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LATS activity, exophthalmos and digital clubbing associated with myxoedema

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THE ASSOCIATION of exophthalmos and finger clubbing with thyrotoxicosis is well known (Malkinson, 1963). It has been postulated that the long acting thyroid stimulator (LATS) might be the common aetiological factor.

The case described is that of a patient with proven myxoedema, who had never had any previous episodes of hyperthyroidism, who exhibited exophthalmos and digital clubbing, and in whom the serum LATS level was raised. In addition she had rheumatoid arthritis and pernicious anaemia. The significance of these associations is discussed.

Case report

The patient, a 67-year-old spinster, was admitted to Hillingdon Hospital in June 1966. In 1944 she had experienced gradual 'slowing down' together with changes in her skin and hair. Myxoedema was diagnosed clinically and treatment with thyroxine had continued from that time until 4 months before when she had neglected to take her tablets. In 1964 proptosis developed and has progressed. Tarsorrhaphy was performed in 1965 for a left-sided corneal ulcer. She developed joint symptoms in 1960 which led to a diagnosis of rheumatoid arthritis. At this time she had an ESR of 50 mm/hr and a negative test for the rheumatoid factor. By 1966 she was unable to walk and surgical arthrodesis of the left knee joint was later carried out.

Pernicious anaemia was diagnosed in 1966 during routine investigation of a symptomless anaemia. In 1930 she had rheumatic fever but there were no apparent sequelae. She had never had a goitre.

There was no family history of thyroid disorder, arthritis or pernicious anaemia.

Examination. The patient was a middle-aged lady with sparse, coarse hair, a dry thickened skin and the facial appearance characteristic of myxoedema (Fig. 1). Her height was 5 ft 2 in. (152.5

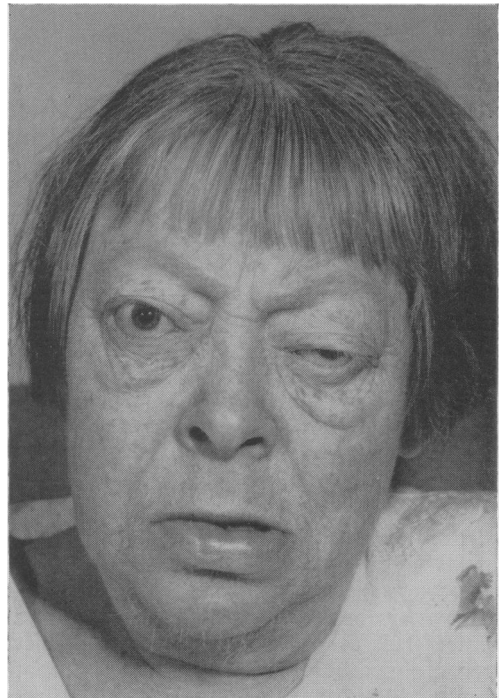


FIG. 1.

cm) and weight 10 st 3 lb (141.5 kg). She was slow in thought and action, her voice was gruff and her tendon reflexes exhibited delayed relaxation. The thyroid gland was impalpable.

Marked finger clubbing was present (Fig. 2) and pretibial myxoedema affected the shins and both feet (Fig. 3). In these areas the skin was raised in irregular firm dimpled swellings.

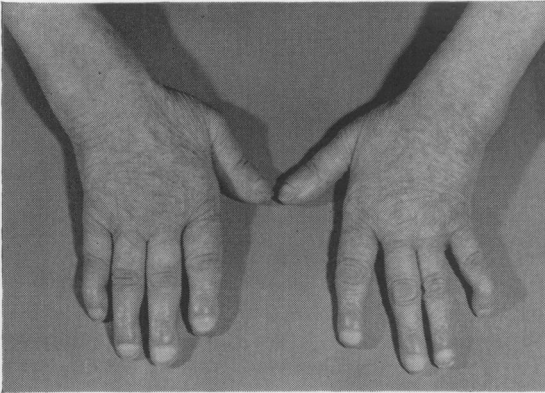


FIG. 2.

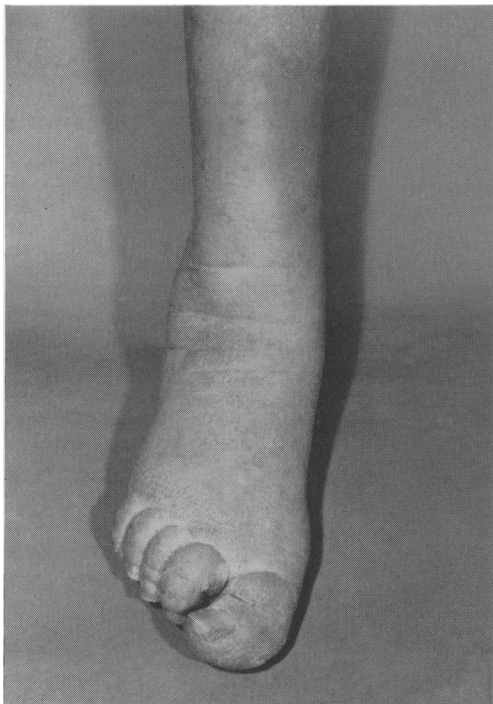


FIG. 3.

There was bilateral exophthalmos and a divergent strabismus. In the left eye, in particular, there was poor elevation, and depression and convergence were limited.

She had moderately severe rheumatoid arthritis in both hands with ulnar deviation and periarticular thickening, together with partial subluxation in the metacarpophalangeal joints. The left knee and wrist joints and both elbow joints were also affected, while large rheumatoid nodules were found on both forearms.

The patient was clinically anaemic, but there was neither splenomegaly nor peripheral neuritis.

Investigations. Haemoglobin 65%. RBC 2.7 million/mm³ WBC 7000/mm³ with a normal differential count. ESR 120 mm/hr. Blood film: anisocytosis and poikilocytosis. Diagnex test indicative of achlorhydria. serum vitamin B₁₂ 60 μg/ml (normal 140–900 μg/ml). Serum iron 57 μg/100 ml. Iron-binding capacity 199 μg/100 ml. Serum proteins 7.4 g/100 ml, albumin 2.8, globulin 4.6 g/100 ml. Electrophoresis: reduced albumin, raised γ-globulin. Serum cholesterol 322 mg/100 ml. Wassermann and Kahn Test negative. Latex test for Rheumatoid Factor negative. Coombs' test negative. FIGLU negative. Serum urea and electrolytes, liver function tests, ECG, chest X-ray normal.

X-rays of the joints showed changes of a rheumatoid type of arthropathy, while the histology of a biopsy specimen was characteristic of a rheumatoid nodule.

Thyroid function studies, performed at a time when all therapy had been withheld for 3 months showed a diminished uptake of ¹³¹I, while administration of thyroid stimulating hormone caused no change in uptake of ¹³¹I.

Thyroid uptake of ¹³¹I at 2 hr=6% (normal 10–30%) at 24 hr=8% (normal 25–55%).

These findings were consistent with the diagnosis of primary hypothyroidism.

Antibody tests: She had a trace of thyroid antibodies as shown by a positive fluorescent test for thyroid cytoplasmic antibodies. The tests for gastric parietal cell and intrinsic factor antibodies were also positive, as was the test for the non-organ-specific antinuclear factor. The McKenzie test for the long acting thyroid stimulator (LATS), performed by Dr David El Kabir of Oxford University, showed a moderately high LATS level: 2 hr response=288 ± 34%, 7 hr response=407 ± 44%, 24 hr response = 346 ± 38%, normal response = 100 ± 25%.

Discussion

This case presents several interesting features.

The occurrence of exophthalmos, pretibial myxoedema and clubbing in association with thyrotoxicosis are well known and thyroid acropachy following thyroidectomy for hyperthyroidism has been described (Sharvill, 1965). However, the presence of exophthalmos in primary myxoedema is said to be extremely infrequent (McKenzie, 1965).

The exophthalmos occurring in thyrotoxicosis was for many years thought to be due to overproduction of thyrotropin (Means, 1944). However, the long acting thyroid stimulator was later described (Adams, 1958) and came to be considered responsible for both exophthalmos and thyrotoxicosis (Pimstone, Hoffenberg & Black, 1964). Other investigations showed no correlation between LATS assays and exophthalmos (McKenzie, 1961). In a recent group of LATS assays it has been shown that LATS occurred in the majority of cases of a series of patients with exophthalmos and thyrotoxicosis. However, in the same investigation LATS was found in only one of seven cases of exophthalmos occurring without thyrotoxicosis (Pinchera, Pinchera & Stanbury, 1965).

Our case has a moderately high LATS level, in the presence of exophthalmos and primary myxoedema. This finding has not been previously recorded, possibly because this uncommon association has not been previously investigated in this way.

Another interesting feature of this case is the coexistence of diseases with an autoimmune background. The patient had pernicious anaemia, rheumatoid arthritis and myxoedema, with positive laboratory evidence of autoimmune disorder. This association of conditions with an autoimmune basis has been described frequently (McEachern & Parnell, 1948; McNicol, 1961) and the occurrence of gastric parietal-cell antibodies in thyroid disorders has been discussed (Doniach, Roitt & Taylor, 1963). LATS might well be a 7S γ -globulin (Kriss, Pleshakov & Chien, 1964) and it has been postulated that it is an autoantibody, produced in response to antigenic

stimulation from the thyroid (Adams, 1965). This theory has not yet been substantiated. However, the occurrence of LATS in this case, with its pronounced autoimmune diathesis, fits appropriately into this concept.

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