Case Report

Hyperthyroidism Associated with Autoimmune Hemolytic Anemia and Periodic Paralysis: A report of a case in which antihyperthroid therapy alone was effective against hemolysis

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We describe a case of a 29-year-old man with hyperthyroidism associated with autoimmune hemolytic anemia and periodic paralysis. Euthyroidism, which was achieved by propylthiouracil, brought inhibition of hemolysis and amelioration of anemia in spite of continuously positive direct and indirect Coombs' tests. Neither adrenocortical steroid nor blood transfusion was administered. Since indirect monospecific Coombs' test was negative against anti-human complements serum, the membrane of red blood cells may be less fragile. This is one reason why hemolysis was inhibited by anti-hyperthyroid therapy only. This may indicate that the hyperdynamic circulatory state secondary to hyperthyroidism plays an important role in the destruction of red blood cells which were coated by anti-red blood cell antibody.

Key Words: Inhibition of hemolysis, Monospecific Coombs' test

Graves' disease is often associated with other autoimmune disorders, but the combination with autoimmune hemolytic anemia is very rare. In none of the previously reported patients with hyperthyroidism and autoimmune hemolytic anemia was hemolysis inhibited by anti-hyperthyroid therapy alone. We describe here a case of man with hyperthyroidism associated with autoimmune hemolytic anemia and periodic paralysis, whose hemolysis was inhibited by anti-hyperthryroid therapy only.

CASE REPORT

A 29-year-old Japanese man was admitted to Hiratsuka City Hospital because of a question of periodic paralysis. He had been well until 2 months earlier, when he began to experience palpitation and transient gait disturbance after taking a big dinner or drinking alcohol. During the 2 months before entry, he lost 7.5 kg in weight. There was no history of blood transfusion or administration of alphamethyldopa, sulfazide or antibiotics. There was a family history of hyperthyroidism.

On admission, his blood pressure was 144/60 mmHg, heart rate was 130/min and body temperature was 37.7°C. He had anemia, jaundice and bilateral diffuse soft goiter with a smooth surface. His extraoccular movement was normal and there was no exophthalmus. He had a fine finger tremor at rest. The first and second heart sounds were accentuated and a systolic ejection murmur (Levine I/VI) was audible at the apex. In the bilateral pulmonary field, the respiratory sound was normal. The liver and spleen were not palpable. There was no edema. A neurologic examination was negative. There was neither muscle weakness nor atrophy in his extremities.

Diagnosis of Hyperthyroidism

Laboratory studies showed a serum T_3 of 6.6 ng/ml, T_4 was 28.9 μg/100 ml, TSH was less than 1.3 μU/ml, free T_4 was more than 8.0 ng/100 ml and the ^{123}I uptake (3 hrs) was 84%. A scintigram

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of the thyroid gland showed bilateral swelling. These findings were compatible with a diagnosis of Graves' disease.

Diagnosis of Autoimmune Hemolytic Anemia

Laboratory findings showed normocytic normochromic anemia with decreased haptoglobin and increased indirect bilirubin. Both the direct and indirect Coombs' tests were positive. The indirect monospecific Coombs' test was positive against anti-human IgG serum, but was negative against anti-human complements (C_3, C_3d, C_4) serum and anti-human complement (C_3d) serum. Cold agglutinin and anti-mycoplasma antibody were negative. A myelogram showed erythroid hyperplasia with slight megaloblastic change. These results confirmed the diagnosis of warm type autoimmune hemolytic anemia.

Diagnosis of Periodic Paralysis

An electromyogram disclosed normal discharge from muscles and the conduction velocity of the bilateral peroneal nerves was normal. These findings and the history were compatible with the diagnosis of periodic paralysis. However the provocation test of periodic paralysis using glucose was not performed because his general condition did not warrant it.

Clinical Course

Figure 1 shows the time course of T_3, T_4, hemoglobin and total bilirubin during treatment. Direct bilirubin ranged from 0.6 to 0.7 mg/100 ml. Propylthiouracil (PTU) was used to treat the hyperthyroidism because leukopenia occurred after the administration of methimazole. The euthyroidism achieved by PTU brought inhibition of hemolysis and amelioration of anemia in spite of continuously positive direct and indirect Coombs' tests. Neither adrenocortical steroid nor blood transfusion was administered.

DISCUSSION

We describe a case of 29-year-old Japanese man with hyperthyroidism associated with autoimmune hemolytic anemia and periodic paralysis. These are the first associations with hyperthyroidism as far as we are aware. Three cases of hyperthyroidism associated with autoimmune hemolytic anemia have been reported in the English literature,[1-3] and 5 cases in the Japanese literature.[4-8] Five of the 8 cases were Japanese,[4-8] one was Japanese-American,[1] one was Chinese[3] and the other one was a Sri Lankan.[2] It is interesting to note that all of the patients were of oriental or Asian origin.

The following problems are worth noting. The first is whether the pathogenesis of the combination of Graves' disease and autoimmune hemolytic anemia can be explained by a common mechanism. Measurement of TSH binding inhibitor immunoglobulin (TBII) showed a value of 26% dur-

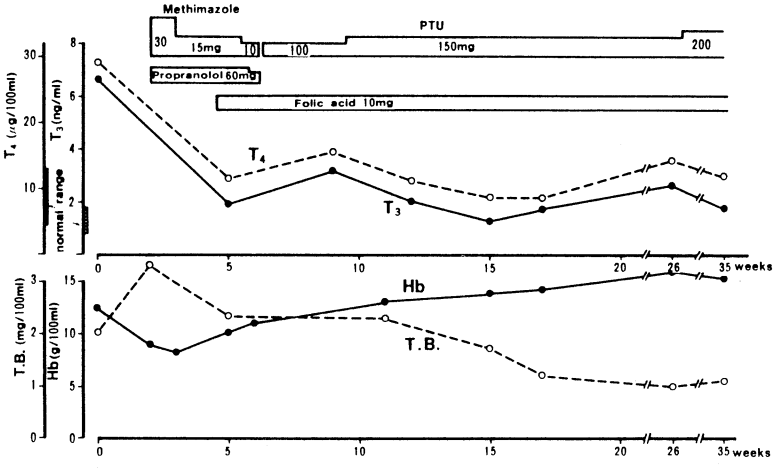

Fig. 1. Time course of triiodothyronine, thyroxine, hemoglobin and total bilirubin during treatment. T_3= triiodothyronine, T_4=thyroxine, Hb=hemoglobin, T.B.= total bilirubin, PTU=propylthiouracil.

ing the therapy, which was higher than the normal range. TBII is related to IgG globulin. The indirect monospecific Coombs' test revealed that the red blood cells of this patient was precipitated against anti-human IgG serum. Thus this patient had both TBII and anti-red blood cell antibody which related to IgG immunoglobulin. There is a possibility that a part of the mechanism which ensues from hyperthyroidism and autoimmune hemolytic anemia may be explained by a common immunological abnormality.

The second problem is to determine why the euthyroidism achieved by PTU brings inhibition of hemolysis and amelioration of anemia in spite of continuously positive direct and indirect Coombs' tests, without administration of adrenocortical steroid. In none of the previously reported patients with hyperthyroidism and autoimmune hemolytic anemia was hemolysis inhibited by anti-hyperthyroid therapy alone. Administration of adrenocortical steroid or blood transfusion or both were required to improve those patients. Since the indirect monospecific Coombs' test was negative against anti-human complements serum, the membrane of red blood cells may be less fragile. This is one reason why hemolysis was inhibited by anti-hyperthyroid therapy only. This may indicate that the hyperdynamic circulatory state secondary to hyperthyroidism plays an important role in the destruction of red blood cells which were coated by anti-red blood cell antibody.

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