Graves' disease mimicking β -thalassaemia trait

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Summary: A case of Graves' disease associated with splenomegaly, lymphadenopathy, microcytic hypochromic anaemia, and a raised haemoglobin A₂ is presented. The haematological indices returned to normal after conventional treatment with anti-thyroid medication.

Introduction

Haematological abnormalities associated with hyperthyroidism are well recognized and may have an immunological basis or be due to thyroid hormone excess *per se*. The presence of microcytic hypochromic anaemia with raised haemoglobin A₂ and splenomegaly, and generalized lymphadenopathy have been described separately in hyperthyroidism.^{1,2} A case of Graves' disease is presented in which all the aforementioned features occurred and were corrected after treatment with anti-thyroid drugs. This case draws attention to haematological changes occurring in Graves' disease that risk being misinterpreted by the unwary physician.

Case report

A 26 year old Jordanian male patient was diagnosed at another hospital as having Graves' disease in 1985, investigated by thyroid isotope scan, blood thyroid hormones and other blood tests of which no record could be obtained, Carbimazole 20 mg/day and propranolol 120 mg/day were administered for a few months. There was apparent remission until June 1992 when he developed palpitations, tremors, dyspnoea, increased sweating with heat intolerance and had lost one stone in weight over a period of 6 weeks. His appetite was good, there was increased frequency of his bowel motions, but no history of melaena or haematemesis. There was no history of previous blood transfusions or anaemia.

His mother had insulin-dependent diabetes mellitus and his father has pernicious anaemia. Haemoglobin electrophoretic studies subsequently showed haemoglobin A₁ 100% in both parents. On examination he had bilateral exophthalmos and lid lag, and a diffuse non-tender goitre with bruit. Generalized non-tender lymph nodes varying in

size 1–2 cm and splenomegaly 3 cm below the costal margin were also found. There was generalized hyperreflexia.

Laboratory data

Packed cell volume (PCV) 35%, white blood cells (WBC) 8,600/cm³ with normal differential, erythrocyte sedimentation rate (ESR) 45 mm/first hour. Blood film showed microcytic hypochromic changes, mean corpuscular volume 72 fl (normal 87 ± 7 fl), mean corpuscular haemoglobin 27 pg (normal 29 ± 2 pg), mean corpuscular haemoglobin concentration 34 g/dl (normal 35 ± 2 g/dl). Stool guaic was negative. Free thyroxine (FT4) 87 pmol/l (normal 10–36 pmol/l). Free tri-iodothyronine (FT3) 15 pmol/l (normal 3.3–8.2 pmol/l). Thyroid stimulating hormone (TSH) <0.2 mU/l (normal 1.5–5 mU/l). Serum iron 29 µmol/l (normal 14–32 µmol/l), total iron binding capacity (TIBC) 67 µmol/l (normal 45–82 µmol/l). Serum ferritin 128 µg/l (normal 18–300 µg/l). Blood culture, monospot, toxoplasma, brucella agglutination, heterophil antibodies, anti-nuclear antibodies, Venereal Disease Research Laboratory (VDRL), anti-microsomal and anti-thyroglobulin antibodies were negative. Haemoglobin electrophoresis by cellulose acetate method showed haemoglobin A₂ 4.8% (normal range 1.5–3.2%), haemoglobin A₁ 95.2%. Chest X-ray was normal, abdominal ultrasound showed diffuse homogeneous enlargement of the spleen and no abdominal lymph node enlargement. Thyroid isotope scan showed diffuse enlargement with increased uptake suggestive of Graves' disease. Barium meal, follow-through radiology and bone marrow examination were normal.

The patient was started on carbimazole 20 mg/day and propranolol 120 mg/day. Folic acid 5 mg/day was started considering an initial diagnosis of Graves' disease and β -thalassaemia trait. His symp-

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toms abated within a month. Four months later he was clinically and biochemically euthyroid with no palpable lymph nodes or spleen. No heart murmur could be auscultated. The deep tendon reflexes were normal and the patient has put on one and a half stone. His laboratory data revealed PCV 45%, blood film was normal, haemoglobin electrophoresis A₂ 2.8% and haemoglobin A₁ 97.2%.

Discussion

Abnormalities of erythrocytes, leucocytes, platelets and coagulation factors that have been reported to be associated with hyperthyroidism are of unusual clinical importance.¹ Thyroid hormones stimulate erythropoietin production by increasing the general metabolism, resulting in increased oxygen requirements.³ The reduced mean corpuscular volume observed in hyperthyroidism contrasts with the macrocytosis of hypothyroidism and

points to a role for thyroid hormone in determining erythrocyte size.

The increase in erythropoiesis in hyperthyroidism is reflected in the bone marrow which undergoes erythroid hyperplasia.⁴ Ineffective erythropoiesis is evidenced by reduced iron utilization and a reduced mean corpuscular volume is frequently observed.⁵ The mean percentage haemoglobin A₂ level (3.21) in a group of untreated hyperthyroid subjects was significantly ($P < 0.001$) higher than in a group made euthyroid with anti-thyroid drugs.⁶ These results suggest that thyroid hormones can modulate the synthesis of globin chains.⁷ The initial findings of microcytic hypochromic anaemia, lymphadenopathy, splenomegaly and a raised haemoglobin A₂ mislead the treating physician to diagnose the β -thalassaemia trait. Thus this case originating in the Mediterranean region, where thalassaemia is common, demonstrates that Graves' disease can be associated with haematological and clinical changes that could be misinterpreted as β -thalassaemia trait.

References

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