Muscle pain and wasting in osteomalacia[1]

D N Golding MD FRCPI
Princess Alexandra Hospital, Harlow, Essex

Osteomalacia often presents with pain in the back and limbs. Proximal muscle weakness is not uncommon in this condition, though profound muscle wasting is very unusual. In the following case the symptoms resembled polymyalgia rheumatica and there was progressive weakness and wasting of the leg muscles.

Case report

A 42-year-old baker with Crohn's disease had been advised to adhere to a high bran diet and exclude milk products as these seemed to exacerbate the abdominal symptoms. In 1969 the enteritis became worse so the ileum was resected and thereafter he had no further bowel trouble. In the past year he had complained of marked weakness and stiffness of the legs which resulted in a very awkward gait.

Examination showed weakness of the ileopsoas and rhomboid muscles and moderate leg oedema, which was thought to be due to hypoproteinaemia as the serum albumin was 20 g/l (normal 36–52). The blood count, ESR, urea, creatinine and electrolytes were normal, as were radiographs of the chest, spine and pelvis. The liver was enlarged 3 cm below the costal margin and liver function tests showed the gamma glutamyl-transferase to be slightly raised at 44 U/l. The alkaline phosphatase was raised at 318 U/l, and was thought at the time to be hepatic in origin. It seemed that the patient had a form of myopathy, but serum muscle enzymes and electromyography were normal and a needle biopsy of the quadriceps revealed only a moderate degree of atrophy involving both types I and II fibres with no evidence of myositis. He became progressively weaker and lost 2–3 stone (9.2–12.8 kg) in weight.

Some weeks later he complained of generalized joint pains and morning stiffness, especially involving the central joints. The blood count and ESR were normal, tests for rheumatoid and antinuclear factor negative and serum immunoglobulins within normal limits. The pain and stiffness became more severe and it was thought he might have polymyalgia rheumatica, but there was no improvement following prednisolone 15 mg daily. By this time there was profound muscle wasting. The alkaline phosphatase rose to 600 U/l: isoenzyme revealed that 170 units of this were of hepatic origin, 432 units from bone. Repeat spine and pelvic radiographs showed marked, generalized osteoporosis with Looser's zones suggesting osteomalacia. The serum calcium was 1.68 mmol/l (normal 2.1–2.7), phosphate 1.25 mmol/l (normal 0.8–1.4), 24 h urinary calcium 1 mmol/l (normal 2.5–7.5). Biopsy of an iliac crest showed uncalcified osteoid seams around the trabeculae, confirming osteomalacia. This was found to be due to vitamin D deficiency consequent upon malabsorption (which often occurs in Crohn's disease) as there was increased xylose excretion over five hours, a flat glucose tolerance curve, and the faecal fat measured 142 mmol in three days (normal less than 18 mmol/day). The low serum calcium was considered to be partly due to low vitamin D levels and partly to lack of milk foods in the diet.

The patient was given high doses of vitamin D intramuscularly (60 000 units weekly for four weeks) followed by oral alfacalcidol (One-Alpha) 0.5 mg daily and calcium supplements. Within a few weeks the pain and stiffness had subsided and he was feeling much stronger, being able to lift loads up to 25 kg. Subsequent gain in weight and muscle mass was rapid.

Discussion

Osteomalacia must be considered in patients developing weakness of the legs for no apparent reason once other conditions including neurological disorders (upper and lower motor neurone lesions and ataxia), primary muscle disease (myopathies and polymyositis), metabolic and endocrine disorders (such as hypothyroidism and hypokalaemia) have been excluded. Initially radiographs of the spine and pelvis may not reveal the typical features of osteomalacia (or even osteoporosis) because muscle weakness often antedates radiological changes. The early stages of osteomalacia may be revealed by reduced serum calcium and high serum alkaline phosphatase in the absence of obvious bone disease (Albright & Reifenstein 1948), so it is important to include these in the investigation of patients with unexplained weakness of the legs.

Muscle weakness ('pseudomyopathy') is a well-known feature of osteomalacia, but severe weakness and wasting as in this case is very unusual. The reason for muscle weakness in this condition has not been established. Lack of vitamin D in its active form ($1,25(OH)_2$ vitamin D) is thought to be important for the function of connective tissue, as deficiency *in vitro* has been shown to interfere with several aspects of cell activity (Kahn *et al.* 1981). It is not thought that deficiency of calcium ions is responsible for the weakness; for example, measurement of quadriceps strength, plasma calcium, phosphorus and alkaline phosphatase in 4 vegetarian Asian women with weak quadriceps and hypophosphataemia revealed that after treatment with vitamin D and calcium there was

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biochemical improvement but no increase in quadriceps strength (Isenberg *et al.* 1982).

The polymyalgic-like episode – severe central joint pain and morning stiffness – is also interesting. The normal ESR and negative response to systemic steroids excluded polymyalgia rheumatica, and it appears that osteomalacia should be included in the differential diagnosis of this condition.

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Intractable polymyositis: prolonged remission induced by total body irradiation[1]

S H Morgan MB MRCP[2]
R M Bernstein MA MRCP
G R V Hughes MD FRCP
Rheumatology Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

Polymyositis may run a chronic, debilitating course. Permanent disability may result from fibrosis and atrophy of muscle, and death can occur as a result of pneumonia, cardiac involvement or complications of treatment. Preliminary results of treatments with total body irradiation (TBI) were reported by Engel *et al.* (1981) and Hubbard *et al.* (1982). We now report the successful use of TBI to induce prolonged remission in a patient whose disease had not responded to conventional therapy.

Case report

Early in 1979, a 49-year-old metallurgist developed a febrile illness with some pain in the small joints of both hands. A week later he began to notice difficulty with walking and rising from a chair, and by the following week he could not get out of a bath without help. At his local hospital a diagnosis of polymyositis was made on the basis of elevated serum muscle enzymes, electromyography and muscle biopsy. In the past he had noticed grittiness of his eyes and described classical Raynaud's phenomonen. A search for occult malignancy was negative.

His initial response to prednisolone was good, but because of a relapse in 1979 azathioprine was added. This induced a prolonged remission lasting until 1981, when a further 'flare' occurred. An increase in his dose of prednisolone failed to control this, and intravenous methotrexate was started (25 mg weekly increasing to 50 mg) with little benefit.

He was referred to the Rheumatology Unit at Hammersmith Hospital for consideration of treatment with TBI. On admission he was febrile, and serial measurements of peak flow showed a gradual decline in ventilatory function. There was a slight anaemia (Hb 10.1 g/dl and his ESR was 90 mm/h. The serum muscle enzymes were elevated, with a creatinine phosphokinase (CPK) of 1200 iu/l (normal 170) and myoglobinuria. A needle muscle biopsy showed an intense inflammatory cell infiltrate with necrosis. Anti-Jo-l-antibody was detected in his serum and a chest radiograph showed patchy shadowing consistent with pulmonary fibrosis.

In view of his profound weakness and declining clinical condition a trial of TBI was given (200 cGy over 10 weeks). The response was dramatic, with a fall in CPK two weeks after starting treatment, paralleled by development of a lymphopenia and improvement in muscle strength measured by strain-gauge myometry (Edwards & McDonnel 1974). A month later he left hospital and was able to return to work. Eighteen months later he remains well on 5 mg prednisolone daily, although his CPK has remained persistently elevated (1000–2000 iu/l).

Discussion

Muscle destruction in myositis probably involves a subset of cytotoxic lymphocytes (Daukins & Mastaglia 1973), the role of myositis-specific autoantibodies being unclear (Nishikai & Reichlin 1980, Matthews & Bernstein 1983). Irradiation has diverse effects on lymphocytes but is immunosuppressive. A lymphopenia occurred in this patient within two weeks of starting treatment with TBI, concomitant with improvement in muscle strength and a fall in CPK.

The long-term benefit of TBI is uncertain. In one other patient thus treated (Hubbard *et al.* 1982) remission was short-lived, lasting less than six months; and in another reported case (Shon *et al.* 1982) attempts to induce remission were unsuccessful.

Technically, TBI is easier to administer than total lymphoid irradiation, which has been used

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[2]Present address: CRC, Northwick Park Hospital, Harrow, Middlesex

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