Neurogenic muscle hypertrophy

Report of two cases

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Summary. Muscle hypertrophy is rare in denervating diseases. A patient with calf enlargement associated with L5-S1 radiculopathy and another with thenar, hypothenar, forearm and calf muscle hypertrophy in the course of chronic relapsing inflammatory demyelinating polyneuropathy are described. Gastrocnemius muscle biopsy revealed both type I and type II fibre hypertrophy in the former case and predominant type I fibre hypertrophy in the latter. Passive stretching and abnormal spontaneous muscular activity might have played a role in the origin of hypertrophy in both patients, but a satisfactory explanation for denervation hypertrophy has yet to be provided.

Key words: Muscle hypertrophy – Neuropathies – Spontaneous muscular activity – Stretching

Both true muscle hypertrophy and pseudohypertrophy may be encountered in the course of several different diseases affecting the central nervous system or the muscle itself, e.g. in dystonias and muscular dystrophies. In some of these disorders, muscular hypertrophy is so frequent that it is a characteristic finding. Exceptional, but well described, is the occurrence of true muscle hypertrophy in denervating processes. It has been reported in patients with anterior horn cell diseases [5, 7, 10, 21], radiculopathies [3, 6, 14, 19, 20], nerve injuries [16–18], and inherited as well as acquired peripheral neuropathies [13, 26–28]. We report two further cases of muscle hypertrophy, one associated with radiculopathy and one with chronic inflammatory demyelinating polyneuropathy (CIDP).

Case reports

Case 1

During the previous year, a 47-year-old man had gradually developed painful right calf enlargement with cramps and impairment of right foot dorsiflexion. Two years earlier he had had an episode of low back pain radiating into the lateral region of the right thigh, leg and heel, which resolved within 1 month.

Neurological examination revealed muscle hypertrophy of the posterior and anterolateral compartment of the right leg (Fig. 1), the enlarged muscles being firmer than normal, with numerous fasciculations, cramps and percussion myotonia. The right calf was 5 cm larger in circumference than the left. The right ankle jerk was not elicitable and the right Achilles tendon was shortened. Pain and touch sensation were decreased in the anterolateral aspect of the right leg, dorsum of the foot and great toe. Routine laboratory blood tests were normal except for an increased serum creatine kinase level (224 U/l, normal value < 70 U/l).

Electromyographic examination of the right gastrocnemius muscle showed nearly continuous pseudomyotonic discharges at rest, which occurred spontaneously, and with needle movements or mechanical percussion of the muscle belly. Voluntary activity was characterized by a greatly reduced recruitment pattern with early recruitment of large motor unit potentials at a high firing rate; motor unit potential amplitude and duration were consistent with chronic denervation. Comparative leg CT and MRI disclosed hypertrophy of muscle bulk of the right leg with reduced fatty tissue (Fig. 2). Lumbar myelogram, lumbar CT and surgery demonstrated bilateral fourth and fifth lumbar disk herniation compressing L5 and S1 right roots. One year after surgery the pain had disappeared, the right foot dorsiflexion had improved and calf enlargement was reduced by 3 cm.

Case 2

A 59-year-old man developed subacute muscle weakness of all limbs with both proximal and distal distribution at the age of 57. Weakness reached its maximum within 30 days, when he was admitted to another hospital, underwent CSF examination which showed an albuminocytologic dissociation, and was discharged with the diagnosis of acute Guillain-Barré syndrome. Almost complete remission occurred in the next 4 months, but in the following 2 years the disease ran a relapsing course; on three occasions he experienced rapid (over 2–3 weeks) deterioration of muscular strength, cramps, myotonic phenomena and distal limb paraesthesias with incomplete recovery in the following months.

At the age of 59 years he was admitted to our hospital because of a new episode of rapid worsening. He was bed-ridden, unable to stand or sit and needed assistance when eating. Neurological examination revealed severe trunk and limb muscle weakness, the distal muscle groups being more severely affected. There was proximal limb muscle wasting, but the calf, thenar, hypothenar and forearm muscles were strikingly enlarged bilaterally (Fig. 3). The hypertrophic muscles were increased in bulk, firm and tense. Spontaneous and per-
Fig. 1. Case 1: right calf enlargement

Fig. 2. Case 1: comparative leg MRI showing hypertrophy of right leg muscles with reduced fatty tissue

Fig. 3. Case 2: hypertrophy of posterior compartment of both legs

Fig. 4. Case 1: needle gastrocnemius muscle biopsy. A small angulated fibre is surrounded by hypertrophic fibres with central nuclei and some splitting. Haematoxylin and eosin, × 335

Fig. 5. Case 2: needle gastrocnemius muscle biopsy. Normal, atrophied and hypertrophied fibres with some target formations are seen. NADH dehydrogenase, × 165

cussion myotonia of both hands was present. All tendon jerks were abolished. Mild distal sensory loss of all modalities was found in glove and stocking distribution. Routine blood tests were normal; muscle enzymes were within normal values. CSF protein levels were increased (93 mg/dl, normal value = 20–45 mg/dl), with no cellularity.

Electromyographic examination showed signs of severe denervation in the proximal and distal muscles examined of all limbs. Intense abnormal spontaneous activity was present particularly in the hypertrophic muscles (first dorsal interosseous and opponens pollicis muscles) with rhythmic motor unit activity in doublets and/or triplets or prolonged high-frequency repetitive discharges. Motor nerve conduction velocities were generally slowed: 38 and 23 m/s in right and left common peroneal nerves respectively (normal lower limit for the age: 43.9 m/s), 29 and 30 m/s in right and left median nerves (normal lower limit for the age: 54.5 m/s).

Sural nerve biopsy showed features of demyelinating chronic neuropathy, and CIDP was diagnosed. Treatment with 50 mg prednisone daily, then 25 mg on alternate days led to a rapid and lasting improvement, with relapses on attempts to reduce the dosage. Improvement in strength was accompanied by a reduction of muscle hypertrophy.

Muscle biopsy

Needle muscle biopsy of right gastrocnemius was performed in both patients. The muscle specimens were frozen in isopentane cooled in liquid nitrogen. Routine histological and histochemical stains were performed [9]. A histogram of fibre diameter was obtained, and atrophy and hypertrophy factors were calculated according to Dubowitz [8].

Case 1. There was a slight increase in connective tissue and a wide variation in fibre size with groups of both small angulated and hypertrophied fibres (Fig. 4). Some pseudomyopathic changes, such as internal nuclei and splitting, were found. ATPase staining showed slight predominance and grouping of