Isolated muscle hypertrophy as a sign of radicular or peripheral nerve injury

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Abstract

Two patients with isolated neurogenic hypertrophy of the trapezius muscle due to accessory nerve injury and a patient with neurogenic hypertrophy of the anterior tibial muscle due to chronic radicular lesion L4 are described. Electromyography of the affected muscles showed dense continuing spontaneous discharges of complex potentials. Muscle biopsy performed in two patients showed abundant hypertrophic muscle fibres, identified in one case by ATP-ase reaction as being of predominantly type I. In the majority of previously reported patients with neurogenic muscle hypertrophy confined to the calf muscle, a passive stretch mechanism was suggested as a cause of the hypertrophy. It is assumed that the excessive spontaneous muscle activity gave rise to the hypertrophy in these patients. This may also be true in previously reported patients with neurogenic hypertrophy and similar spontaneous activity in electromyography.

Neurogenic lesions normally cause muscle wasting. But occasionally a neurogenic lesion results in hypertrophy of a single muscle. In 1848 R J Graves reported a man with sciatica and subsequent calf enlargement.¹ A second case was published in France: in 1918 Lhermitte noticed a man with calf enlargement after a bullet injury to the sciatic nerve.² In 1932 he reported a second³ and a third patient with the same enlargement after sciatica.⁴ Further cases of calf enlargement after sciatica were published later.⁵⁻¹⁷ Both Valenstein *et al*¹⁸ and Vasilescu *et al*¹⁹ described calf enlargement with chronic relapsing polyneuropathy. In his first report² Lhermitte also commented on a soldier who experienced a thenar hypertrophy after a forearm injury, and neurogenic hypertrophy of the hand and forearm muscles with chronic relapsing inflammatory polyneuropathy has been described in a recent report.¹⁶

Our three patients illustrate that neurogenic hypertrophy of muscles due to radicular or peripheral nerve lesions is not restricted to the calves and may also affect the trapezius and anterior tibial muscles. They suggest a common pathogenetic pathway for neurogenic muscle hypertrophy.

Case reports

Patient 1 This 39 year old athletic man was involved in a head-on car collision nine years previously. He was wearing a seat belt and suffered only minor injuries. Subsequently he noticed increasingly painless wave-like muscle motions above his right shoulder. There was no weakness or sensory disturbance. The right trapezius muscle bulk gradually increased, and because of two episodes of torticollis the patient sought medical advice.

The family history for muscle or nerve disease was negative. The clinical examination showed normal cranial nerves, normal neck mobility, and symmetrical tendon jerks. The Babinski sign was negative. Motor and sensory functions, coordination, and gait were normal. Sweating was symmetrical. There was increased muscle bulk of his right trapezius muscle (fig 1) and frequent muscle twitching. General physical examination was normal. Laboratory tests such as erythrocyte sedimentation rate (ESR), white cell count (WCC), serum chemistries including glucose and calcium, and creatine phosphokinase (CPK) were unremarkable. Radiographs of the chest, shoulders, and scapulae and EKG were normal. CT (fig 2) of the cervico-thoracic region confirmed an increased size and decreased density of the right trapezius muscle.

Electrophysiological studies: electromyography of the right trapezius muscle showed continuous spontaneous activity at all sites as numerous mostly polyphasic and large potentials (peak to peak amplitudes of up to 1.2 mV)

Figure 1 Patient 1 presenting with a hypertrophied right trapezius muscle (R=right).

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Figure 2 CT scan of an axial section through the trapezius muscles of patient 1. Note the enlarged right trapezius muscle compared with the normal left side (R = right).

occurring at random or as brief grouped discharges. The interference pattern during maximal voluntary effort was normal. Motor unit potential analysis revealed a moderate prolongation of the average potential duration (18.6 ms, 23 potentials measured). Electromyography of the right sternocleidomastoid muscle was normal. Both accessory nerves showed normal motor latencies to the trapezius muscles.

Muscle biopsy from the right trapezius showed sections with abundant hypertrophic fibres predominantly of type I as well as sections with small groups of atrophic, elongated type II fibres according to the ATP-ase reaction, and type grouping was evident (figs 3, 4). The overall distribution of type I and II fibres was normal. A diagnosis of right accessory nerve lesion was made.

Patient 2 The family history of this 20 year old asthenic man was negative. At the age of 18 he had a scalenic lymph node biopsy on his left side. The lymph node histology was compatible with a cat scratch disease. Approximately one month later he felt pain in his left shoulder and subsequently noticed weakness of his left shoulder and arm. He was referred six

Figure 3 Muscle fibre histogram of the biopsy from the trapezius muscles of patient 1 showing fibre diameters and type distribution. There are abundant hypertrophic fibres, predominantly of type I and also atrophic type II fibres. Fibre type distribution is normal (Specimen 860916, ATP-ase, pH 4.6, 10 $\times$).

Figure 4 Biopsy from the same specimen as in fig 3 showing a sample with groups of atrophic, angulated fibres, all belonging to type II. Type grouping and targetoid fibres are also present (ATP-ase, pH 4.6, 7 $\times$).

months after the lymph node biopsy. Except for the atrophy of the upper part of his left trapezius muscle, the general physical and neurological examinations were normal. Bulk and function of the sternocleidomastoid muscle was normal. ESR, WCC, CPK, and radiographs of the shoulder were normal. The clinical diagnosis was a left accessory nerve lesion and it was corroborated by electromyography.

As there was no spontaneous improvement, the patient had surgery for his nerve lesion. The surgical findings showed a completely transected left accessory nerve at the site of the lymph node biopsy. The proximal and distal nerve endings were easily found, an anastomosis was made, and the nerve was sutured. Six months later electromyography showed "high frequency complex repetitive discharges" in the left trapezius muscle. A year later there was a prominent hypertrophy of the left trapezius muscle. The muscle weakness was still present, with force against very slight resistance (Grade 3 to 4 according to the MRC scale).

Electromyography of the upper portion of the left trapezius muscle showed continuous and dense repetitive discharges of simple or polyphasic potentials mostly of high frequency (> 10 Hz) at all sites in the completely relaxed muscle. Additional discharges were triggered by needle movements and voluntary contractions. There was a fair amount of voluntary activity, which yielded an intermediate pattern at maximal voluntary activation. Stimulation of the left accessory nerve produced a muscle response of prolonged latency in the trapezius muscle. A diagnosis of left accessory nerve lesion was made.

Patient 3 This was a 41 year old farmer and ski instructor with a negative family history for muscle and nerve diseases. At the age of 29 he

Figure 5 CT scan through the lower legs of patient 3. Note the hypertrophic left anterior tibial muscle (arrowheads) compared with the normal right side (R = right).

Figure 6 Needle-EMG from the left tibialis anterior muscle of patient 3 showing continuous slow frequency rhythmic repetitive activity of complex potentials typical of "myokymic discharges".

had an operation for a left lumbar 3/4 disc hernia and a spondylodesis. In the following years he had intermittent back pain radiating to his left thigh distally and medially and to his lower leg anteriorly and medially. Nonsteroidal anti-inflammatory drugs reduced the pain. At the age of 40, however, he experienced a substantial increase in discomfort, and for the first time noticed a gradually increasing swelling, lateral to his left tibia. Suspecting a muscle sarcoma, a biopsy was taken and was considered negative. CT showed an increased bulk of the anterior tibial muscle with a normal density (fig 5). One year later he was referred for further investigation since the muscle swelling was still increasing.

The clinical examination showed a painless swelling of the left anterior tibial muscle. Elevation of the left foot was slightly weaker than on the right side. The left knee jerk was decreased. The remaining tendon jerks were symmetric and brisk. The circumference of the thighs was equal, but the left lower leg measured 34 cm and the right only 32 cm. There were no other neurological abnormalities. Skin temperature was 32°C over both anterior tibial muscles ruling out an inflammatory process. ESR, WCC, electrolytes, glucose, creatinine, serum aspartate aminotransferase, alkaline phosphatase, and chest radiographs were normal. Serum alanine aminotransferase was 46 mU/ml (normal up to 27 mU/ml) and CPK was 159 mU/ml (normal up to 125 mU/ml).

The muscle biopsy specimens obtained a year earlier in another laboratory were revised. Only HE and van Gieson stains were available. The fibre size showed an abnormal variability. Hypertrophic fibres were present in large number, some with segmentation and an increased number of central nuclei. The aspect was non-specific and was considered consistent with both a myopathic process and with secondary myopathic changes due to a chronic denervation.

Electromyography of the left anterior tibial muscle showed continuing high and low frequency repetitive discharges of mostly polyphasic potentials at all sites in the relaxed muscle (fig 6). In addition, there were grouped discharges of regularly occurring bursts of several potentials. The density of this spontaneous activity obscured the motor unit potentials of volitional activation at the optical signal display. The left gastrocnemius muscle showed a reduced pattern at maximal voluntary activity but no spontaneous activity. Electromyography of the left lateral vastus muscle was

normal. The motor conduction velocity of the left peroneal nerve was normal over all segments.

A diagnosis of muscle hypertrophy due to longstanding left L4 root lesion was made.

Discussion

Hypertrophy is a physiological response of muscle to work.^{20,21} Stretch may also induce muscle hypertrophy,²² even in the absence of innervation. Pathological conditions leading to muscle hypertrophy include myotonia congenita and other forms of myotonias,²³ dystonias, acromegaly, chronic spinal muscle atrophy,^{24,26} a familial²⁷ and a sporadic ataxia,²⁸ the Schwartz-Jampel syndrome,^{29,30} the Hoffmann's syndrome,³¹ post-poliomyelitis muscle hypertrophy,³² and polyneuropathy associated with continuous spontaneous activity.^{18,19,33-35} Muscle hypertrophy following nerve injury has been the subject of experimental work.³⁶ The phenomenon has been reported occasionally in humans¹⁻¹⁷ but rarely cited in textbooks.³⁷

All reported human cases of muscle hypertrophy due to radicular or peripheral nerve injuries were restricted to the calves except one of Lhermitte's cases.² Bernat and Ochoa proposed combined work- and stretch-induced post-denervation muscle hypertrophy as an explanation.⁸ They supported their hypothesis with biopsy findings from the gastrocnemius muscle. These showed changes of partial denervation and reinnervation, with small groups of type I and II atrophic muscle fibres and abundant hypertrophic fibres of both types but mostly type II. They postulated that, in addition to compensatory work-induced type II muscle fibre hypertrophy, there was an element of stretch-induced type I hypertrophy of denervated fibres. Such a condition has been well recognised experimentally but had not been documented previously.

The assumption of work- and stretch-induced hypertrophy of denervated fibres is not an entirely satisfactory explanation. If it was, then calf hypertrophy would be a much more common finding in longstanding S1 root lesions. The hypothesis might explain some of the effects on the calf muscles, which are the muscles most often used and stretched in the daily activities because of the upright posture of humans. Biopsy findings in two of our patients are compatible with this assumption and also with chronic denervation and reinnervation.³⁸ However, the fact that in two of our patients the trapezius muscle and in another patient the anterior tibial muscle were hypertrophied weakens the hypothesis of combined work and stretch as a major cause and raises the question of further pathogenetic factors.

In our three patients dense continuing spontaneous discharges of complex potentials were the prominent finding in electromyography of the hypertrophied muscles. Lapresle *et al*,⁶ Mielke and Ricker,⁹ Cooper *et al*,¹¹ Lagueny *et al*,¹⁴ Valenstein *et al*¹⁸ and Vasilescu *et al*¹⁹ also described striking spontaneous activity in the needle electromyography of the hypertrophied

muscles denoted as "spontaneous motor unit potentials", "fasciculations", "myotonic", "pseudomyotonic", or "trains of repetitive" discharges.

Depending on firing rate and rhythm, different terms have been used to characterise complex discharges: "fasciculations" generally denote motor-unit type potentials firing at random. The terms "pseudomyotonic", "bizarre high frequency", or "complex repetitive" discharges have been used, when the potentials fire at a uniform frequency of 5 to 100 Hz. The terms "grouped fasciculations" or "bizarre low frequency", "bizarre repetitive" and "myokymic" discharges have been used for more or less rhythmical firing at 5 Hz or less either of single complex potentials or of short bursts of potentials. Common to all these types of complex discharges is that they usually occur in chronic or longstanding neuromuscular disorders. High frequency complex repetitive discharges have been found in a variety of peripheral neurogenic disorders such as muscular dystrophy, polymyositis, spinal muscular atrophy, amyotrophic lateral sclerosis, and chronic neuropathies.⁴⁰ Myokymic (low frequency) discharges and fasciculations have frequently been found in partial old nerve lesions such as chronic entrapment,^{41 42} mechanical nerve injury,³⁹ radiation-induced⁴²⁻⁴⁴ or inflammatory neuropathy,^{18 19 42 45} and hereditary neuropathy with liability to pressure palsy.⁴⁵ The polyphasic or serrated action potentials of complex discharges are generated by groups of functionally linked muscle fibres, whereas fibrillations and sharp positive waves typical of acute denervation are generated by single denervated muscle fibres. The site of origin of the ectopic impulses causing the complex discharges is as yet uncertain and may not be the same in all types. While (high frequency) complex repetitive discharges have been shown to arise in the partially denervated or diseased muscle itself^{46 47} myokymic discharges and fasciculations may arise in nerve fibres, and both, the actual locus of the causal nerve lesion^{42 43} as well as distal nerve sprouts⁴⁸ have been proposed as possible sites of origin.

Electrical muscle activity normally reflects muscle fibre contraction. Therefore, when occurring excessively in a muscle, continuous spontaneous muscle activity may well give rise to hypertrophy, regardless of the anatomical location and function of the muscle. We therefore propose that the muscle hypertrophy was caused by the spontaneous activity. Such a pathogenesis has also been postulated in muscle hypertrophy of polyneuropathies with "pseudomyotonia".^{19 33 35} Similarly, Valenstein *et al*¹⁸ noted that a patient with chronic recurrent polyneuropathy showed the most spontaneous activity in those muscles which were hypertrophied. It could be assumed that the considerably hypertrophic muscle fibres in our biopsies were the ones which produced the spontaneous activity. It is interesting that in our specimen these were predominantly "tonic" type I fibres.

The clinician must be aware that isolated

muscle hypertrophy can be a sign of partial peripheral nerve or root lesion, and it probably may occur in any skeletal muscle. Since neurogenic muscle hypertrophy is rare, focal myositis or primary muscle neoplasms might be suspected. This may lead to unnecessary, costly, and sometimes invasive investigations which could be avoided when the possibility of neurogenic hypertrophy is considered. The electromyographic finding in a hypertrophied muscle of profuse spontaneous activity confirms the diagnosis.

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