CASE REPORTS

Hyperthyroidism and steatorrhoea

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ENDOCRINOPATHIES may, by their secondary effects, produce symptoms which overshadow those directly attributable to the primary affection. We report two patients with proven hyperthyroidism who presented with steatorrhoea and in whom treatment produced rapid and complete remission of symptoms. There appears to be only one previous report stressing this association (Crane & Evans, 1966).

Case reports

Case No. 1

A 57-year-old man became acutely ill with high fever (103°F), tachycardia and substernal pain in January 1966. The pain and temperature subsided in 72 hr with symptomatic treatment but tachycardia persisted. During the following weeks he noticed frequent loose stools, anorexia, intense tiredness, irritation of the skin and weight loss of one stone. He was seen at Crumpsall Hospital in March and was found to have generalized skin pigmentation and rapid atrial fibrillation (ventricular rate 130/min). Blood pressure 130/90 mmHg. Chest radiograph normal. ECG: rapid atrial fibrillation and right bundle branch block. The rhythm disturbance, in the absence of other cardiac pathology, was attributed to the recent infection. Digitalis rapidly controlled the ventricular rate.

The patient continued to pass four to five semi-solid normal coloured stools each day and was admitted for investigation.

Investigations (April 1966). Weight 128 lb. Hb 12.3 g/100 ml; WBC 9900/mm³; ESR 52 mm/hr; serum sodium 146, potassium 4.5, chlorides 110 mEq/l. Blood urea 39 mg/100 ml; serum bilirubin 0.5 mg/100 ml. Alkaline phosphatase 8 KA units/100 ml. Thymol turbidity 3 units; thymol flocculation incomplete; colloidal gold 2. Total serum proteins 7.2 g/100 ml. Electrophoresis showed a slight increase in α_2 -globulin. SGOT 12 units/ml; SGPT 12 units/ml. Urine n.a.d. Faecal culture—no pathogens isolated. Barium meal normal.

The patient was considered to have post-influenzal depression and began treatment with amitriptyline,

25 mg three times daily. He rapidly regained his appetite, felt less tired and gained weight. He continued to pass four semi-solid stools each day.

Investigations (August to November 1966). Weight 142-145 lb. ESR 21 mm/hr. Alkaline phosphatase 16 KA units/100 ml. Colloidal gold 3. Serum calcium 9.8 mg/100 ml; serum phosphorus 3.4 mg/100 ml. Serum folate 1.3 ng/ml (normal 3-8). Urine 17 ketosteroids 8 mg/24 hr; 17-hydroxycorticosteroids 12 mg/24 hr. Xylose absorption test normal. Faecal occult blood negative on three occasions. Daily faecal fat estimations (on normal ward diet): 7, 4, 2, 5, 28, 12, 4, 7, 8, 7, 4, 4, 11, 6 g total fat. Barium enema (10 August 1966) normal. Jejunal biopsy (11 November 1966): 'some of the villi are rather stunted while others show some rounding and flattening of their tips. There is an increased round cell infiltrate present in the lamina propria. The picture is that of partial villous atrophy'. Liver biopsy (18 November 1966): normal histology.

In January 1967, the patient complained of central abdominal pains, alternating diarrhoea and constipation and rapid weight loss—13 lb over 4 weeks. Rectal examination was normal although the faeces were observed to be soft and pale. Repeat barium enema (3 February 1967) showed 'some narrowing of the lumen in the upper part of the ascending colon just below the hepatic flexure, possibly due to neoplasm'. At laparotomy (22 February 1967), no abnormality was found but a thickened appendix was removed. Histology of this organ showed no abnormal features. The immediate post-operative course was complicated by pneumonia and, subsequently, a penicillin-resistant staphylococcal enteritis.

The patient continued to pass large, pale, unformed stools with a daily fat content of 7, 1, 11, 4, 10 and 14 g. In April he was seen for the first time by one of the authors (W.D.R.) who noticed a moderately enlarged, firm goitre and suspected thyrotoxicosis. The clinical diagnosis was confirmed by the ¹³¹I uptake—58% at 2 hr. The thyroglobulin precipitin reaction was negative and tanned red cell

titre 1:50. Within a few weeks of starting carbimazole, 15 mg every 8 hr, the stools were normal, skin irritation had ceased and considerable weight gain had occurred. The patient has continued to remain well on a low maintenance dose of carbimazole and digitalis and, when last seen in November 1968, was asymptomatic and weighed 158 lb.

Case No. 2

A woman of 57 years, was seen at another hospital in February 1967 having lost 49 lbs in weight over 4 years. She complained of vague abdominal pains and distension but had no bowel disturbance. Thyrotoxicosis was suspected because of tremor, lid-lag and rapid atrial fibrillation. The radioiodine uptake was borderline—31% at 2 hr. No treatment was given.

She was admitted to Crumpsall Hospital in April 1968 with a 3-month history of swelling of the legs, abdominal discomfort and frequent (up to five a day) loose motions which were pale, frothy and difficult to flush. Her appetite was good. Examination revealed generalized skin pigmentation, fine tremor of the hands, marked bilateral lid-lag and a moderately enlarged diffuse goitre. She had rapid atrial fibrillation (ventricular rate 140/min). Blood pressure 160/80 mmHg. Oedema of the legs, sacrum and lower abdominal wall. The liver was enlarged and palpable three fingers below the costal margin.

Investigations. Weight 119 lb. Haemoglobin 9.9 g/100 ml; WBC 6000/mm³; ESR 23 mm/hr. The blood film showed normochromia, moderate anisocytosis and poikilocytosis. Reticulocytes 2%. Serum iron 40 µg/100 ml. Serum B₁₂ 205 pg/ml. Serum folate 1.6 ng/ml. Folate absorption was subnormal. Sternal marrow was normal apart from low iron stores. Serum electrolytes normal. Serum bilirubin 2.2 mg/100 ml. Alkaline phosphatase 37 KA units/100 ml. Total serum proteins 6.7 g/100 ml; albumen 2.8, globulin 3.9. Transaminases normal. Prothrombin activity 35%. 2-hour ¹³¹I uptake 86%. Protein bound iodine 14 µg/100 ml. Thyroglobulin precipitin reaction negative. Tanned red cell titre 1:50. Serum calcium 9.0 mg/100 ml; serum phosphorus 2.1 mg/100 ml. Glucose tolerance test showed a flat curve. Xylose absorption normal. Chest radiograph showed marked cardiac enlargement with congestive changes in the lung fields and a right basal effusion. Skeletal survey revealed Paget's disease in the left pelvis. ECG—rapid atrial fibrillation. Daily faecal fat estimations (on normal ward diet): 40, 60, 31, 21 g total fat. Liver biopsy showed 'early changes of fatty infiltration. Increase in small bile ducts with plasma cells in surrounding collagen'. Jejunal biopsy normal.

The patient began treatment with carbimazole,

15 mg every 8 hr, on 25 April and 8 days later started to have a single daily motion. Faecal fat remained intermittently elevated for a period of about 4 weeks—faeces on five occasions yielding 5, 22, 2, 10 and 18 g total fat. In August, faecal fat was normal—2 g on each of 3 successive days.

After an initial weight loss of 6 lb, a result of the response to diuretics, there was a steady weight gain to 149 lb on 21 September. On this date the return of sinus rhythm was first noted. Repeat folate absorption (14 June 1968) was normal. Serum bilirubin gradually fell to 0.7 mg/100 ml while alkaline phosphatase rose to 110 KA units/100 ml. Plasma albumen rose to 4.7 g/100 ml. Electrophoresis now shows an increase in γ-globulin.

Discussion

The association between disorders of the thyroid gland and abnormalities of the gastro-intestinal tract has been recognized for many years. The best known association is that of hyperthyroidism and diarrhoea, first reported by Moebius (1906).

Verbruycke (1931) in an analysis of thirty-four patients coming for gastro-intestinal diagnosis, and in whom the underlying cause was found to be 'masked' hyperthyroidism, noted the common occurrence of abdominal pain, nausea, vomiting, flatulence, diarrhoea and constipation. Zellman & Spielberg (1966) in a review of bizarre manifestations of hyperthyroidism, stress that anorexia, abdominal pain, nausea and vomiting are occasional features.

Hyperthyroidism is not generally regarded as a cause of steatorrhoea. Neither Badenoch (1960) in his masterly review of steatorrhoea, nor Frazer (1968) in his monograph on malabsorption syndromes, mention hyperthyroidism in exhaustive lists of causes. According to Hawkins (1963), the diarrhoea of hyperthyroidism is rarely accompanied by steatorrhoea. However, slight increases in faecal fat excretion may be common. Cook, Nassim & Collins (1959) in metabolic studies on nine hyperthyroid patients, found faecal fat above normal limits in eight, but in only one patient was faecal fat in excess of 10 g daily. Faecal fat tended to decrease after treatment. They considered that the high faecal fat was caused by an excess of calcium in the gut although the highest values for faecal calcium were not directly related to the highest values for faecal fat. In a similar study, Adams *et al.* (1967) found faecal fats of 10, 8.7 and 7.5 g/day in three of ten hyperthyroid patients.

Friedenwald & Morrison (1933) describing the stool as liquid, often bile-stained and at times containing undigested food remains, suggested that diarrhoea was due to over-activity of the vagus nerve, hyperchlorhydria or a direct effect of in-

creased circulating thyroxine on the motility of the bowel, either singly or in combination. In an investigation of forty-two patients with hyperthyroidism before and after sub-total thyroidectomy, Shirer (1933), using barium studies, demonstrated hypermotility of the bowel in 92.8% of the patients although only 14.2% had diarrhoea. Motility returned to normal in the majority of patients post-operatively. Shirer suggested that the hypermotility may disturb digestive and absorptive functions and attributed the low serum proteins in his patients to incomplete assimilation of ingested food. Brown, Pendergrass & Burdick (1941) confirmed hypermotility in both small and large bowel in barium studies on twenty-four patients.

In recent studies with rats fed thyroid extract, Middleton & Thompson (1968) found an increased faecal fat extraction and malabsorption of both triglyceride and fatty acid. They found no evidence of a primary defect of pancreatic, biliary or mucosal function but were clearly able to demonstrate a more rapid gastric emptying and intestinal transit which, they suggest, is the cause of the steatorrhoea in hyperthyroidism.

The symptoms and signs of hyperthyroidism may closely resemble those of a malabsorption syndrome. In our patients, weight loss, vague abdominal pains, generalized skin pigmentation and frequent loose pale stools were notable features. In the first patient a diagnosis of malabsorption was pursued for a period of 15 months, and it is not unreasonable to surmise that, where the secondary effects of hyperthyroidism dominate the clinical picture, failure to consider an endocrine cause may lead to repetition of such a course in other patients.

Abnormal liver function tests, which were found in both our patients, and histological changes similar to those described in Case 2, have been reported in hyperthyroidism (Klotz & Darnis, 1960).

The low serum folate, noted in both patients, may have resulted from the increased metabolic requirements, impaired absorption or a combination

of these factors. In Case 2 the return of folate absorption to normal following treatment may be significant but, since the earlier studies were performed without preliminary saturation, the validity of the observation must remain in doubt.

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