

Propylthiouracil and Hepatitis: A Case Report

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A 10-year-old girl initially presented with clinical features and thyroid function tests consistent with hyperthyroidism. She was treated with propylthiouracil, 100 mg, three times a day. She developed jaundice and hepatitis following treatment with propylthiouracil for 40 days. Clinical features of hepatitis improved after the discontinuation of propylthiouracil and she became euthyroid. At this time, an immunofluorescent technique revealed antibodies consistent with autoimmune thyroiditis. From this report, it appears that hepatitis is one of the infrequent complications of treatment with propylthiouracil and transient hyperthyroidism may be associated with autoimmune thyroiditis.

Sporadic case reports of liver dysfunction temporarily associated with propylthiouracil (PTU) treatment have been reported over the past 30 years.¹⁻⁴ Another patient who developed hepatitis following the use of PTU is described in this report.

Case Report

A ten-year, four-month-old girl gave a history of painless thyroid swelling of one week duration. She complained of palpitations, excessive tiredness, nervousness, prominence of the eyes, heat intolerance, and excessive sweating two weeks prior to hospitalization. There was a family history of goiter, but no known history of thyrotoxicosis. At the evaluation, her height was 137.1 cm and weight was 28 kg. The resting pulse rate was 110. The goiter was diffuse and firm. Bilateral exophthalmos, lid-retraction, and lid-lag were noted. Hyperkinetic movements and fine

finger tremors were present. The skin was warm and moist.

Hematologic studies, serum chemistries, and urinalysis were normal. The total thyroxine level, 23 $\mu\text{g}/100\text{ ml}$, and T_3 resin uptake, 52.4 percent, were consistent with hyperthyroidism. The tanned red blood agglutination and immunofluorescent tests for thyroid antibodies were negative. Skull x-rays were reported as normal. Sick cell preparation was positive and hemoglobin electrophoresis was consistent with sickle cell trait. The patient was treated with PTU 100 mg three times daily for 17 days. The symptoms gradually improved except thyroid swelling and exophthalmos.

She was discharged from the hospital on a maintenance dose of 100 mg of propylthiouracil three times a day. Twenty-three days later, she developed jaundice and hepatic tenderness. Her total bilirubin was 10.5 mg/100 ml, alkaline-phosphatase 400 IU/L (90-230 IU/L), LDH 325 IU/L (40-140 IU/L), and SGOT 350 IU/L (5-20 IU/L). But they returned to normal levels after the therapy with PTU was discontinued. The hemoglobin, hematocrit, and reticulocyte count were normal. The total leukocyte count and peripheral blood smear were normal. Responses to di-

rect and indirect Coomb tests were negative. Glucose-6-phosphate dehydrogenase enzyme level in the serum was normal. Serum hepatitis B antigen and antinuclear antibodies were negative. Tests for LE and rheumatoid factors were negative. Immunofluorescent test for microsomal antibodies was greater than 1:2560, but the tanned red blood agglutination test for thyroid antibodies was negative. Thyroid function studies revealed euthyroidism, but the patient had a goiter and exophthalmos. She was given one grain of desiccated thyroid daily and the goiter diminished in size. After three weeks of therapy with desiccated thyroid, antibodies by the immunofluorescent technique were positive with a titer of 1:1250.

Comment

Hashimoto thyroiditis is a common cause of goiter in children. The association of thyrotoxicosis, transient hyperthyroidism, and autoimmune thyroiditis has been reported by several authors.⁵⁻⁷ These disorders are autoimmune diseases and the development of clinical features of thyrotoxicosis or those of Hashimoto thyroiditis in any particular patient de-

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depends on the stimulus applied to the thyroid gland.⁸ Initially, the above case presented with hyperthyroidism, which lasted for two weeks; subsequently, the patient developed euthyroidism. Appropriate clinical pattern and positive immunofluorescent antibody studies are adequate for the diagnosis of chronic lymphocytic thyroiditis in children.⁵ In this patient, diagnosis of Hashimoto's thyroiditis was made by positive immunofluorescent technique for antimicrosomal antibodies.

Liver dysfunction and jaundice have been very rarely reported in association with PTU therapy.¹⁻⁴ Hepatitis in a nine-year-old girl with Graves disease was reported by Parker¹ in association with PTU treatment of 100 mg three times daily for two months. Clinically, the patient developed jaundice, hepatic tenderness, and the following laboratory values: SGOT 2,424 Karmen units/ml, lactic dehydrogenase 672 Walker units/ml, and bilirubin 48/100 ml total and 28 mg/100 ml direct. A 32-year-old woman with Graves disease, following a six-month PTU therapy, suddenly developed rash and malaise.²

Her SGOT was 250 mU/ml. All of the patients improved after discontinuation of PTU except a 60-year-old woman.³ Her clinical course was also complicated by hepatic congestion secondary to cardiac failure and probable sepsis complicating agranulocytosis. A case of nonfatal toxic hepatitis with agranulocytosis following six weeks of treatment with PTU has been reported.⁴ The patient, age 68, had previous treatment with thiouracil and PTU and the possibility of sensitization by previous administration of the drug was not ruled out completely.

The symptoms of the present patient developed after 40 days of PTU therapy. Clinical and laboratory observations were those of hepatitis. She gradually improved after discontinuation of PTU. The pathogenesis of liver dysfunction in these patients remains unclear at the present time and the possibility of drug toxicity may be considered in this patient as well as those described in the literature.¹⁻⁴ Thus, hepatitis appears to be one of the infrequent complications of propylthiouracil treatment.

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Literature Cited

1. Parker LN: Hepatitis and propylthiouracil. *Ann Intern Med* 82:228-229, 1975
2. Medical Tribune Report: Drug reaction with Graves' disease. 10:8, May 15, 1969
3. Colwell AR, Sando DE, Lang SJ: Propylthiouracil induced agranulocytosis, toxic hepatitis and death. *JAMA* 148:639-641, 1952
4. Livingston HJ, Livingston SF: Agranulocytosis and hepatocellular jaundice. *JAMA* 134:422-425, 1947
5. Monteleone JA, Danis RK, Tung KSK, et al: Differentiation of chronic lymphocytic thyroiditis and simple goiter in pediatrics. *J Pediatr* 83:381-385, 1973
6. Fatourechhi V, McConahey WM, Woolner LB: Hyperthyroidism associated with histologic Hashimoto's thyroiditis. *Mayo Clin Proc* 46:682-689, 1971
7. Sato T, Takato I, Taketani T, et al: Concurrence of Graves' disease and Hashimoto's thyroiditis. *Arch Dis Child* 52:951-955, 1977
8. Masi AT, Hartmann WH, Reba RC: Serial clinical histopathologic observations on 34 chronic (Hashimoto's) thyroiditis patients with implications concerning the pathogenesis of the lesion. Program of the annual meeting of the American Thyroid Association, Ann Arbor, Michigan, September 14 to 16, 1967, p 41

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