A CASE OF CHRONIC THYROTOXIC MYOPATHY*

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Muscular weakness is part of the general clinical picture of thyrotoxicosis as Graves[1] and Basedow[2] observed in their classical description of the disease. In rare instances, however, extreme muscle weakness amounting almost to paralysis may be the only clinical sign of thyrotoxicosis and such a case is presented in this paper. The condition was first described by Bathhurst[3] in 1895. In 1961 Whitfield and Hudson[4] in a review of the literature could find only 60 published records of chronic thyrotoxic myopathy and added 5 cases of their own; since then a few more examples have been described.

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The condition causes great disability and although it is rare the prospects of recovery are so good that it is considered worth while describing yet another example.

CASE REPORT

Mrs. O., aged 36 years, gave the following story: In June 1959, 5 months after the birth of her first baby, she became aware of weakness affecting her legs and to a lesser extent her arms. This steadily increased so that she found difficulty in climbing stairs and later in walking. Later her back muscles became involved; she found difficulty in straightening her back or getting out of a deep chair. Her arms tired quickly when she carried her infant. She had noticed no abnormality in speaking, swallowing or sphincter control. Because of the severe muscle weakness she consulted a neurologist who did the following investigations which were either normal or negative:

Full blood count, virus complement-fixation tests, virus culture of blood and faeces, blood serology, L.P. and cerebrospinal fluid examination. She was told that she had a 'spinal infection' and was treated with steroids for about a month. Over the ensuing 9 months her condition persisted unchanged. In March 1960 when we first saw her, she still complained of weakness, but she was distressed by the recent appearance of large unsightly pouches under her eyes. Systematic enquiry elicited no other abnormal symptoms and, in particular, she did not mention any loss of weight.

Examination

The patient was a big woman, height 5 ft. 8 inches, weight 150 lb. The striking clinical feature was generalized, symmetrical muscle weakness; the muscles of the shoulder girdle, back and thighs were most severely affected. There was weakness of the deltoids, triceps, and quadriceps; she could not sit up from the supine position without the help of her hands, and she found straight leg-raising difficult. There was no obvious wasting or fibrillation, but there was some evidence of hypotonia, the outstretched hand showing the 'dinner fork posture'. The tendon reflexes were brisk. Intravenous administration of prostigmine, 2·5 mg., with atropine gr. 1/100, produced no improvement in muscle power.

Signs of hyperthyroidism. It should be emphasized that no clinical signs of thyrotoxicosis were evident. There were large pouches under the eyes, but none of the characteristic ocular signs of hyperthyroidism. There was no goitre, no retrosternal mass on X-ray, no tremor and no excessive sweating. The blood pressure was 120/80 mm.Hg and the pulse rate was 100 per minute.

Clinical Investigations

The serum protein bound iodine level repeated on several occasions ranged between 10·8 and 11·5 μg./100 ml. The urine showed persistent creatinuria (Table I). Radioactive iodine studies confirmed the presence of thyrotoxicosis. The 24-hour uptake of ^{131}I was 73·5% and after daily administration of 80 μg. of triiodothyronine for 7 days was 80·5% (Werner's Test). The 24-hour conversion ratio was 93% and the red cell uptake of ^{131}I-labelled T_3 was 30%. Other tests were normal or non-contributory and included total neutral 17-ketosteroids, full blood count, blood urea and proteins, serum calcium, sodium and potassium.

Progress

For certain personal reasons the patient was not seen for 2 months after these tests were completed. During this period she had lost 14 lb. in weight although her appetite was excellent. She had developed palpitations and diarrhoea and the swelling around her eyes had become more obvious. Examination now revealed definite lid retraction and lid lag, a palpable thyroid gland, a fine tremor and a moist skin. In short she now showed clinical signs of thyrotoxicosis for the first time; and this a year after the onset of her weakness. At this stage, treatment was instituted using potassium perchlorate, G 1·0 daily, in divided doses. Her response was dramatic. Within 3 months she had gained 15 lb. in weight and thought her muscle power was better. After 18 months she had no subjective or objective signs of muscle weakness and had lost all evidence of thyrotoxicosis. The biochemical response is shown in Table I.

DISCUSSION

The way in which this patient presented illustrates the main feature of this condition. She was so disabled by muscle weakness that her house doctor referred her to a neurologist. Nine months later, although iodine studies proved that she was thyrotoxic, it was difficult to find any of the accepted clinical signs to support this diagnosis. It was fully a year after the onset of weakness that she first began to show recognizable clinical signs of thyrotoxicosis. Faced with such a case of muscle weakness other conditions have to be considered and differentiated; Cushing's syndrome, the myopathy following prolonged steroid therapy, particularly triamcinoline and dexamethasone; the myopathy associated with visceral neoplasm; porphyria, diabetes mellitus, potassium lack and chronic polymyositis. Moreover, myasthenia gravis and periodic paralysis may be associated or may complicate the picture.

From a review of the literature the condition appears to be more frequent in females in keeping with the female preponderance of thyrotoxicosis. The weakness affects mainly the pelvic girdle, the quadriceps, the shoulder girdles and upper arms, hence patients complain of difficulty in walking, climbing stairs, raising the arms or combing their hair. The bulbar muscles are rarely involved. The affected muscles are not obviously wasted and do not fibrillate; tendon reflexes are normal and sensation is not disturbed. Muscle power is not enhanced by the injection of prostigmine. Reports on muscle biopsies have been conflicting; in some series there was no abnormality[5, 8] but another study[9] showed almost universal lesions, including atrophy of fibres and increase in sarcolemmal nuclei. Serum-potassium levels, where they have been estimated, have been normal.[4]

Relation to Myasthenia Gravis and Periodic Paralysis

Occasionally thyrotoxicosis may be complicated by myasthenia gravis in which case thyrotoxic myopathy may be simulated. Prostigmine evokes the usual improvement in muscle power and treatment of the thyrotoxicosis does not influence the myasthenia.[6]

Thyrotoxic Periodic Paralysis

Some 40 cases of periodic paralysis in association with thyrotoxicosis have been reported.[6, 10] In some series of periodic paralysis as many as half the patients have been thyrotoxic. In this type of case reversal of the hyperthyroidism abolishes the periodic paralysis. It is postulated that the thyrotoxicosis exposes a latent disease.

TABLE I. CLINICAL INVESTIGATIONS

	Urine					*Blood*				
	24-hr. vol. (ml.)	*Na (mEq./l.)*	*K (mEq./l.)*	*Creatinine (G/l.)*	*Creatine (G/l.)*	*Na (mEq./l.)*	*K (mEq./l.)*	*PBI (μg./100 ml.)*	*$RCUT_3$* %*	*Cholesterol (mg./100 ml)*
Before treatment	1,145	159	58·5	1·51	0·13	143	4·6	11·0	30	—
After treatment:										
1 week	1,500	228	93	1·12	0·53	—	—	—	—	—
2 weeks	1,600	—	—	1·04	0·12	—	—	—	—	—
12 weeks	790	—	—	0·81	0·16	—	—	5·0	11·8	286
15 weeks	1,600	—	—	1·04	0·12	—	—	—	—	—
17 weeks	940	—	—	1·46	0·09	—	—	3·6	—	—
72 weeks	—	—	—	—	—	—	—	7·0	15·4	225

*$RCUT_3$ = Red-cell uptake of ^{131}I.

Mechanism

In occasional cases the 'toxic' thyroid notoriously produces profound effects on one target rather than on the general system; thus some patients may show extreme muscle wasting[11] and others severe mental apathy (apathetic hyperthyroidism); in the cardiovascular system persistent atrial premature contractions, atrial fibrillation, angina pectoris or unexplained heart failure may be due to masked thyrotoxicosis.

The occurrence of muscular weakness in thyrotoxicosis has been known as long as the disease itself, but the fundamental metabolic abnormality cannot as yet be defined in precise biochemical terms, and no acceptable explanation is available for cases like the present one, where muscular weakness predominates and even masks the other features of thyrotoxicosis. The characteristic anatomical distribution of the myopathy would, in addition, appear to require that the biochemical abnormality was operative in particular muscle groups. Thyroxine is known to increase oxygen uptake or respiration of cells and tissues, and an excess of thyroid hormone could interfere with the intracellular integration of multienzyme systems. Thyroxine can, for example, 'uncouple' oxidative phosphorylation. This means that while thyroxine stimulates oxidative reactions, it retards the transfer of the energy derived thereby to ADP which is normally phosphorylated to ATP. The high-energy bond which is generated in this reaction enables the cell to store energy. In the muscle cell the immediate energy required for mechanical contraction appears to be derived from ATP, which is then converted back to ADP; the phosphate plus the high-energy bond is transferred to creatine which acts as a phosphate acceptor and forms creatine phosphate. While this transphosphorylation is independent of oxidation or respiration, it is possible that an overproduction of thyroid hormone may, by decreasing ATP production, indirectly decrease the formation of creatine phosphate in muscle, and thus produce muscle weakness. Several authors[5, 9, 12] have, however, found little or no correlation between the degree of muscular weakness or wasting and the extent of creatinuria. Thorn and Eder[12] found no striking increase of creatine excretion in chronic thyrotoxic myopathy over that seen in uncomplicated thyrotoxicosis. The demonstration of an abnormal creatine tolerance has also not proved to be completely reliable as a differential diagnostic finding in thyrotoxic myopathy. The unravelling of the metabolic disturbance must thus await further studies.

SUMMARY

A young married woman complained of severe weakness affecting the muscles of the back, the shoulder and pelvic girdles. Iodine studies proved that she was thyrotoxic although she showed no clinical signs of hyperthyroidism.

She recovered her muscle power after treatment with potassium perchlorate.

She is a further example of a rare condition—chronic thyrotoxic myopathy. The clinical picture is defined and the differential diagnosis is discussed.

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