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CASE REPORT

Asymmetric Calf Hypertrophy of Neurogenic Origin

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A 47-year-old male presented with painful swelling of the right calf. His medical history was negative, except for a herniation of disc LIV-V 5 years before. Physical examination revealed unilateral calf hypertrophy with moderate weakness of plantarflexion, mild paresis of dorsiflexion. Electromyography showed a peripheral neurogenic lesion in the right anterior tibial muscle, but normal findings were obtained from the unaffected quadriceps muscle. Histological examination of the right gastrocnemic muscle showed neurogenic changes with typical targetoid fibers, but no pathological changes were present in the quadriceps muscle. Chronic asymmetric spinal muscular atrophy is an infrequent neuromuscular disease and because of asymmetric appearance, it might be difficult to distinguish from other, acquired neurogenic muscle diseases such as radiculopathy caused by intervertebral disc herniation. Our case confirms that muscular hypertrophy can follow partial denervation in humans. (Pathology Oncology Research Vol 12, No 4, 254–256)

Key words: asymmetric atrophy, muscle biopsy, neuropathy, spinal muscular atrophy

Introduction

Muscle atrophy usually develops due to denervation caused by various pathologic conditions. In contrast, hypertrophy is a rare result of neurogenic muscle damage.[6,14,17] Occasionally myopathy, focal myositis, muscle neoplasm or injury might be responsible for swelling of the related muscles.[5,9] We present a case where the right calf was found to be selectively enlarged. Muscle biopsy suggested true muscle hypertrophy and neurogenic origin. The possible causes are discussed.

Case report

A 47 year-old male patient was examined because of painful swelling of the right lower extremity. His family and medical history was unremarkable, except mild degenerative changes of the lumbar spine and herniation of disc LIV-V discovered 5 years ago. His complaints started 3 years before the admission. He felt stiffness of the right calf muscles, which was increased during exercises. Later on painful swelling and weakness developed.

Physical examination: His body weight was 104 kg. Hypertrophy of the right calf muscles was detected, the circumference of the right calf was 5 cm greater than that of the left one (*Figure 1a*). Mild paresis in the foot dorsiflexion, decreased Achilles tendon reflex, S1 hypesthesia and hypalgesia were found on the right side.

Laboratory tests revealed moderately elevated creatinin kinase (400 U/l, normal up to 200 U/l) and moderately low phosphate level (0.8 g/l). CSF showed slightly elevated protein content (0.64 g/l, normal up to 0.5 g/l) and decreased albumin ratio (116, normal >130). Serological tests were negative for viruses (EBV, adenovirus, RSV, VZV) and Borrelia burgdorferi.

Electromyography showed neurogenic lesion in the right anterior tibial muscle (motor unit potential difference from normal controls was +39%), but it was normal in the unaffected quadriceps muscle and in the deltoid muscle. Electroneuronography of the median nerve was normal, but conduction velocity of the peroneal nerve was slightly reduced (40.9 m/s).

MRI of legs: The density and structure of bones and thigh muscles were normal and symmetrical. The right gastrocnemic and long digital flexor muscles were swollen and showed high signal intensity with T1, T2 and STIR methods, and slight contrast enhancement was found (*Figure 1b*).

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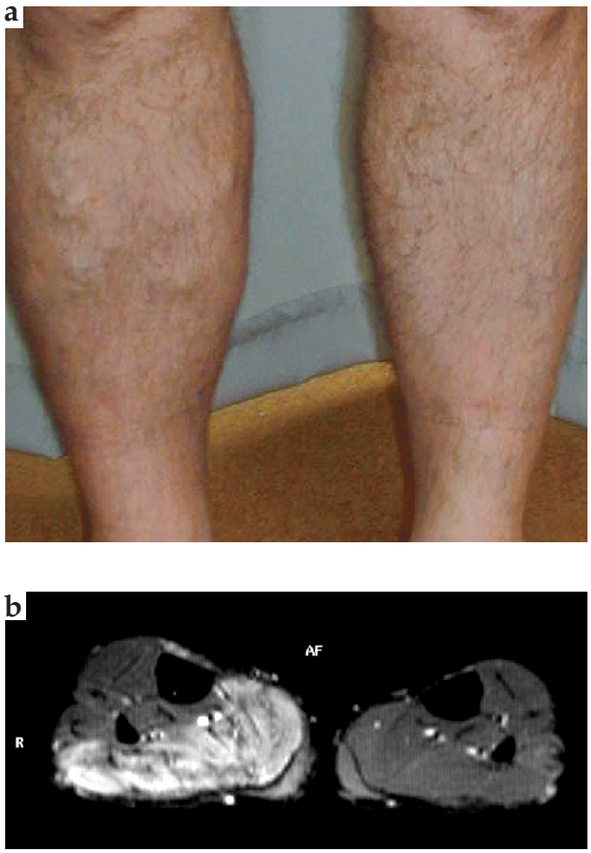

Figure 1. (a) *Enlargement of the right calf.* ***(b)*** *MRI scans of calves. The circumference of the right calf is significantly greater, and the signal intensity of the gastrocnemic muscle is altered. STIR images show bright signal in the involved muscles.*

SPECT: the activity of tracer (99mTc-2-methoxy-isobutylisonitrile [99mTc-MIBI]) was measured during perfusion and 1 h later (metabolic phase). The perfusion was similar on both sides, but slightly decreased metabolic activity was seen in the right calf muscles.

Angiological examination found normal arterial and venous blood flow with color duplex ultrasonography. Lumbosacral MRI showed slight degenerative changes of lumbar discs and vertebrae (osteochondrosis et retrospondylophytosis).

Muscle biopsy specimens were evaluated according to standard quidelines.[8] The right quadriceps muscle showed no pathological features (*Figure 2a*). Histological examination of the clinically involved right gastrocnemic muscle showed marked variation in fiber size, with small angular fibers and fiber-type grouping. The number of internal nuclei was slightly elevated (3%) and some pycnotic nuclear clumps were found. The amount of perifascicular connective and adipose tissue was slightly increased. There was type 1 fiber predominance (65%) and the ratio of type 2/C fibers was increased (5%). NADH staining showed disorganized intermyofibrillar network, type 1 fibers appeared as targetoid, type 2 fibers were hypertrophic (*Figure 2b*). Electronmicroscopic examination showed core structures in the targetoid fibers and, in several regions, disorganization of muscle fibers.

Discussion

Enlargement of a muscle (group) may be resulted due to increase of number, or the size of muscle fibers (true hypertrophy), or from infiltration of the muscle by collagen, fat, parasites, tumor or inflammatory cells (pseudohypertrophy).[1] Unilateral painless hypertrophy may occur in focal myositis and due to primary muscle neoplasm.[9] Muscle hypertrophy appears physiologically in work-induced fashion and pathologically in a variety of muscle disorders. Calf hypertrophy is known to occur in muscle diseases of neurogenic origin.[11]

We found only few presentations of L5-S1 radiculopathy followed by calf hypertrophy. The majority was radiologi-

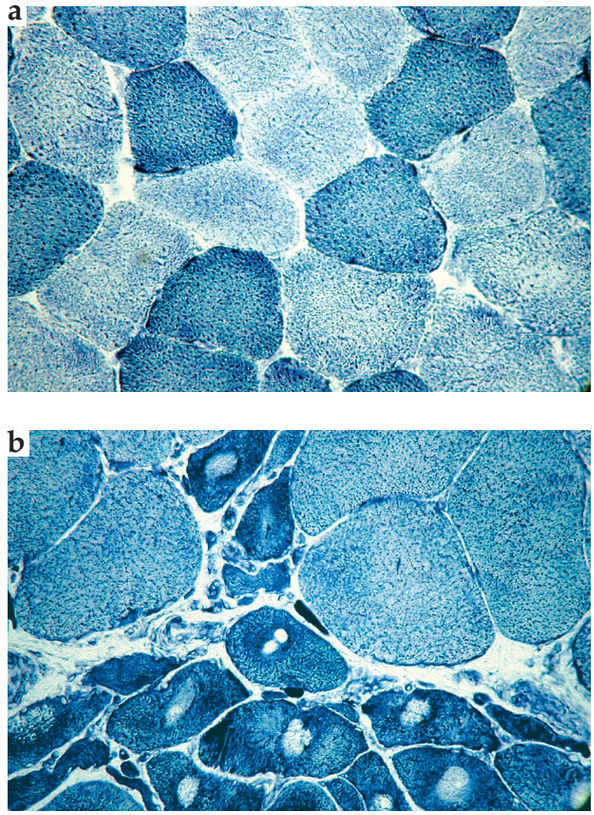

Figure 2. *Normal mosaic pattern is preserved in the right lateral vastus muscle* ***(a).*** *Fiber type grouping in the right gastrocnemic muscle. Marked hypertrophy of type 2 (bright), and targetoid structure in type 1 (dark) fibers* ***(b).*** *NADH staining, 40X.*

cally and histologically proven to be true muscle hypertrophy,[3,6,13] while in a few patients pseudohypertrophy was supposed to develop due to proliferation of the connective tissue and fat replacement.[7] Mielke et al.[12] described cases, and they suggested the role of both above-mentioned mechanisms, depending on at which stage of process is investigated. In our patient the biopsy proved neurogenic origin (selective type 2 fiber enlargement) and revealed many target fibers, which is an uncommon finding in this particular condition.[3]

In our case, lumbar disc herniation and signs of S1 radicular lesion were also present. Laminectomy did not influence the clinical course as reported in chronic radiculopathy.[13,16] In such cases several hereditary and acquired diseases should be considered, such as amyotrophic lateral sclerosis, different types of spinal muscle atrophy (SMA), hereditary neuropathies and focal myositis.[2,9,15,17]

Several variants have been described within the SMA group, based on the onset, progression, inheritance and the muscles involved.[15] Pearn at al.[14] reported a new type of spinal muscular atrophy syndrome. It was characterized by symmetric hypertrophy, slow progression and onset in adolescence. Bundey and Lovelace[4] described two brothers with adolescent onset of SMA with calf hypertrophy. This newly described syndrome should also be considered when single male cases of SMA were found within otherwise unaffected families. However, the symptoms were usually symmetric in these cases.

A rare asymmetric form of SMA was also described, which was not accompanied by calf hypertrophy.[10]

Chronic asymmetric spinal muscular atrophy is an infrequent neuromuscular disease, and because of asymmetric appearance we have to distinguish it from other, acquired neurogenic muscle diseases such as radiculopathy caused by intervertebral disc herniation. Our case confirms that calf hypertrophy can follow partial denervation in humans.

References

1. *Adams RD, Denny-Brown D, Pearson CM*: Diseases of Muscle. A Study in Pathology. Second Edition. Harper and Row, Hagerstown, Maryland, 1962, pp. 349-353, 666-669.
2. *Barron SA, Heffner RR*: Abnormal spontaneous electrical activity and gross enlargement of muscle. Arch Neurol 40: 515-518, 1983.
3. *Bernat JL, Ochoa JL:* Muscle hypertrophy after partial denervation: a human case. J Neurol Neurosurg Psychiat 41: 719-725, 1978.
4. *Bundey S, Lovelace RE*: A clinical and genetic study of chronic proximal spinal muscular atrophy. Brain 98: 455-472, 1975.
5. *Celesia GG, Andermann F, Wiglesworth FW, Robb JP:* Monomelic myopathy: Congenital hypertrophic myotonic myopathy limited to one extremity. Arch Neurol 17: 69-77, 1967.
6. *Costa J, Graca P, Evangelista T, de Carvalho M:* Pain and calf hypertrophy associated with spontaneous repetitive discharges treated with botulinum toxin. Clin Neurophysiol 116: 2847-2852, 2005.
7. *De Visser M, Verbeten B, Lyppens KC:* Pseudohypertrophy of the calf following S1 radiculopathy. Neuroradiol 28: 279-280, 1986.
8. *Dubowitz V, Brooke MH, Neville HE*: Muscle biopsy: A Modern Approach. Saunders W.B. Co, London, 1973, pp 20-33.
9. *Gobbele R, Schoen SW, Schröder JM, et al:* S1 radiculopathy as a possible predisposing factor in focal myositis with unilateral hypertrophy of the calf muscles. J Neurol Sci 170: 64-68, 1999.
10. *Harding AE, Bradbury PG, Murray NM:* Chronic asymmetrical spinal muscular atrophy. J Neurol Sci 59: 69-83, 1983.
11. *Korczyn AD, Kuritzky A, Sandbank U:* Muscle hypertrophy with neuropathy. J Neurol Sci 36: 399-408, 1978.
12. *Mielke U, Ricker K, Emser W, Boxler K:* Unilateral calf enlargement following S1 radiculopathy. Muscle Nerve 5: 434-438, 1982.
13. *Montagna P, Martinelli P, Rasi F, et al:* Muscular hypertrophy after chronic radiculopathy. Arch Neurol 41: 397-398, 1984.
14. *Pearn J, Hudgson P:* Anterior-horn cell degeneration and gross calf hypertrophy with adolescent onset. A new spinal muscular atrophy syndrome. Lancet 1: 1059-1061, 1978.
15. *Pearn JH:* Classification of the spinal muscular atrophies. Lancet 1: 919, 1980.
16. *Ricker K, Rohkamm R, Moxley RT*: Hypertrophy of the calf with S-1 radiculopathy. Arch Neurol 45: 660-664, 1988.
17. *Valenstein E, Watson RT, Parker JL:* Myokymia, muscle hypertrophy and percussion myotonia in chronic recurrent polyneuropathy. Neurology 28: 1130-1134, 1978.