

Hypothyroidism presenting with musculoskeletal symptoms

D. N. GOLDING

Princess Alexandra Hospital and Harlow Group, Hertfordshire and Essex

The possibility of hypothyroidism should be considered in patients presenting with rheumatic pains of uncertain aetiology. While it is established that this condition can occasionally present with muscle weakness due to myopathy (Fessel, 1968), it is per-

haps less well appreciated that muscle pain and stiffness may predominate over weakness, and in this paper nine hypothyroid patients who presented with musculoskeletal symptoms of this kind are described. Their principal features are summarized in Table I.

This paper was presented at a meeting of The Heberden Society at Burgenstock, Switzerland, in June, 1968.

Table I Clinical features in nine hypothyroid patients presenting with musculoskeletal symptoms

Case no.	Age (yrs)	Presenting symptoms				Median nerve delay	Hypothyroid	
		Pain	Stiffness	Cramp	Acroparaesthesiae		Delayed ankle-jerk relaxation	ECG changes
1	27	+ generalized	+	+	+	ND	+	+
2	54	+ generalized mainly wrists and arms	+	+	+	+(unilateral)	+	+
3	53	+ generalized mainly lower limbs	+	+	-	ND	+	+
4	67	+ mainly neck and back	-	-	-	ND	-	-
5	56	+ generalized mainly back	+	+	-	ND	+	+
6	65	+ generalized mainly wrists	+	+	+	+(unilateral)	+	+
7	43	+ generalized mainly wrists and arms	+	-	-	ND	+	+
8	64	+ mainly neck and ankles	+	+	+	ND	-	+
9	38	+ generalized	+	-	+	+(bilateral)	+	+

ND = Nerve conduction not tested.

Diagnosis of hypothyroidism

Hypothyroidism was suspected when there was lethargy, sensitivity to cold, weight-gain, mental dullness, bradycardia (pulse-rate under 60/min.), or a combination of these features. Only one patient (Case 3) looked typically myxoedemic. The diagnosis was confirmed by delayed recovery phase of the Achilles tendon reflex (which occurred in all but one case), and two or more of the following:

- (1) Serum cholesterol over 280 mg./100 ml.
- (2) Serum protein-bound iodine (PBI) under 3.5 µg./100 ml.
- (3) Radioactive iodine (I^{132}) uptake by the thyroid under 15 per cent. in 2 hrs; under 18 per cent. in 4 hrs.
- (4) Low-voltage complexes or flat/inverted T-waves in most leads of the electrocardiogram.

Illustrative case histories**CASE 1 (Hypothyroidism presenting with pain and lethargy)**

A 27-year-old male student had been troubled by aching in the muscles for 4 years, particularly in the neck and shoulder regions and in the thighs. These symptoms were worse in the cold weather. When first seen (October, 1966) he appeared pale and sluggish, with striking poverty of thought processes and slow limb movements. The shoulder-girdle posture was poor, but the neck and spine movements were full and painless. The peripheral joints were rather stiff on passive movement but not tender. X-ray examination excluded osteoarthritis. The pulse was slow and regular and the ankle-jerks showed the delay in the relaxation phase characteristic of hypothyroidism. Serum cholesterol 300 mg./100 ml.; protein-bound iodine 0.7 µg./100 ml.; I^{132} uptake 9 per cent. in 2 hrs, 8 per cent. in 4 hrs. Tests for rheumatoid factor and thyroid antibodies negative. Electrocardiogram showed low-voltage

<i>features</i>			<i>Other symptoms</i>	<i>Duration at first attendance (yrs)</i>	<i>Relief by thyroid therapy</i>	<i>Improvement in ECG</i>	<i>Follow-up (yrs)</i>
<i>Serum cholesterol (mg./100 ml.)</i>	<i>I^{132} uptake</i>	<i>Protein-bound iodine (mg./100 ml.)</i>					
300	Low	0.7	None	2	+	+	1
453	Low	ND	None	Several	+	+	1
540	Low	1.4	Macrocytic anaemia	9/12	+	+	2½
320	Low	5.5	None	6/12	+	+	3
300	Low	5.8	None	5/12	+	+	2½
328 (taking thyroid extract)	Low	6.5	None	2/12	+	-	2½
334	Low	1.3	None	8	+	+	9/12
246	Low	3.4	Cerebellar features	20	±	+	2
143	Low	1.2	None	6/12	+	+	6/12

complexes and flat or inverted T-waves in many leads.

L-thyroxine 0.2 mg. daily was prescribed, and after 3 weeks the patient reported that he had much less pain and stiffness, stating that his joints felt as though they had been 'oiled with an oil-can'. The electrocardiogram after treatment showed marked improvement.

CASE 6 (Hypothyroidism presenting with carpal tunnel syndrome)

A 65-year-old woman presented with a 2 months' history of pain in the forearms and tingling in the hands, worse in the right (dominant) side, and inability to hold small objects firmly. The paraesthesiae affected the index, third, and fourth fingers and the thumb. She also complained of diffuse 'rheumatism' and of weakness of the legs on climbing stairs. She felt generally tired and unwell. She had been found to be hypothyroid 5 years before (serum cholesterol 352 mg./100 ml.; radioactive iodine uptake 15 per cent. in 2 hrs, 15 per cent. in 4 hrs), and had been given thyroid extract 7.5 mg. twice daily which she had taken ever since.

She was found to have weakness of the abductor pollicis brevis and hypoalgesia in the median nerve distribution of the right hand. She was thought to have a carpal tunnel syndrome, but an injection of hydrocortisone into the right carpal tunnel was without effect. Serum cholesterol on this occasion was 328 mg./100 ml.; Hb 86 per cent., erythrocyte sedimentation rate 20 mm./hr (Westergen); latex-test negative; serum uric acid 3.2 mg./100 ml.; radiographs of the hands normal. Motor conduction tests on the right median nerve from wrist to thenar eminence showed a latency of 6 msec. as compared with 3 msec. on the left side. Sensory conduction times from wrist to index finger were respectively 3 and 2 msec.

Thyroid extract 15 mg. daily was replaced by L-thyroxine 0.1 mg. three times daily. The symptoms gradually improved, and when she was seen 4 months later she no longer complained of tingling and clumsiness on using the right hand. She remained well on this regime, and was symptom-free at her last review in October, 1968.

CASE 7 (Hypothyroidism presenting with pain and stiffness)

A 43-year-old woman had complained of diffuse aches and pains in the muscles and joints since her pregnancy in 1959. Recently the pains in her arms had become 'intense' and on occasion had caused her to drop objects she was holding. Severe morning stiffness affecting the shoulders initially raised suspicion of rheumatoid arthritis, but there was no joint swelling or tenderness, the erythrocyte sedimentation rate was normal, and tests for rheumatoid factor were negative. The limbs were cold on palpation and the ankle-jerks showed delay in the relaxation phase. Serum cholesterol 334 mg./100 ml.; protein-bound iodine 1.3 µg./100 ml.; radioactive iodine uptake low. Electrocardiogram showed flat T-waves and low voltage complexes. The patient volunteered that a previous course of phenylbutazone had greatly aggravated the pains.

She improved after only 2 weeks' treatment with L-thyroxine 0.2 mg. daily; by this time she had lost most of her pain and stiffness and was left with only mild aching

in the wrists and forearms. The electrocardiogram showed marked improvement in QRS and T-wave voltage in all leads.

Discussion

Table I summarizes the principal clinical and laboratory features of the nine patients, with particular reference to presenting symptoms of a musculo-skeletal nature, investigations for hypothyroidism, duration of symptoms, length of follow-up, and effect of thyroid replacement therapy. All patients also had full blood counts, erythrocyte sedimentation rate, tests for rheumatoid factor (latex-fixation and Waaler-Rose), serum uric acid estimations, and radiographs of hands and feet. These investigations showed no abnormalities.

Generalized pain referable to muscles or joints, usually a diffuse aching and sometimes described as 'fibrositis', was common to all. Occasionally the pain was very severe, and various parts of the body seemed to be affected at different times. Frequently cold weather aggravated the pain. The administration of phenylbutazone aggravated the symptoms (rather than relieving pain, as was the intent) in one case: this is of interest because the drug has an antithyroid effect and also antagonizes thyroxine peripherally (von Rechenberg, 1962).

In some of the more severe cases muscle pain was associated with fatigue giving rise to a sensation similar to that commonly experienced after a bout of strenuous exercise. Sometimes the pain 'settled' in the wrists, hands, and fingers. Carpal tunnel syndrome was proven electrodiagnostically in all three patients in whom the wrists were the predominant site of pain. Muscle stiffness was a feature in eight patients. This was frequently most pronounced in the early morning when it could last for more than 30 minutes, raising suspicion of rheumatoid disease or polymyalgia rheumatica. Muscle cramps, usually nocturnal and affecting the calf muscles, occurred in eight patients.

Five patients had paraesthesiae of the hands and sometimes also of the feet. Carpal tunnel syndrome was established by motor and sensory median nerve conduction tests in three, but the degree of conduction delay was slight in all but one patient.

There was a good symptomatic response to thyroid administration within a few weeks, or occasionally months. Relief of muscle stiffness was, in general, more dramatic than alleviation of pain. Acroparaesthesiae were always abolished by therapy.

Electrocardiograms were carried out after treatment in six patients and all but one showed significant improvement in QRS voltage and T-waves.

The various musculoskeletal conditions which have previously been described in association with hypothyroidism are listed in Table II. The literature is mainly concerned with muscle weakness and

Table II Muscular features in hypothyroidism

General muscle weakness
Pain and stiffness
Carpal tunnel syndrome
Muscle hypertrophy { Hoffmann's syndrome (adults) Debré and Semelaigne's syndrome (infants)
'Pseudomyotonia'
Muscle cramps ('pseudo-tetany')

wasting in this condition. In tabulating the features of 25 patients with myxoedema, Nickel, Frame, Bebin, Tourtellotte, Parker, and Hughes (1961) reported that all had subjective weakness, and a quarter had objective loss of muscle strength primarily affecting the proximal limb-girdle muscles; the hands and feet were rarely involved. Histological changes of myopathy were found in all of twelve biopsies performed. The syndrome of Hoffmann (1897) is a rare condition characterized by hypertrophic, weak, and sometimes painful limb muscles; first described in a patient who had previously had several thyroidectomies, this condition is probably identical to the syndrome of hypertrophica musculorum vera described by Hesser (1940). The syndrome of Debré and Semelaigne (1935) is a similar, though very rare, muscular hypertrophy occurring in infants with cretinism. In both children and adults, the hypertrophy is reversible on return to the euthyroid state. 'Myxoedematous pseudo-myotonia' refers to significant muscular weakness associated with delayed muscle contraction as well as relaxation. Since delayed return of the ankle-jerks occurs in at least 75 per cent. of hypothyroid persons, minor degrees of 'pseudo-myotonia' must be common in most of these patients. The abnormal tendon reflex response is not due to defect in the neural components of the reflex arc or of muscle excitation, but is thought to be a result of alteration of the contractile mechanism itself (Lambert, Underdahl, Beckett, and Mederos, 1951). The electromyogram does not show the high frequency after-discharge characteristic of true myotonia, but long trains of repetitive polyphasic discharges have been described in some cases (Waldstein, Bronsky, Shrifter, and Oester, 1958; Salick and Pearson, 1967). In Salick's case of myxoedema associated with severe myopathy, the electromyogram suggested an active myopathic process with marked spontaneous irritability. Proximal myopathy has also been described in eight patients by Aström, Kugelberg, and Muller (1961).

Muscle and joint pains are not, however, usually stressed as symptoms of hypothyroidism. In the opinion of an endocrinologist (A. Stuart Mason, personal communication), aches and pains are far more common than genuine muscle weakness and more important from a diagnostic viewpoint;

proximal muscle weakness has been so often sought for because of the frequency of myopathy in thyrotoxicosis. In medical text books, Bayliss (1966) stated that 'stiffness and aching in muscles attributed to "rheumatism", or weakness with tingling in the hands (carpal tunnel syndrome) may be the presenting symptom'. Muscle pains are not mentioned by Selenkow and Ingbar (1966) nor by Stanbury (1967), though it is stated in the latter textbook that 'vague pains in the extremities and back are common, and stiffness in the joints is a frequent complaint'. Wilson and Walton (1959) reported three cases of post-thyroidectomy hypothyroidism, in which pain and stiffness were prominent symptoms. One of their patients had proximal muscle hypertrophy, another had aching after exertion described as an 'after-tennis feeling' but clinically normal muscles, and the third complained of painful cramps in the hands and feet resembling tetany. Fessel (1968) reported three patients with muscle pains, who were thought at first to have polymyositis but were subsequently found to be suffering from hypothyroid myopathy.

Acroparaesthesiae in hypothyroidism were formerly thought to be due to myxoedematous infiltration of the nerve sheaths. That this does sometimes occur is suggested by the deposition of large amounts of pseudomucinous substance in tendon sheaths and subcutaneous tissue in occasional cases, giving an appearance not unlike scleroderma. It is now well recognized that paraesthesiae in hypothyroidism usually result from the pressure of oedematous or pseudomucinous material on the median nerves at the wrists causing the carpal tunnel syndrome; this often occurs in the absence of muscular pains or weakness and may in fact be the only presenting feature of the condition. However, Fincham and Cape (1968) demonstrated the existence of an intrinsic myxoedematous neuropathy in addition to the carpal tunnel syndrome in some cases.

Summary

(1) Nine patients presenting with musculoskeletal symptoms were found to be hypothyroid.

(2) The symptoms were generalized muscle and joint pains, muscle stiffness, cramps, and acroparaesthesiae.

(3) In all cases the symptoms were alleviated by the administration of thyroid hormone.

(4) The literature concerning hypothyroidism associated with musculoskeletal features is discussed.

(5) It is suggested that hypothyroidism should be considered in the differential diagnosis of patients presenting with 'rheumatism'.

I wish to thank Dr. A. Stuart Mason for reading this paper and for his helpful comments.

References

- ASTRÖM, K.-E., KUGELBERG, E., AND MULLER, R. (1961) *Arch. Neurol. (Chicago)*, **5**, 472 (Hypothyroid myopathy).
- BAYLISS, R. I. S. (1966) In 'Price's Textbook of the Practice of Medicine', 10th ed., ed. R. Bodley Scott, pp. 423-5. Oxford University Press, London.
- DEBRÉ, R., AND SEMELAINNE, G. (1935) *Amer. J. Dis. Child.*, **50**, 1351 (Syndrome of diffuse muscular hypertrophy in infants causing athletic appearance: its connection with congenital myxedema).
- FESSEL, W. J. (1968) *Ann. rheum. Dis.*, **27**, 590 (Myopathy of hypothyroidism).
- FINCHAM, R. W., AND CAPE, C. A. (1968) *Arch. Neurol. (Chicago)*, **19**, 464 (Neuropathy in myxedema; a study of sensory nerve conduction in the upper extremities).
- HESSER, F. H. (1940) *Bull. Johns Hopk. Hosp.*, **66**, 353 (Hypertrophia musculorum vera associated with hypothyroidism: a case study).
- HOFFMANN, J. (1897) *Dtsch. Z. Nervenheilk.*, **9**, 278 (Weiterer Beitrag zur Lehre von der Tetanie).
- LAMBERT, E. H., UNDERDAHL, L. O., BECKETT, S., AND MEDEROS, L. O. (1951) *J. clin. Endocr.*, **11**, 1186 (A study of the ankle jerk in myxedema).
- NICKEL, S. N., FRAME, B., BEBIN, J., TOURTELLOTE, W. W., PARKER, J. A., AND HUGHES, B. R. (1961) *Neurology (Minneapolis)*, **11**, 125 (Myxoedema neuropathy and myopathy: a clinical and pathologic study).
- RECHENBERG, H. K. VON (1962) 'Phenylbutazone', pp. 57-61. Arnold, London.
- SALICK, A. I., AND PEARSON, C. M. (1967) *Neurology (Minneapolis)*, **17**, 899 (Electrical silence of myxedema).
- SELENKOW, H. A., AND INGBAR, S. H. (1966). In 'Principles of Internal Medicine', ed. T. R. Harrison, R. D. Adams, I. L. Bennett, W. H. Resnik, G. W. Thorn, and M. M. Wintrobe, 5th ed., p. 421. McGraw-Hill, New York.
- STANBURY, J. B. (1967) In 'Cecil-Loeb Textbook of Medicine', ed. P. B. Beeson and W. McDermott, 12th ed., p. 1297. Saunders, Philadelphia.
- WALDSTEIN, S. S., BRONSKY, D., SHRIFTER, H. B., AND OESTER, Y. T. (1958) *Arch. intern. Med.*, **101**, 97 (The electromyogram in myxedema).
- WILSON, J., AND WALTON, J. N. (1959) *J. Neurol. Neurosurg. Psychiat.*, **22**, 320 (Some muscular manifestations of hypothyroidism).

RÉSUMÉ

L'hypothyroïdisme se manifestant par des symptômes musculosquelettiques

- (1) Neuf malades présentant des symptômes musculosquelettiques ont été trouvés comme étant hypothyroïdes.
- (2) Les symptômes étaient des douleurs généralisées aux muscles et aux articulations, de la rigidité musculaire, des crampes et de l'acroparesthésie.
- (3) Dans tous les cas les symptômes étaient soulagés par l'administration de l'hormone thyroïde.
- (4) La bibliographie concernant l'hypothyroïdisme avec des signes musculosquelettiques est discutée.
- (5) Il est suggéré que l'hypothyroïdisme devrait être considéré pendant le diagnostic différentiel des malades se présentant avec du 'rhumatisme'.

SUMARIO

Hipotiroidismo concurrente con síntomas esquelomusculares

- (1) Se descubrió que nueve pacientes que presentaban síntomas esquelomusculares padecían de hipotiroidismo.
- (2) Los síntomas eran, en general, dolores musculares y articulares, rigidez muscular, calambres y acroparestesia.
- (3) En todos los casos, los síntomas fueron aliviados mediante la administración de hormona tiroidea.
- (4) Se discute la literatura concerniente al hipotiroidismo con características esquelomusculares.
- (5) Se sugiere que el hipotiroidismo debería ser tomado en cuenta en el diagnóstico diferencial de pacientes con 'reumatismo'.