Hypothyroidism presenting with musculoskeletal symptoms

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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 perhaps 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

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (yrs)</th>
<th>Presenting symptoms</th>
<th>Median nerve delay</th>
<th>Hypothyroid</th>
<th>Delayed ankle-jerk relaxation</th>
<th>ECG changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pain</td>
<td>Stiffness</td>
<td>Cramp</td>
<td>Acroparesthesiae</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>54</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (unilateral)</td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>ND</td>
</tr>
<tr>
<td>5</td>
<td>56</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>ND</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+ (unilateral)</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>ND</td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>ND</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+ (bilateral)</td>
</tr>
</tbody>
</table>

ND = Nerve conduction not tested.
Hypothyroidism presenting with musculoskeletal symptoms

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 (131I) 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.; 131I 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 features.

<table>
<thead>
<tr>
<th>features</th>
<th>Other symptoms</th>
<th>Duration at first attendance (yrs)</th>
<th>Relief by thyroid therapy</th>
<th>Improvement in ECG</th>
<th>Follow-up (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum cholesterol (mg./100 ml.)</td>
<td>Protein-bound iodine (mg./100 ml.)</td>
<td>131I uptake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>300</td>
<td>Low</td>
<td>0·7</td>
<td>None</td>
<td>2</td>
<td>+</td>
</tr>
<tr>
<td>453</td>
<td>Low</td>
<td>ND</td>
<td>None</td>
<td>Several</td>
<td>+</td>
</tr>
<tr>
<td>540</td>
<td>Low</td>
<td>1·4</td>
<td>Macrocytic anaemia</td>
<td>9/12</td>
<td>+</td>
</tr>
<tr>
<td>320</td>
<td>Low</td>
<td>5·5</td>
<td>None</td>
<td>6/12</td>
<td>+</td>
</tr>
<tr>
<td>300</td>
<td>Low</td>
<td>5·8</td>
<td>None</td>
<td>5/12</td>
<td>+</td>
</tr>
<tr>
<td>328 (taking thyroid extract)</td>
<td>Low</td>
<td>6·5</td>
<td>None</td>
<td>2/12</td>
<td>+ (after increasing dose of thyroid extract)</td>
</tr>
<tr>
<td>334</td>
<td>Low</td>
<td>1·3</td>
<td>None</td>
<td>8</td>
<td>+</td>
</tr>
<tr>
<td>246</td>
<td>Low</td>
<td>3·4</td>
<td>Cerebellar features</td>
<td>20</td>
<td>±</td>
</tr>
<tr>
<td>143</td>
<td>Low</td>
<td>1·2</td>
<td>None</td>
<td>6/12</td>
<td>+</td>
</tr>
</tbody>
</table>
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 hypoalgiesia 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 msc. as compared with 3 msc. on
the left side. Sensory conduction times from wrist to index
finger were respectively 3 and 2 msc.

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 labora-
tory 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

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 syn-
drome 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 conduc-
tion 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. Acropara-
esthesiae were always abolished by therapy.

Electrocardiograms were carried out after treat-
ment in six patients and all but one showed signifi-
cant 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
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 hypothyrophia 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 Medeross, 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, Shritfer, 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 textbooks, 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 '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 pseudosubcutaneous 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.

<table>
<thead>
<tr>
<th>Table II</th>
<th>Muscular features in hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>General muscle weakness</td>
<td></td>
</tr>
<tr>
<td>Pain and stiffness</td>
<td></td>
</tr>
<tr>
<td>Carpal tunnel syndrome</td>
<td></td>
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<tr>
<td>Muscle hypertrophy</td>
<td></td>
</tr>
<tr>
<td>Hoffmann's syndrome (adults)</td>
<td></td>
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<tr>
<td>Debré and Semelaigne's syndrome (infants)</td>
<td></td>
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<tr>
<td>'Pseudomyotonia'</td>
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<tr>
<td>Muscle cramps ('pseudo-tetany')</td>
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</tr>
<tr>
<td>Histological features of muscular weakness:</td>
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</tr>
<tr>
<td>Objective loss of muscle strength</td>
<td></td>
</tr>
<tr>
<td>Disturbance of tendon reflexes</td>
<td></td>
</tr>
<tr>
<td>Delays in muscle contraction</td>
<td></td>
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<tr>
<td>Abnormal muscle responses to nerve stimulation</td>
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</table>

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RéSUMÉ

L'hypothyroïdisme se manifestant par des symptômes musculosquelettiques

(1) Neuf malades présentant des symptômes musculosquelettiques ont été trouvés comme étant hypothyroïdiques.
(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 thyroïdienne.
(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 esqueletomusculares

(1) Se descubrió que nueve pacientes que presentaban síntomas esqueletomusculares padecían de hipotiroidismo.
(2) Los síntomas eran, en general, dolores musculares y articulares, rígidez 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 esqueletomusculares.
(5) Se sugiere que el hipotiroidismo debería ser tomado en cuenta en el diagnóstico diferencial de pacientes con 'reumatismo'.