NOTE

A Case of Thyrotoxicosis with Pancytopenia

TAKESHI SOEKI, YOSHIYUKI TAMURA, NORIYASU KONDO, HISANORI SHINOHARA, HIDEJI TANAKA, KANJI BANDO AND NOBUO FUKUDA

Department of Internal Medicine and Clinical Research, National Zentsuji Hospital, Senyu-cho 2–1–1, Zentsuji, Kagawa 765–8507, Japan

Abstract. We report a 49-year-old man with primary hyperthyroidism who presented with pancytopenia. The patient presented with leg edema, sinus tachycardia, cardiomegaly, and pleural effusions, all from congestive heart failure. Laboratory data showed pancytopenia and primary hyperthyroidism; echocardiogram showed diffuse hyperkinesis of the left ventricular wall and right ventricular overloading. The bone marrow was moderately hypercellular and compatible with arrested hematopoiesis. Pancytopenia and heart failure improved after administration of methimazole and diuretics. However, high levels of thyroid hormone recurred with pancytopenia 4 months after admission. Therefore, subtotal thyroidectomy was performed, and the levels of thyroid hormones and peripheral blood cell counts have remained normal. Pancytopenia may be caused by hyperthyroidism.

Keywords: Thyroid, Pancytopenia, Hematopoiesis

(Endocrine Journal 48: 385–389, 2001)

THYROID hormone stimulates the production of erythrocytes via erythropoietin [1] and by stimulating hemopoietic stem cells directly [2]. Patients with hypothyroidism demonstrate anemia, but there are few reports of hematologic disorders, such as iron deficiency anemia [3], pernicious anemia [4, 5], or idiopathic thrombocytopenic purpura [6–8], in patients with hyperthyroidism.

We report here an interesting case of hyperthyroidism with severe anemia, leukocytopenia, and thrombocytopenia, all of which were resolved with successful treatment of the endocrinopathy.

Case Report

A 49-year-old man presented with leg edema of 1 month duration. The patient was 159 cm tall and weighed 54 kg. Blood pressure was 114/52 mmHg, pulse rate 100/min regular, and temperature 36.4°C. He was pale, but not icteric. A rubbery firm diffuse goiter was palpated. Decreased breath sounds were noted over the lower region of the right lung, but auscultation of the heart sound was normal. There was no abnormality in the abdomen. There was moderate edema of the legs and feet.

Laboratory data on admission are shown in Table 1. Urinalysis was normal. The peripheral blood smear showed pancytopenia. Anemia was normocytic and normochromic. Blood chemistries revealed decreased concentrations of triglyceride and total cholesterol, and slight elevation of alkaline phosphatase. There was a mild decrease in serum iron and ferritin. Thyroid function tests showed abnormally high concentrations of free T₃ (FT₃) and free T₄ (FT₄) (FT₃: 11.4 pg/ml, FT₄: 5.8 ng/ml), with a thyroid stimulating hormone (TSH) concentration below the detection limit. High concentrations of thyroglobulin (Tg), antibodies to thyroid peroxidase (TPOab), TSH-binding inhibiting immunoglobulin (TBII), and thyroid stimulating antibody were found. The serum erythropoietin level was...
high, and haptoglobin was low. Direct and indirect Coombs tests were negative. Antinuclear antibodies were negative and complement hemolytic activity was within the normal range. Both platelet surface-associated IgG (PA-IgG) and free antibodies to platelets were negative. Plasma concentrations of atrial and brain natriuretic peptides were mildly and markedly increased, respectively. Plasma
levels of prothrombin time and fibrinogen were decreased and activated partial thromboplastin time was prolonged, but plasma level of fibrin degradation products was within normal limit. The bone marrow was moderately hypercellular with normal megakaryocytes and almost normal myeloid and erythroid differentiation (nucleated cell count: 34.3 × 10⁴/µl), compatible with arrested hematopoiesis. There were no findings of chromosomal aberrations indicating a myelodysplastic syndrome (MDS).

Chest roentgenogram on admission showed marked cardiomegaly (cardiothoracic ratio (CTR) = 69%) and mild bilateral pleural effusions with mild pulmonary congestion. An electrocardiogram on admission revealed sinus tachycardia, low voltage in the limb leads, and slight ST segment depression in leads V₅ and V₆. Echocardiogram showed diffuse hyperkinesis of the left ventricular wall and right ventricular overloading.

Ultrasound tomogram of the thyroid showed mild diffuse enlargement with a regular parenchymal pattern. Scintigram of the thyroid revealed increased radiiodine uptake (55.6% at 24 hours). Abdominal ultrasonogram showed no abnormal findings including hepatosplenomegaly.

From these results, the patient was diagnosed with congestive heart failure associated with primary hyperthyroidism. However, the origin of pancytopenia was unclear on admission. Diuretics improved the edema and the pulmonary findings within 1 month. An antihyperthyroid drug (thiamazole; dose at initiation: 30 mg/day) was started. His FT₃ and FT₄ levels decreased gradually and pancytopenia improved after 3 months. However, high levels of FT₃ and FT₄ recurred immediately after reduction of thiamazole, as did pancytopenia at 4 months after admission. The patient did not have symptoms suggestive of thyroid crisis at that time. Injection of thiamazole 60 mg/day and the use of lugol fluid stabilized his FT₃ and FT₄ concentrations and pancytopenia. Subtotal thyroidectomy was performed (Fig. 1). The resected thyroid weighed 46 g on the left lobe and 44 g on the right. Histopathologic findings showed cuboid cylindrical follicular epithelial cells, mamilliform proliferation, and vacuoles in the marginal part of the colloid, compatible with Basedow's disease. After thyroidectomy, the TSH level increased to the normal range, and FT₃, FT₄, and peripheral blood counts maintained normal levels without antihyperthyroid drugs.

**Discussion**

This patient presented with hyperthyroidism and pancytopenia. Cell counts fluctuated with thyroid function. He had received no drugs before admission. Bone marrow showed arrested hematopoiesis and no signs of MDS. These results suggest that pancytopenia was caused by hyperthyroidism.

The prevalence of anemia among patients with hyperthyroidism ranged from 10 to 15% [9]. In association with hyperthyroidism, iron deficiency anemia [3], pernicious anemia [4, 5], and hemolytic anemia have been reported. Our patient had mild iron deficiency, but this did not cause severe anemia since his red blood cell remained normocytic and normochromic. Vitamin B₁₂ was normal. Hemolytic anemia was not present, and Coombs tests were negative. The pathogenesis of anemia in hyperthyroidism could be caused by impaired utilization of iron [10] or shortened survival time of erythrocytes [11, 12]. In this patient, neither ferrokinetics nor survival times were measured. However, these disorders may demonstrate arrested hematopoiesis. Decreased haptoglobin level in the present case might be due not to hemolysis but to arrested hematopoiesis.

With regard to thrombocytopenia with hyperthyroidism, autoimmune mechanisms such as idiopathic thrombocytopenic purpura are associated with hyperthyroidism [6-8]. Hypersplenism may also link thrombocytopenia and hyperthyroidism [13]. In the present case, high titers of Tg and TPOAb, TBI, and thyroid stimulating antibody were present, whereas antinuclear antibodies, platelet antibodies, and complement hemolytic activity were unrevealing. These findings do not suggest an autoimmune mechanism for thrombocytopenia in this patient with hyperthyroidism. The findings of decreased plasma level of prothrombin time, prolonged activated partial thromboplastin time, and decreased plasma fibrinogen level in the present case support potential existence of disseminated intravascular coagulation causing thrombocytopenia. However, plasma level of fibrin degradation products were not increased and there were no fundamental diseases causing disseminated intravascular coagulation and symptoms.
suggestive of bleeding tendency in the present case, which may deny the existence of disseminated intravascular coagulation. Decreased plasma levels of prothrombin time and prolonged activated partial thromboplastin time may be due in part to persistent diarrhea before admission.

Leukopenia may complicate hyperthyroidism (before starting antithyroid treatment) but is usually associated with pancytopenia [14–17]. All of these cases demonstrated an improvement in cell counts with improvement of thyroid function, similar to the clinical course in the present case. These findings support the thyrotoxic state itself causing the arrested hematopoiesis which leads to pancytopenia. Recently, Kinjo et al. reported a case of Graves’ disease complicated with MDS, in which thiamazole improved pancytopenia [17]. In their report, diagnosis of MDS was made on the basis of characteristic chromosomal aberration and increased ringed sideroblasts in bone marrow. However, the present case had no findings indicating MDS. Another pathogenic mechanism for pancytopenia might be reduced survival of blood cells due to hypersplenism induced by hyperthyroidism. In fact, patients with primary hyperthyroidism may have hypersplenism [18]. Although organic hepatosplenomegaly was not found in the present case, it could not be denied that functional hypersplenism caused the reduced lifespan of blood components. It was not considered that dilution by increased circulating plasma volume associated with congestive heart failure caused pancytopenia in the present case because edema and pulmonary findings were improved in spite of persistent pancytopenia 1 month after the treatment.

Further studies are needed to clarify the unexplained mechanisms of pancytopenia associated with hyperthyroidism.
References


