

## Pancytopenia in severe hyperthyroidism : A case report

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*Pancytopenia is very rare in hyperthyroidism. We report here a 66-year-old man presenting with pancytopenia in severe hyperthyroidism. This case shows the relationship of severity of pancytopenia and degree of hyperthyroidism. Pancytopenia recovers after administration of anti-thyroid drugs. Therefore, anti-thyroid drug should not be contraindicated for the treatment of hyperthyroidism in the setting of pancytopenia.*

**Keywords :** *Pancytopenia, Hyperthyroidism.*

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ภาวะแพนไซโตพีเนียพบได้น้อยมากในผู้ที่มีภาวะธัยรอยด์เป็นพิษรุนแรง คณะผู้นิพนธ์ได้รายงานผู้ป่วยชายอายุ 66 ปี มาด้วยภาวะแพนไซโตพีเนียโดยที่มีภาวะธัยรอยด์เป็นพิษรุนแรงร่วมด้วย พบว่าความรุนแรงของภาวะแพนไซโตพีเนียสัมพันธ์กับระดับความรุนแรงของภาวะธัยรอยด์เป็นพิษ และภาวะนี้สามารถดีขึ้นหลังจากได้รับยาต้านธัยรอยด์ ดังนั้นยาต้านธัยรอยด์ไม่ควรเป็นข้อห้ามใช้ในการรักษาผู้ป่วยธัยรอยด์เป็นพิษที่มีภาวะแพนไซโตพีเนียร่วมด้วย

**คำสำคัญ :** ภาวะแพนไซโตพีเนีย, ภาวะธัยรอยด์เป็นพิษ

Hyperthyroidism can affect single lineage abnormality in hematology, e.g., anemia; however, pancytopenia is very rare. We, hereby, report a man presenting with pancytopenia in severe hyperthyroidism. Pancytopenia recovers after administration of anti-thyroid drugs. The pathogenesis of pancytopenia in thyrotoxicosis is poorly understood. A review of the literature and possible pathophysiological mechanisms are discussed.

### Case Report

A 66-year-old-man presented with anorexia and diarrhea for 2 months. He had no palpitation nor excessive sweating. His weight decreased 15 kg in 2 months. He had developed icteric sclera for 1 week prior to admission. On admission he was a febrile with blood pressure of 110/80 mmHg. Heart rate was 84/min, with total irregularity. He had normal mental status. His conjunctiva was moderately pale. He had icteric sclera, warm and moist skin. Thyroid gland was about 20 g. His complete blood count (CBC) showed a white blood count (WBC) of 2,600 / mm<sup>3</sup> an absolute neutrophil count(ANC) of 685/ mm<sup>3</sup>, hemoglobin (Hb) of 10.0 g/dL, mean corpuscular volume (MCV) of 82.5 fL and platelet of 57,000 / mm<sup>3</sup>. There is no evidence of hemolysis from peripheral blood smear. His bone marrow aspiration and biopsy were adequate. Megakaryocytes, myeloid precursors and erythroid precursors were present in normal numbers with normal morphology. Iron stores were normal. No megaloblast or macrophage activation were identified. Liver function tests were as followed: direct bilirubin 6.1mg/dL (0.0-0.4); total bilirubin 10.9mg/dL(0.0-1.1); ALP 127 IU/L (32-92); SGOT 44 IU/L(10-42); SGPT 20 IU/L(10-40). The ultrasonography of

whole abdomen was normal. His thyroid function tests revealed a pattern of primary hyperthyroidism: TSH <0.027  $\mu$ IU/ml (0.27-4.2); FT4 4.98 ng/dl (1.01-1.79); FT3 13.36 pg/ml (2.57-4.43). Anti-thyroid drug (propylthiouracil 150 mg 3 times daily) was started for 2 months. Thyroid scintigraphy showed changes consistent with Graves' disease. A 24-h RAI uptake revealed 85 % uptake. The patient underwent treatment with 5 mCi of I<sup>131</sup> orally. He had clinical improvement. And the improvements of his blood counts were correlated to the degree of hyperthyroidism.

He is currently mild hyperthyroid (FT4 1.47 ng/dl, FT3 5.75 pg/ml. His complete blood counts (CBC) showed a white blood count (WBC) of 3,160/ mm<sup>3</sup> an absolute neutrophil count (ANC) of 1,780/ mm<sup>3</sup> hemoglobin (Hb) of 15.7 g/dl, and platelet of 106,000 / mm<sup>3</sup>.

### Discussion

Hyperthyroidism can affect single lineage abnormality in hematology; however, pancytopenia is very rare. Anemia occurs in 10 % to 25 % of hyperthyroid patients which may be normocytic, microcytic or macrocytic and usually mild.<sup>(1)</sup> Causes of anemia in hyperthyroidism are ineffective erythropoiesis or deficiency of iron, vitamin B12 and folate.<sup>(2)</sup> Granulocytopenia occurs in about 20 % of hyperthyroid patients. In a study of 63 patients with thyrotoxicosis, 27 % of patients had a granulocyte count less than 1,500 / mm<sup>3</sup>, 57 % of patients had a granulocyte count of 2,000-4,000 / mm<sup>3</sup> and the mean granulocyte count was 3,100 / mm<sup>3</sup> compared with 3,600 / mm<sup>3</sup> in normal subjects.<sup>(3)</sup> Hypothesis of granulocytopenia is the antigen crossing between TSH receptors and polymorphonuclear neutrophils.<sup>(4)</sup>

Others have suggested that in hyperthyroidism the granulocytes have a decreased circulating time.<sup>(5)</sup> Many studies found that the granulocyte count rises during antithyroid drug treatment. Thrombocytopenia is also observed in thyrotoxicosis patients. In a study, 42 % of thyrotoxicosis patients have platelet count less than 150,000 / mm<sup>3</sup>. Patients with Graves' disease occasionally has clinically important thrombocytopenia (platelet count below 100,000/ mm<sup>3</sup> ).<sup>(6)</sup> Thrombocytopenia may be immunologically mediated, e.g., antiplatelet antibodies in autoimmune thrombocytopenic purpura. Thyroid antibodies may be reactive with proteins on platelets and thyrotoxicosis itself may increase the phagocytic activity of the reticuloendothelial system. Thrombocytopenia also improves during antithyroid therapy.

Five cases of pancytopenia are reported in the literature.<sup>(5)</sup> Three patients had mild pancytopenia which responded completely to antithyroid therapy. One case was hyperthyroidism during autologous stem-cell transplantation for multiple myeloma. This case had a prolonged period of pancytopenia post-transplantation but after antithyroid therapy pancytopenia showed sustained improvement.<sup>(5)</sup> Another case is the pediatric patient with chronic relapsing severe aplastic anemia and delayed diagnosis of Graves' disease. There is low prevalence of Graves' disease in young boy, and no reported association between severe aplastic anemia and Graves' disease has been reported in a child before. The treatment in the young boy includes immunosuppressive and radioactive ablation of thyroid gland. Anti-thyroid drugs were not used in the young boy due to the precaution of agranulocytosis

from anti-thyroid drugs.<sup>(7)</sup> But our case shows that pancytopenia is correlated with the degree of hyperthyroidism itself, therefore, anti-thyroid drug may not be contraindicated in pancytopenic patients with thyrotoxicosis.

The pathogenesis of pancytopenia in thyrotoxicosis is poorly understood. The postulated pathogenesis of pancytopenia is the immunologic or toxic effect of thyroid hormone that disturbs maturation and differentiation of the pluripotential stem cell.<sup>(6)</sup> Two of previous reports found the bone marrow showed macrophage activation.<sup>(6)</sup> Some authors suggest that pancytopenia in thyrotoxicosis is only coincidence of two autoimmune diseases (aplastic anemia and Graves'disease). However a case shows that pancytopenia can occur with normocellular marrow and the severity of pancytopenia is closely correlated to the degree of hyperthyroidism, therefore, pancytopenia probably results from toxicity of thyroid hormone itself.

## References

1. Fein HG, Rivlin RS. Anemia in thyroid diseases. *Med Clin North Am* 1975 Sep;59(5): 1133-45
2. Iitaka M, Noh JY, Kitahama S, Fukasawa N, Miura S, Kawakami Y, Kawasaki S, Yamanaka K, Ishii J, Katayama S, et al. Elevated serum granulocyte colony-stimulating factor levels in patients with Graves' disease. *Clin Endocrinol (Oxf)* 1998 Mar;48(3): 275-80
3. Adrouny A, Sandler RM, Carmel R. Variable presentation of thrombocytopenia in Graves' disease. *Arch Intern Med* 1982 Aug;142(8): 1460-4

4. Weitzman SA, Stossel TP, Harmon DC, Daniels G, Maloof F, Ridgway EC. Antineutrophil autoantibodies in Graves' disease. Implications of thyrotropin binding to neutrophils. *J Clin Invest* 1985 Jan;75(1): 119-23
5. Shaw B, Mehta AB. Pancytopenia responding to treatment of hyperthyroidism: a clinical case and review of the literature. *Clin Lab Haematol* 2002 Dec;24(6):385-7
6. Braverman EL, Utiger DR. The blood in thyrotoxicosis. In: Braverman EL, Utiger DR, eds. *Werner & Ingbar's The Thyroid: A Fundamental and Clinical Text*. 8<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins, 2000: 627-30
7. Kumar M, Goldman J. Severe aplastic anaemia and Grave's disease in a paediatric patient. *Br J Haematol* 2002 Jul;118(1):327-9