

The spectrum of disease in weakness and wasting of the quadriceps muscles

Case reports

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Summary

Three patients who presented with weakness and wasting of the quadriceps muscles ('quadriceps myopathy'), are reported. In each, electrophysiological and biopsy studies revealed completely different pathological processes, including motor unit disease, polymyositis and muscular dystrophy. Double biopsies performed in 2 of the patients showed the disease process to involve upper as well as lower limbs. The diffuse and heterogeneous nature of this form of neuromuscular disease is confirmed.

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Weakness and associated wasting, when apparently confined to the quadriceps muscles, is an uncommon clinical finding which nevertheless enjoys, among clinicians, the popular title of 'quadriceps myopathy'. This term is attributed to Bramwell,¹ who described 2 cases of symmetrical, atrophic paresis of the quadriceps muscles in 1922. Since then, the nosology of the condition has been debated intermittently.²⁻⁴ It has been suggested⁵ that quadriceps myopathy is a syndrome rather than a specific disease entity, although Walton⁶ makes the authoritative assertion that it is almost certainly a variety of limb girdle muscular dystrophy. We report 3 cases, in which the differing pathogenetic mechanisms underlying this selective form of muscle atrophy are clearly indicated.

Case reports

Case 1

In January 1979 a 53-year-old White woman presented with a history of slowly progressive weakness in the lower limbs. At school she had been exempted from gymnastics because of a tendency to fall. At the age of 20 she began to experience difficulty in rising from the sitting position and climbing stairs. There had been a gradual deterioration over the years and she was particularly susceptible to buckling of the knees if bumped on the backs of her legs. Except for 4 miscarriages, the previous medical history was unremarkable.

It appeared from the family history that the patient's mother, an aunt, niece and great-grandmother (all of them in the maternal line) had developed weakness in the legs. At an

advanced age her great-grandmother was also reported to have lost power in her hands. Further details could not be obtained.

On examination, the patient was alert and co-operative. Although somewhat obscured by fat, there was obvious wasting of the lower parts of both quadriceps muscles, particularly the vastus medialis (Fig. 1), and extension and flexion of the knees was grade 2-3 power (British Medical Research Council scale). Motor power and muscle bulk throughout the rest of the body were normal and she showed no difficulty in walking on heels and toes. The patellar reflexes could not be elicited, but the remainder of the tendon reflexes were normal, as were the cranial nerves, sensation and co-ordination.

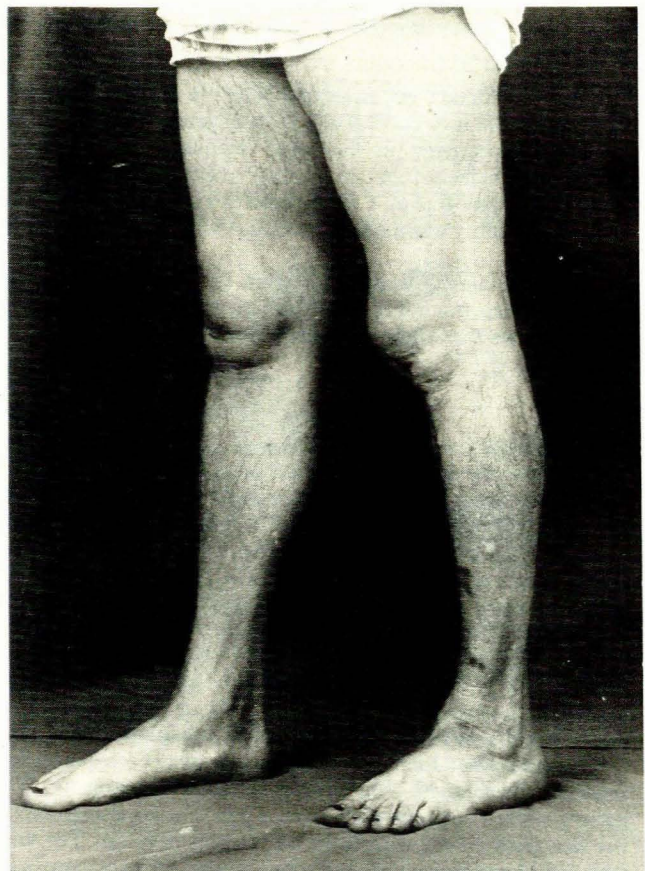


Fig. 1. Case 1 — quadriceps wasting with the typical depression above the patella.

Laboratory tests were carried out and the following were reported as being normal: haematological values, serum urea and electrolytes, albumin-globulin ratio, liver enzymes, serum alkaline phosphatase level, effective thyroid index (ETI). Results of antinuclear factor, antimitochondrial, anti-smooth-muscle, antiparietal, antithyroglobulin and antimicrosomal tests were negative. The ESR was 5 mm/h and serum creatine

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phosphokinase 26 U (normal 40 U); serological reactions were negative.

Electromyography (EMG) of the left vastus medialis and lateralis and rectus femoris muscles, as well as the hamstring muscles, showed 'single motor unit' potentials with an increased duration and a rather low amplitude (Fig. 2). The gastrocnemius, tibialis anterior, deltoid and biceps brachialis muscles all showed normal potentials, and potentials with slightly prolonged duration and a 'poor interference pattern' on full contraction. The intrinsic hand and foot muscles were essentially normal. There were no signs of fibrillations, positive denervation potentials, giant motor unit potentials or fasciculations, and the number of polyphasic potentials was within normal limits.



Fig. 2. Case 1, electromyography: single motor unit pattern on full contraction.

Motor conduction velocities and delays in the right peroneal nerve were 53,8 m/s and 3,8 m/s respectively and 67,4 m/s and 3,0 m/s respectively in the right median nerve. Sensory conduction velocity in the right median nerve (index finger/wrist) was 46,2 m/s. A diagnosis of a hereditary, proximal motor neuropathy was made on clinical and electrophysiological grounds.

Biopsy specimens were taken from the gastrocnemius and deltoid muscles but not from the quadriceps because of the very few potentials that could be evoked during EMG.

Case 2

In May 1978 a 66-year-old woman was admitted to the neurology department because of progressive weakness and wasting of both thighs of about 2 years' duration. A year before admission she began to fall easily and complained of diffuse pains in both legs, particularly during the night. There were no cramps, but she thought her grip had become weaker. She had been seen by a neurosurgeon and an orthopaedic surgeon for these complaints together with low backache, and the atrophy of her thighs had drawn the attention of one of them. Previous medical history included asthma since the age of 25, which was treated with cortisone from 1966 to 1969, and three abdominal operations for large bowel volvulus and subsequent adhesions.

On examination there was striking atrophy of both quadriceps muscles, particularly the vastus medialis component. The patient walked carefully with normal gait, but was compelled to use her arms when rising from the sitting position. The knee jerks could not be elicited, but other tendon reflexes were brisk and symmetrical. No pathological reflexes were present. Global power in hands and feet was slightly reduced and the thenar muscles were small. There was no evidence of myotonia or fasciculation, and sensation and co-ordination were intact.

The following were reported as being normal: ESR, full blood count, serum electrophoresis, glucose and blood urea, electrolytes, serum vitamin B₁₂ and folic acid, calcium and magnesium, ETI. Results of rheumatoid factor, LE cell, C-reactive protein and antinuclear factor tests and the Wassermann reaction in blood and CSF were negative. The liver functions were normal apart from a slight rise in lactic dehydrogenase

level. Creatine phosphokinase was 33 U (normal 40 U). The CSF was normal, as were the results of screening tests for porphobilinogen. Radiology of the spine showed multiple disc degenerations, cervical spondylosis and arthrosis, and lumbar scoliosis. Previous myelography was normal. Radiographs of chest and skull were normal as was the barium meal (apart from the colon resection findings).

EMG performed with concentric monopolar needle electrodes on the left deltoid, quadriceps femoris and anterior tibialis muscles showed many short-lasting potentials with a rather low amplitude and more than the normal amount of polyphasic potentials in places (Fig. 3). No pseudo-divebomber effect was heard and no fibrillations, positive denervation potentials or fasciculations could be demonstrated. Conduction velocities were as follows — left median nerve, upper arm/wrist: 70 m/s, distal latency 4,3 m/s; left ulnar nerve upper arm/wrist: 60,7 m/s, distal latency 3,4 m/s; and left peroneal nerve: 44,6 m/s, distal latency 3,8 m/s.

Tetanic contraction of the left hypothenar muscles with 20 cps and impulse duration of 0,2 m/s resulted in a normal decrease of amplitudes, with a normal expected recovery rate and no reaction on intravenously administered edrophonium bromide.

A clinical diagnosis of a late onset myopathy, possibly a polymyositis, was made, and biopsy specimens were taken from the deltoid and quadriceps muscles.

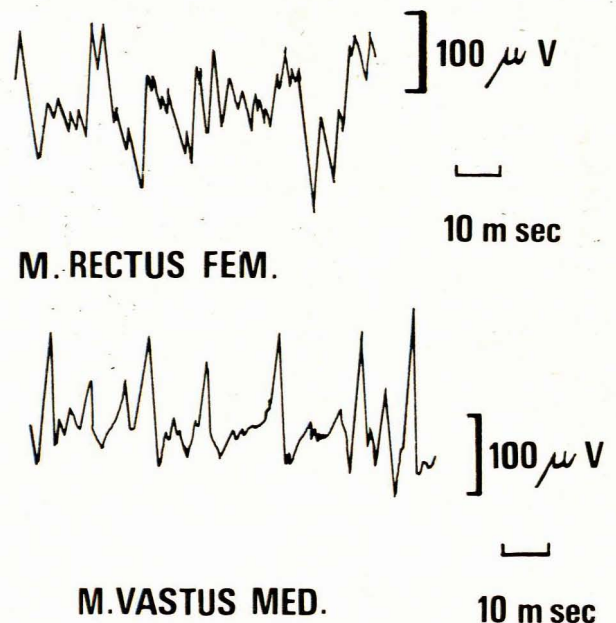


Fig. 3. Case 2, electromyography: short-lasting potentials with low amplitude and polyphasic potentials.

Case 3

In January 1974 a 51-year-old man was seen by the Gloucester Hospital neurologist, Dr David Stevens. A history of difficulty in climbing stairs, which had come on gradually over the previous 4 years, was elicited. The patient also tended to fall easily. On examination there was marked wasting and weakness of the quadriceps muscles, with rather bulky calves which were thought to be possibly hypertrophied. The remainder of the physical examination was normal, including motor power elsewhere, cranial nerves, reflexes and sensation. Upon being questioned he admitted to usually being relegated to the position of goalkeeper in his school sports activities. The family history was non-contributory.

A number of routine laboratory tests were carried out and the results were normal, but the serum CPK value was in excess of 700 U on two occasions (normal 50 - 100 U). EMG revealed an excess of polyphasic potentials in both the quadriceps and calf muscles, with normal activity in the deltoid and biceps muscles. Nerve conduction tests were normal. The clinical impression was that of a quadriceps myopathy due either to muscular dystrophy or polymyositis.

Biopsy was carried out on the rectus femoris on one side.

Pathological findings

All biopsy samples were frozen in liquid nitrogen and cryostat sections were stained routinely, using the following techniques: haematoxylin and eosin (H and E), Gomori trichrome, reduced nicotinamide adenine dinucleotide (NADH₂), succinic dehydrogenase (SDH), lactic dehydrogenase (LDH), myosin ATPase at acid and alkaline incubations, periodic acid-Schiff (PAS) and fat. Formalin-fixed samples were stained with the H and E and Masson trichrome methods.

In case 2, where initial results suggested an inflammatory myopathy, additional frozen sections were incubated with appropriate fluorescein-tagged antibodies for the demonstration of IgG, IgM, IgA, IgE, fibrin and complement C3. Paraffin sections were stained for RNA with the methyl green pyronin method.

Case 1

Both samples showed extensive fibre type grouping, consistent with a neuropathic picture and presumably reflecting a state of reinnervation (motor unit disease). Conversion was predominantly to the type I cell, with a relative 'loss' of type II fibres, although some areas of the biopsy specimens showed numbers of enclosed type II cells (Fig. 4). There was also a degree of abnormal variation in fibre size, with scattered small cells measuring $\pm 20 \mu\text{m}$ against an average diameter of $\pm 60 \mu\text{m}$. There was no evidence of group atrophy, or of target cell formation. Additional stains for acid phosphatase (with normal controls) were negative.

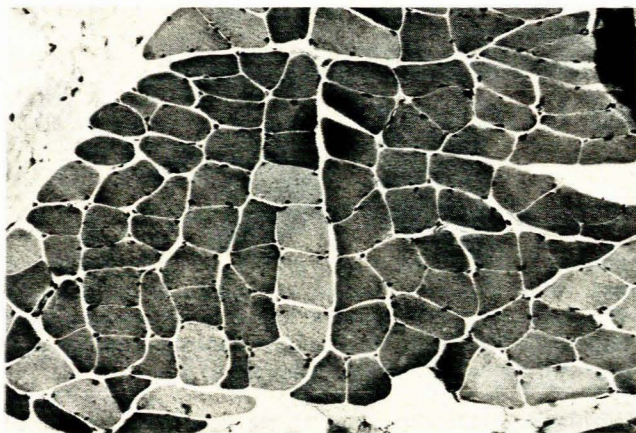


Fig. 4. Fibre type grouping; the dark cells are type 1 (ATPase, pH 4,6 ($\times 210$)).

Case 2

The histological picture was that of a low-grade inflammatory myopathy, more severe in the quadriceps than the deltoid. The inflammatory infiltrate (Fig. 5) consisted predominantly of lymphocytes with occasional plasma cells and affected the muscle fasciculi diffusely, with concentration on small blood

vessels. Occasional myofibre necrosis was present. The histochemical enzyme mosaic was normal, but revealed a mild degree of type II fibre atrophy. Immunohistochemistry was negative.

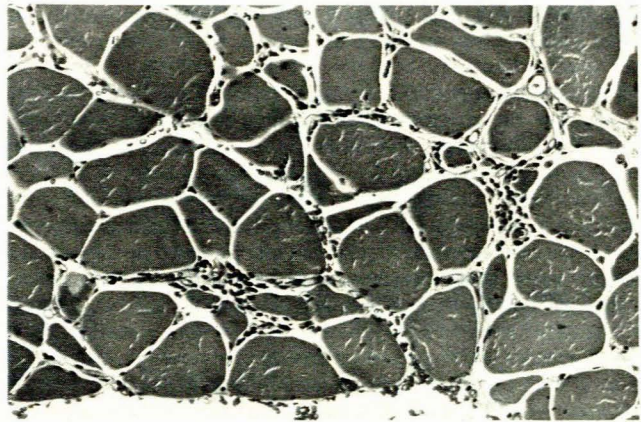


Fig. 5. Lymphocytic infiltrate centred mainly on small intramuscular vessels. Fibre size variation is clearly visible (H and E $\times 250$).

Case 3

The picture was characteristic of a dystrophic myopathy, with enormous variation in cell size (± 10 - $120 \mu\text{m}$), loss of angulation, fibre splitting, hyalinization, necrosis and phagocytosis and greatly increased endomyseal connective tissue (Fig. 6). The enzyme mosaic was lost because of poor cell differentiation. The fasciculi were infiltrated with fat and many cells showed increased lipid content, with poor staining for glycogen.

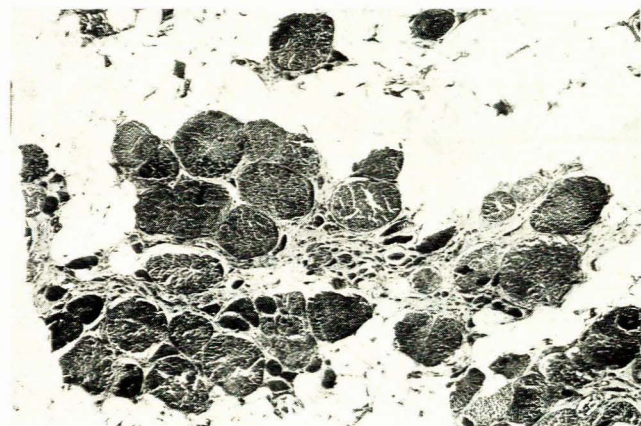


Fig. 6. Typical dystrophic myopathy, showing myofibre atrophy and hypertrophy, fibrosis and fat infiltration (H and E $\times 100$).

Discussion

Weakness and atrophy of selected muscle groups is a not uncommon occurrence in the myopathies and in central neurogenic atrophy, and may be proximal or distal, with or without involvement of muscles innervated by the cranial nerves. The muscular dystrophies probably display this tendency to the most marked degree, but polymyositis has also been shown to be capable of exhibiting a remarkable selectivity.⁷ It is therefore perhaps surprising that this line of reasoning seems to have found little favour in the explanation of apparently isolated involvement of the quadriceps muscles by differing pathogenetic mechanisms. In addition, the pathological process may be exacerbated by what Brooke⁸ has described as the

particular susceptibility of the quadriceps muscles to wasting (especially the vasti). Although weakness and wasting of the quadriceps was the presenting feature in our cases, various combinations of clinical and electrophysiological testing, together with the morphology, indicated that the disease process was more widespread. In case 1 the EMG was diagnostic and in cases 2 and 3 it was very helpful. Patients 1 and 2 were subjected to double biopsies, each of which provided evidence of morphological abnormalities beyond the clinically affected site.

Much of the uncertainty surrounding the pathogenesis of the so-called quadriceps myopathy relates to changes shown at biopsy, which have been described by various authors. Denny-Brown's⁹ case showed isolated myofibre necrosis, a feature depicted in his original article and reproduced again in the paper of Turner and Heathfield² who actually followed up this patient 20 years later. On that occasion, besides interpreting the lesion as a form of polymyositis, they demonstrated myopathic changes in the upper limb on EMG. The second patient, reported by the same authors as a case of quadriceps myopathy, underwent muscle biopsy; the photomicrograph illustrates severe muscle atrophy and fibrosis with what might be a focal collection of inflammatory cells. This case was diagnosed as polymyositis. Two cases reported by van Wijngaarden *et al.*³ are illustrated by myosin-ATPase and oxidative enzyme stains, and in our opinion these stains, together with the fields selected, do not provide firm examples of dystrophic myopathy. Walton's patients¹⁰ had clearly illustrated dystrophic myopathies, a fact which presumably explains the statement in his textbook;⁶ possibly he did not accept the paper of van Wijngaarden *et al.*,³ where the heterogeneous nature of quadriceps myopathy is suggested. We agree with Boddie and Stewart-Wynne⁵ when they conclude that quadriceps myopathy is not a distinct entity, but these authors reported a single case and, if the fibre type grouping shown in

their paper points to a genuinely neuropathic process, there is also a disturbing amount of muscle cell necrosis and hyalinization present.

The double biopsies performed on 2 of our patients confirm another expected finding: while selective weakness and atrophy of the quadriceps may be a remarkable clinical feature, the disease process is, of course, more widespread.

The frequent reference to Bramwell's¹ article of 1922 raises a minor but interesting historical point, for this paper was entitled 'Symmetrical, atrophic paresis of the quadriceps muscles of probable myopathic origin'. His description of 2 patients was entirely clinical, with neither electrophysiological or biopsy studies to help. Despite his caution in designating the underlying pathogenesis, he seems to have been misquoted ever since.

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Nuus en Kommentaar/News and Comment

Levodopa and herpes zoster

It has been shown that levodopa alleviates the pain from bone metastases of cancer of the breast and elsewhere, and over the past few years several uncontrolled studies have been published suggesting that this drug is also useful for the pain associated with herpes zoster.

A controlled study from Paris (Kernbaum and Hauchecorne, *J. Amer. med. Ass.*, 1981, **246**, 132) on 47 outpatients with herpes zoster appears to confirm this finding. The study was double-blind, and benserazide 25 mg was added to 100 mg levodopa in each capsule; the control capsules contained a placebo. Two capsules were taken 3 times a day.

The severity of pain was assessed on an intensity scale of 5, and patients were asked to chart pain intensity on a visual analogue scale. Six patients had to stop treatment because of vomiting. Pain decreased to a significantly greater extent in the levodopa group than in the placebo group after the 3rd day of treatment, both in the group as a whole and in the patients with particularly severe pain. Why the drug works remains unknown.

Psychosomatics of faith and hope

Faith and hope can have two opposite effects on the psyche and soma, argues Professor Stumpf of Cologne (*Dtsch. Arztebl.*, 1981, **78**, 1685). They represent two different psychosomatic reactions. Unlike the animal, man lives in both the present and the future and is much influenced by the latter.

Faith goes further than hope; whereas hope is more concerned with the conscious and intellectual strata of the human subject, faith belongs more to the unconscious and emotional areas. Whereas hope implies uncertainty about the future and therefore leads to restlessness and tension, and thus to passive attitudes, loss of drive and probably lack of physical resistance, faith implies certainty and therefore dictates actions directed towards restoration of health, together with a calm and patient outlook and mobilization of forces, with promotion of healing. Hope has a negative effect on the healing process, faith promotes it. These effects cannot of course be translated as yet into physiological and chemical terms.