Thrombotic Thrombocytopenic Purpura with Hashimoto Thyroiditis: A case Report

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Abstract: Hashimoto's thyroiditis (chronic lymphocytic thyroiditis) and thrombotic thrombocytopenic purpura (TTP) similarly have an autoimmune process as the basic pathogenesis. A case of 89-year-old Thai woman is found to have the history of sudden onset of left hemiparesis as the transient ischemic attack just few hours before admission, microangiopathic hemolytic anemia, thrombocytopenia with multiple purpura, high serum LDH, and mild renal impairment, the classical pentad of TTP, with the severe deficiency of plasma ADAMTS 13 factor activity. The computerized tomography of the brain does not show any intracerebral hemorrhage, just only multiple lacunar infarcts. Her underlying disease is long term well controlled Hashimoto's thyroiditis and hypertension. She responds well to the repeated plasma exchange transfusion and oral corticosteroid. Her clinical and all laboratory manifestations become normal within one month. The occurrence of TTP in case of Hashimoto's thyroiditis may signify their association as the autoimmune diseases but different autoantibodies with different targets, anti-thyroglobulin and anti-thyroperoxidase with thyroid cell destruction in Hashimoto's thyroiditis and anti-ADAMTS13 factor leading to ADAMTS13 factor deficiency in TTP.

บทคัดย่อ: **Thrombotic Thrombocytopenic Purpura ในผู้ป่วย Hashimoto Thyroiditis: รายงานผู้ป่วย 1 ราย**

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Hashimoto's thyroiditis หรือ chronic lymphocytic thyroiditis และ thrombotic thrombocytopenic purpura (TTP) ต่างก็เป็นโรคที่มีพยาธิกำเนิดมาจากขบวนการภูมิคุ้มกันต่อต้านตนเองเช่นเดียวกัน ในรายงานนี้เป็นผู้ป่วยหญิงไทย อายุ 89 ปี มีอาการอัมพฤกษ์ซีกซ้ายกะทันหัน ไม่กี่ชั่วโมงก่อนรับตัวไว้รักษา แต่เป็นชั่วขณะ ร่วมกับอาการแสดงอื่น ๆ เช่น microangiopathic hemolytic anemia, ภาวะเกล็ดเลือดต่ำพร้อมกับมีจ้ำเลือดตามตัว, มี LDH ในเลือดสูง และไตเสื่อมเพียงเล็กน้อย, ทั้งหมดนี้เป็นลักษณะสำคัญ 5 ประการของโรค TTP ผู้ป่วยมีภาวะขาดปัจจัย ADAMTS13 ในเลือดอย่างรุนแรง เอกซเรย์คอมพิวเตอร์สมองไม่พบภาวะเลือดออกในสมอง พบเพียงจุดที่สมองขาดเลือดหลายจุด ก่อนหน้านี้ผู้ป่วยเป็นโรค Hashimoto's thyroiditis และความดันโลหิตสูง ที่ได้รับการรักษาอย่างต่อเนื่องมานานแล้ว ผู้ป่วยตอบสนองดีต่อการรักษาด้วยการแลกเปลี่ยน plasma ทั้งหมด 5 ครั้ง ร่วมกับการให้ผู้ป่วยรับประทานยา steroid ผู้ป่วยตอบสนองต่อการรักษาดีภายใน 1 เดือน ผลการตรวจทางโลหิตกลับเป็นปกติ การพบ TTP ในผู้ป่วย Hashimoto's thyroiditis บ่งว่าทั้งสองโรคอาจจะมีความเกี่ยวข้องกันในฐานะเป็นโรคกลุ่ม autoimmune เหมือนกันแต่แตกต่างกันตรงชนิดของ autoantibodies และเนื้อเยื่อเป้าหมายของการทำลายต่างกัน นั่นคือพบ anti-thyroglobulin และ anti-thyroperoxidase ทำลายเซลล์ของต่อมธัยรอยด์ในโรค Hashimoto's thyroiditis แต่พบ anti-ADAMTS13 factor ทำลาย ADAMTS13 factor จนหมดในโรค TTP

Introduction

Hashimoto's thyroiditis (HT or chronic lympho-cytic thyroiditis) is the inflammatory disease of the thyroid gland mainly from the organ specific T cell mediated autoimmune pathogenesis. Its clinical manifestations 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 or thyroglobulin (Tg), and the thyroid peroxidase (TPO). HT can be often found to coexist with other autoimmune diseases such as type 1 diabetes mellitus, rheumatoid arthritis, multiple sclerosis, vitiligo, including an autoimmune polyendocrine syndrome type 2, which is usually defined by the occurrence of two or more of the following: Addison's disease, autoimmune thyroid disease and/or type 1 DM[1]. The slow reacting autoimmune diseases that can be found in cases of HT include pernicious anemia, Addison's disease, vitiligo, Simmond's panhypopituitarism, etc but thrombotic thrombocytopenic purpura (TTP) has still rarely been reported.

TTP is clinically characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia with or without neurological deficit[2]. Other findings may include the high LDH and fever. An acquired deficiency of plasma ADAMTS13 activity due to its autoantibody, defined as < 10% of normal, is a common characteristic in TTP[3,4]. Actually the ADAMTS13 factor is needed to cleavage the large multimer of von Willebrand factor for the prevention of the over-aggregation of platelet leading to formation of microthrombi in the arteries. It can happen itself or can be found secondarily to be associated with other autoimmune diseases such as HT, SLE, psoriasis and celiac disease[5]. Herein we report one case of TTP found in HT.

Case Report

A Thai 89 year old female was referred to hematologist because of the sudden onset of left hemiparesis, multiple ecchymoses at trunk and limbs with thrombocytopenia. Her underlying diseases had been well controlled Hashimoto's thyroiditis (HT) for many years and hypertension. Her current drugs consisted of amlodipine (5 mg), atenolol (50 mg), and simvastatin (10 mg).

On physical examination, she had some degree of confusion with irrelevant speech and completely recovered from left hemiparesis, BT 37.0 deg Celsius, BP 120/90 mmHg, multiple ecchymoses 1-2 cm at chest wall, and limbs.

The blood tests: WBC 22,700/mm^3, Hb 9.8 g%, Hct 29.4 %, MCV 89.0 fL, MCH 29.7 pg, RDW 16.1%, platelet 80,000/mm^3 N 75%, L 15%, M 9%, and frequent fragmented red blood cells on peripheral blood smear.

FBS 91 mg%, cholesterol 137 mg%, triglyceride 146 mg%, HDL 26 mg%, LDL 82 mg%, BUN 28.0 mg%, creatinine 1.34 mg%, GFR 37 ml/min/m^2, LDH 973 IU, CK-MB 2 CPK 42, troponin-I 0.11, TSH 6.31

Plasma ADAMTS13 factor activity <3%, VDRL-ve, ANA homogeneous+ve 1:80 AFP 1.42, CEA 0.98, CA-125 14.5 (0-35 u/mL), CA19-9 3.1 (0-37 U/mL), normal urinalysis, morning cortisol 7.35, anti-thyroglobulin >4,000 IU/ml (normal 0-115 IU/ml), anti-microsomal antibody >600 IU/ml (normal 0-34 IU/ml)

The computerized tomography of the brain revealed the multiple small lacunar infarcts.

The final diagnosis was thrombotic thromyboctopenic purpura and the underlying diseases were Hashimoto's thyroiditis and hypertension.

The treatment for TTP consisted of plasma ex-change transfusion for 5 times, and oral prednisolone.

Within one month, she completely recovered, no new ecchymosis or neurological deficit, WBC 14,100/mm^3, Hb 14.0 g%, Hct 41.1%, MCV 88.9 fL, MCH 30.3 pg, RDW 14.1 %, platelet 221,000/mm^3, FT4 0.4, TSH 3.868, LDH 393, creatinine 1.12 mg%.

Discussion

Our case is diagnosed as TTP because she fulfills nearly all classic criteria, viz., she has (i) micro-angiopathic hemolytic anemia (Hb 9.8 g%), (ii) thrombocytopenia (platelet 80,000/mm^3), (iii) CNS involvement: hemiplegia and confusion, and (iv) renal involvement (creatinine level 2.2 mg%) and strongly confirmed by the deficiency of ADAMTS13 factor[6].

The development of TTP in the case of HT may signify their association because both of them similarly have the autoimmune processes as the main basic pathogenesis. However each disease has its own autoantibodies specific to different target tissues. In HT, nearly all patients have antibodies against thyroid tissues such as anti-Tg or anti-TPO but the apoptotic destruction of the thyroid cells is mainly the role of the activating cytotoxic T cells[7]. On the other hand, TTP has autoantibody (IgG) specific to ADAMTS13 factor leading to the deficiency of ADAMTS13 factor[8]. In fact, among five autoimmune diseases which are significantly found in cases of TTP, HT, SLE, ITP, psoriasis and celiac disease, the first one is the most common with the HLA-based connection of both diseases that are possibly proposed[5].

Our case develops TTP after hypothyroidism

of HT has been well controlled with eltroxin for many years. In fact, only the problem of hypothyroidism in HT is concerned while its underlying autoimmune process is still left to continue (anti-Tg >4,000) and this may explain why the new autoimmune diseases can occur such as TTP as in our case, SLE[9], rheumatoid arthritis, pernious anemia, Addison's disease, celiac disease and vitiligo[10].

Our case is treated with prednisolone and the plasma exchange that is considered effective treatment of TTP because it can remove the ADAMTS13 autoantibodies and UL-vWFMs, and also supply the ADAMTS13 factor[8].

Conclusion

An 89-year-old Thai woman develops full blown thrombotic thrombocytopenic purpura consisting of neurological deficit, microangiopathic hemolytic anemia, thrombocytopenia, high serum LDH and mild renal impairment with underlying Hashimoto's thyroiditis and hypertension. Her diagnosis is confirmed by the severe deficiency of the ADAMTS13 factor activity. She responds well to multiple plasma exchange transfusion and oral steroid. Her clinical and laboratory manifestations become normal within one month after therapy.

References

1. Chistiakov DA. Immunogenetics of Hashimoto's thyroiditis. *J Autoimmune* Dis 2005, 2:1 doi: 10.1186/1740-2557-2-1.
2. George JN. Diagnosis of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome in adults. In: Up ToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2013.
3. Tsai HM. Pathophysiology of thrombotic thrombocytopenic purpura. Int J Hematol 2010; 91: 1-19.
4. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. Blood 2010; 116: 4060-9.
5. John ML, Scharrer I. Autoimmune disorders in patients with idiopathic thrombotic thrombocytopenic purpura. Hamostaseologie 2012; 32 Suppl 1: S86-9.
6. George JN, Al Nouri ZL. Diagnostic and therapeutic challenges in the thrombotic hrombocytopenic purpura and hemolytic uremic syndromes. Am Soc Hematol Book 2012; 2012: 604-9.
7. Davies TF. Pathogenesis of Hashimoto's thyroiditis (chronic autoimmune thyroiditis). In: UpToDate, Basow DS (Ed), Waltham MA, 2008.
8. Matsumoto M. Anti-ADAMTS13 autoantibodies in patients with thrombotic thrombocytopenic purpura. Nihon Rinsho Meneki Gakkai Kaishi 2013; 36: 95-103.
9. Kobak S, Hudaverdi O, Keser G, Oksel F. Coexistence of systemic lupus erythematosus, Hashimoto's thyroiditis and IgA nephropathy in the same patient. Mod Rheumatol 2011; 21: 89-91.
10. Boelaert K, Newby PR, SiSmmonds MJ, Holder RL, Carr-Smith JD, Heward JM, et al. Prevalence and relative risk of other autoimmune diseases in subjects with autoimmune thyroid disease. Am J Med 2010; 123: 183.e1-9.