Propylthiouracil (PTU) is commonly used in the treatment of hyperthyroidism, and is reported to have several adverse effects such as antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, Wegener’s granulomatosis, hepatotoxicity, agranulocytosis, aplastic anemia, medication-induced systemic lupus erythematosus and rheumatic syndromes with or without associated serum antinuclear antibody and splenomegaly. In MEDLINE search, we found only one child report previously in English literature as PTU-induced hemolytic anemia. We described a woman with Graves’ disease who developed hemolytic anemia after PTU therapy.

Case Report

A 41-year-old woman followed at Taipei Veterans General Hospital since August 1992 when, at 33 years of age palpitation was complained. There was no family history of Graves’ disease. Physical examination revealed diffuse grade II goiter and tachycardia with a rate of 108 beat/min. Initial laboratory studies impressed the diagnosis of Graves’ disease: thyroxine (T4) 24.20 µg/dl (6.0 - 12.0 µg/dl), free thyroxine (fT4) > 4.5 ng/dl (0.70 - 2.2 ng/dl), tri-iodothyronine (T3) > 4.5 ng/dl (0.70 - 2.2 ng/dl), tri-iodothyronine (T3) 719 ng/dl (85-165 ng/dl), thyroxine (T4) 24.20 µg/dl (6.0 - 12.0 µg/dl), free thyroxine (fT4) > 4.5 ng/dl (0.70 - 2.2 ng/dl), tri-iodothyronine (T3) 719 ng/dl (85-165 ng/dl), thyroid-stimulating hormone (TSH) 0.04 µU/ml (0.4 - 3.1 µU/ml), anti-thyroglobulin antibody non-reactive and anti-microsomal antibody non-reactive and anti- microsomal antibody non-reactive. In MEDLINE search, we found only one child report previously in English literature as PTU-induced hemolytic anemia.

We described a woman with Graves’ disease who developed hemolytic anemia after PTU therapy.
after 10-month carbimazole therapy.

Unfortunately, the follow-up turned irregular since June 1993. The patient experienced several times of hyperthyroid flare-up and received carbimazole therapy off and on. The patient discontinued anti-thyroid drug therapy during 1996 and 1997 although she was still hyperthyroid biochemically. She took PTU 150 mg daily in divided doses for 7 days in Feb 1998, and received regular PTU therapy since Aug 21, 1998 due to exacerbated symptoms including palpitation and tremor of hands.

On Dec 1, 1998, she was admitted due to headache, dizziness, weakness and limbs numbness for about 3-4 days. The laboratory data showed hemoglobin 5.7 g/dl, MCV 86.6 fl, reticulocytes count 4.66%, hepatoglobulin < 13 mg/dl, ferritin 210 ng/ml (10-300 ng/ml), glucose-6-phosphate dehydrogenase (G-6-PD) 12.5 U/G HB (7.3-18.4 U per gram hemoglobin), mildly elevated serum uric acid, potassium and direct bilirubin (Table 1). The ANA, Coombs’ test (di and in di rect) and sugar water test were all negative. After packed RBC transfusion 500 cc, she was discharged with hemoglobin 9.5 g/dl on Dec 5, 1998. PTU therapy continued at the Outpatient Department. On Dec 16, 1998, she was admitted again due to the same symptoms. The laboratory data showed severe hemolytic anemia with high reticulocytes count (Table 1). The ANA, Coombs’ test (di rect and in di rect) and sugar water test were all negative. After packed RBC transfusion and prednisolone therapy was resumed. The follow-up laboratory data showed prolonged low hepatoglobulin level with mild anemia despite head ache, dizziness and numbness of limbs disappeared. She required low-dose prednisolone (2.5 mg per day) to control hemolysis until Oct 25, 2000, when she discontinued prednisolone by herself again. She was well with out low-dose prednisolone therapy until Jan, 2001.

**Discussion**

PTU-induced hemolytic anemia is extremely rare. To our knowledge, only one case has been reported by a 5 1/2 year-old girl with hyperthyroidism who received PTU 200 mg daily in divided doses. After 18-month therapy, the patient suffered from hemolytic anemia (the lowest Hgb 10.2 g/dl) and granulocytopenia (2500/mm³, 2% polymorphonuclear neutrophils). The diagnosis was confirmed by challenge of low dose (25-50 mg daily) of PTU 2 months later when both hemolytic anemia and granulocytopenia followed. After 1-year follow-up, hemolytic anemia and granulocytopenia did not recur after PTU discontinuation.

In our case, the possibility of cellular membrane defect of red blood cells was excluded by sugar water tests and erythrocyte osmotic fragility test. ANA, Coombs’ tests and cryoglobulin were all negative. Incidental challenge of PTU established the diagnosis.

However, it was some what different from the previously reported case in which prolonged low hepatoglobulin level with suspected mild hemolytic anemia persisted for 19 months after PTU discontinuation. She did not visit our hospital until Feb 8, 1999, while the symptoms persisted. The laboratory data showed hemoglobin 6.6 g/dl, hepatoglobulin 28.5 mg/dl and reticulocytes count 6.6%. She was admitted and treated with packed RBC transfusion and decadron therapy. After discharge, she received prednisolone therapy.

She had been away from PTU after the incidentchal lenge of PTU. The hyperthyroidism improved a lot as it elapsed since I-131 therapy, and the euthyroid state came even to ally. In May 1999, she discontinued prednisolone by her self, and severe hemolytic anemia recurred. The hepatoglobulin level was 8.8 g/dl on July 7, 1999. Packed RBC 2 units were transfused and prednisolone therapy was resumed. The follow-up laboratory data showed protracted low hepatoglobulin level with mild anemia although head ache, dizziness and numbness of limbs disappeared. She required low-dose prednisolone (2.5 mg per day) to control hemolysis until Oct 25, 2000, when she discontinued prednisolone by herself again. She was well with out low-dose prednisolone therapy until Jan, 2001.

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tion. Granulocytopenia did not occur in our case (data not shown). There were two possible explanations for the clinical course. First, the delay in recovery of mild hemolytic anemia after PTU therapy was due to the prolonged effect of PTU itself. The hemolytic anemia was finally resolved without any medication after discontinance of PTU. Such course has not been reported in the literature. Second, the patient might suffer from subclinical idiopathic hemolytic anemia with acute exacerbation by PTU therapy. No matter which possible explanation was, it was worthy to report the rare case.

The pathophysiology of PTU-induced hemolytic anemia is unknown. The hemolytic anemia would be triggered by PTU-induced autoantibody due to mildly decreased C3 on Dec 17, 1998. The management of PTU-induced hemolytic anemia includes prompt discontinuation of PTU. In this case, steroid is useful for the control of the hemolysis. We report this case to show that hemolytic anemia may be one of the complications of PTU therapy.

### References