.79), TSH >100 uIU/mL (normal 0.4-4.5), anti-HIV, VDRL, HBsAg and anti-HCV were all negative.

The bone marrow biopsy showedthe normal cellularity in all trilineage, and the flow cytometry revealed no immunophenotypic evidence of mature B cell non-Hodgkin lymphomaand the absence of iron storage. The chromosome study showed she was normal female.

The computerized tomographyof the chest and the abdomen showed 2 small pulmonary nodules in RML and RLL, and multiple mediastinaland hilarnodes and intra-abdominal lymphadenopathies, 1-2 cm in diameter and mild splenomegaly.

The pathology of a lymph node from the submental areavealedthe reactive lymphoid hyperplasia, normal distribution for CD3 and CD20 reactive lymphoid cells.

She was finally diagnosed as having primary-hypothyroidism with generalized lymphadenopathies with pancytopenia. And she was treated with L-thyroxin 150 microgram/day, all enlarged lymph nodes were gradually diminished and pancytopenia became nearly normal within 3 months. And the CBC showed, Hb 10.5 g%, Hct 32.2 %, WBC 6,400/mm^3, platelet 191,000/mm^3, MCV 75.9 fL, MCH 24.8 pg, MCHC 32.7 g%, RDW 14.9 %, N 44.0 %, L 49.8 %. At 6 months after treatment, Hb 11.7 g%, Hct 36.2 %, WBC 6,600/mm^3, platelet 225,000/mm^3, MCV 70.6 fL, MCH 22.9 pg, MCHC 32.5 g%, RDW 17.3 %, N 58.2 %, L 36.5 %, TSH 2.21 uIU/mL.

Discussion

Our case is proved to be primary hypothyroidism based on the combination of low free T_3, low free T_4 and strikingly high TSH levels. But the presence of the autoimmune disease of the thyroid gland and IgG4 antibody, the most common cause of

hypothyroidism, is not proven. Furthermore, her goiter is not present. Therefore Hashimoto's thyroiditiscould not be concluded[6].

The centroblastic lymphoma[2] as well as the reactive lymphoid hyperplasia may be found in caseswith hypothyroidism especially in Hashimoto thyroiditis, thereforethe biopsy of the enlarged lymph node in these patients is necessary before making any conclusion.

The normochromic normocytic anemia or anemia of chronic disease is the most common hematologic complication in hypothyroidism[7] whereas the pancytopenia with normocytosis is the very rare entity[8]. Pernicious anemia due to antibody against intrinsic factor that may be found in primary hypothyroidism, can affect the hematopoiesis in the bone marrow, leading to the pancytopenia with-megaloblastosis[9]. But our case shows only mild micromocytosisand mild hypochromia (MCV 75.9 fL, MCH 24.8 pg), therefore she is believed to be free from vitamin B12 deficiency even though its serum level has not been explored.

The combination ofthe reactive lymphoid hyperplasia of generalized lymphnodesand pan-cytopenia with normocytosis in our case is proposed to be one of unusual manifestations of primary hypothyroidism.

In case of the enlarged thyroid gland with surrounding palpable cervical lymph nodes, malignancy of the thyroid gland should be firstly excluded[10]. On the contrary, generalized lympha-denopathies in Hashimoto's thyroiditis should signify the malignant disease of the lymphoid tissuewhich is more commonly found in any case suffering from the immune derangement[11,12]. Furthermore, lymphoma of the thyroid gland itself may be more commonly found in the gland that used to be Hashimoto's thyroiditis[13].

Conclusion

A 51-year old woman is found to have the clinical syndrome of generalized lymphadenopathies, pancytopenia and full blown hypothyroidism without the thyroid gland enlargement. The associations among these entities are proposed because the generalized lymphadenopathy and the pancytopenia are improved afterthe treatment with L-thyroxin.

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