

# CALF HYPERTROPHY IN SPINAL MUSCULAR ATROPHY

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## ABSTRACT

Two unusual variants of spinal muscular atrophy with gross calf hypertrophy of adolescent onset were studied clinically, electrophysiologically and histologically.

There have been reports of several variants within this group of spinal muscular atrophies. In Singapore we encountered 2 patients who had an unusual variant of spinal muscular atrophy not well recognised previously with only 3 reports recorded to date. Our cases presented with gross calf hypertrophy and a slowly progressive clinical course. Nerve conduction studies were normal but electromyogram and muscle biopsies revealed a chronic denervation problem of probable central origin.

**Keywords :** Spinal muscular atrophy, Calf hypertrophy, Adolescent onset, Electromyogram, Muscle biopsy.

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## INTRODUCTION

Spinal muscular atrophy has long been recognised as a disease of chronic denervation but it has not been commonly associated with calf hypertrophy.

The only previous reports on this have been the ones by Pearn and Hudson<sup>(1)</sup>, Gobernado et al<sup>(2)</sup> and D'Alessandro et al<sup>(3)</sup>.

We now report on two unusual cases of spinal muscular atrophy.

## CASE 1

This patient was a 31-year-old Chinese female whose history dates back to the age of ten years when she recalled falling over things easily. In the last 3 years there was rapid deterioration and she found it difficult to get up from a squatting posture. Presently she is unable to climb stairs without support. No tremors or muscle twitchings were noted by the patient. Weakness was confined to the lower limbs. There was no difficulty in breathing. There were 3 other siblings in the family, 2 girls and a boy. Both parents and the 3 siblings were all well and did not have any weakness.

Clinical examination did not reveal any abnormalities. Mental status was normal. Cranial nerves were normal and there was no wasting of facial muscles and no fasciculations noted in the tongue. The upper and lower limbs showed severe symmetrical proximal muscle wasting in the shoulder and hip girdle. There was symmetrical hypertrophy of the calf muscles. No fasciculations were seen and there was no spasticity of the limbs. There was bilateral pes cavus and a marked lumbar lordosis. There was weakness of both the upper and lower

limbs, being more proximal in distribution. Reflexes could not be elicited despite reinforcement. Sensory examination was essentially normal. Serum creatinine kinase activity was increased to twice the normal value but the aldolase was normal. Thyroid function tests were normal. The erythrocyte sedimentation rate was within normal limits. Motor and sensory nerve conductions were within normal range, values ranging from 60m/s to 70m/s. Electromyography revealed increased insertional activity with fibrillation potentials and positive sharp waves and giant polyphasic potentials in both deltoids, the right quadriceps and right gastrocnemius, revealing a denervation pattern consistent with anterior horn cell involvement. Recruitment revealed an incomplete interference pattern. Muscle biopsy done showed a denervation pattern with group atrophy and fibre type grouping, hypertrophy of fibres, internal nucleation, fibre splitting and fibre type grouping (Fig 1 & 2).

Fig 1 - Severe group atrophy with cluster of myonuclei and internal nucleation. (H + E x 380)

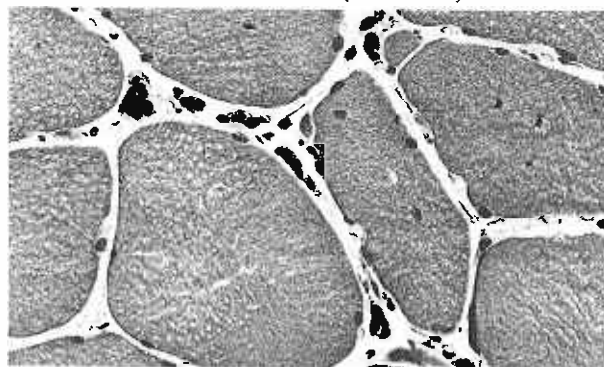
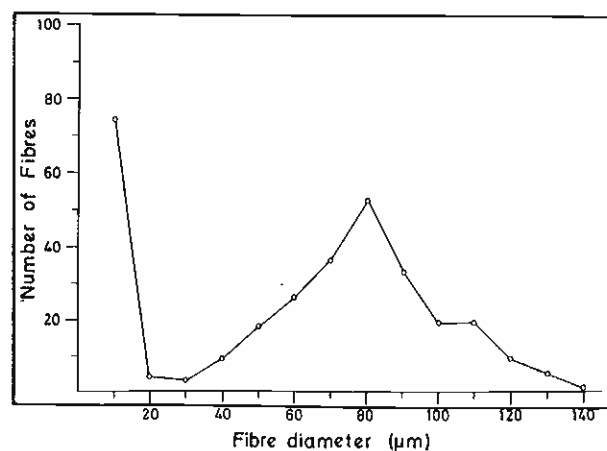


Fig 2 - Distribution of muscle fibres displaying a two peaked configuration



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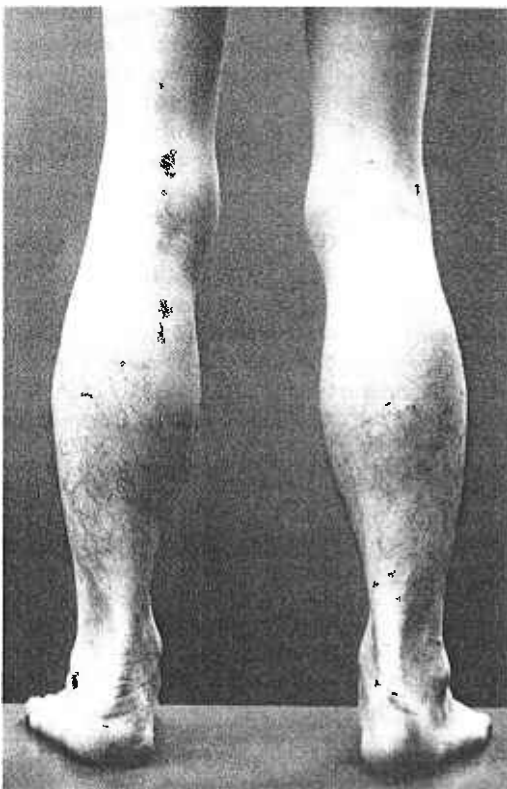
**CASE 2**

This was a 31-year-old man who complained of weakness in walking since young, around the age of 5 to 6 years. He was still able to walk but had difficulty in climbing stairs and getting up from a squatting position. No other members of his family were affected by such weakness. The most striking feature was the gross hypertrophy of both his calves (Fig 3 and 4).

**Fig 3 - Lateral view of calves showing gross hypertrophy**



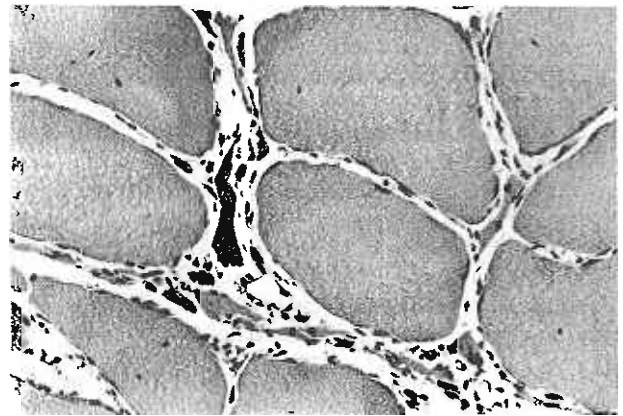
**Fig 4 - Posterior aspect of calves**



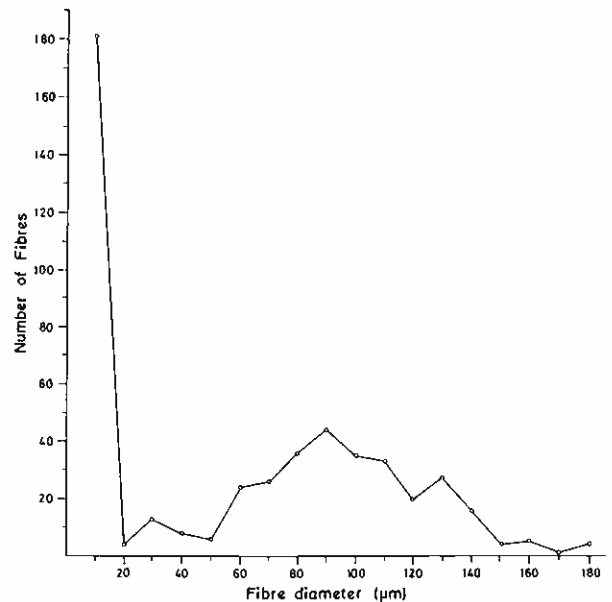
He had a lordotic stance. No fasciculations were seen here. His upper limbs revealed wasting of the deltoids with obvious fasciculations over the same area. There was no obvious wasting of his muscles distally. The tongue was not wasted and had no fasciculations. The facial muscles were unaffected. Muscle power was much weaker proximally as compared to the distal segments and reflexes were present bilaterally but diminished in intensity. The jaw jerk was not brisk. All the sensory modalities of pain to pin prick, touch, vibration sense and proprioception were intact. He had a positive Gower's sign. The cardiovascular system was normal on examination.

The muscle enzymes showed a mild increase in the creatinine kinase activity to almost three times the normal value but the aldolase level was normal. Nerve conduction studies were normal. Muscle sampling in all four limbs revealed a denervation pattern with giant polyphasic potentials indicating a picture of anterior horn cell involvement. A muscle biopsy was then done from the gastrocnemius and deltoid areas. This revealed scattered clusters of grouped atrophy with many of the atrophied fibres reduced to a bag of myonuclei (Fig 5). Internal nuclei were observed in 30% of fibres. Hypertrophy was marked in many fibres, some reaching a size of 180  $\mu\text{m}$  in diameter. Some of the larger fibres showed splitting. Enzyme histochemistry revealed fibre type grouping and moth eaten appearance in many of the type 1 fibres. There was considerable variation in fibre size (Fig 6).

**Fig 5 - Section shows grouped atrophy and internal nucleation of some fibres (H & E x 260)**



**Fig 6 - Distribution of muscle size fibre showing marked variation with atrophied and hypertrophied fibres**



## **PATHOLOGY**

In any muscle biopsy, the purpose is to determine whether the picture is that of a muscle disorder or secondary to denervation. With the recent onset of enzyme histochemistry, this has helped to differentiate between denervation changes in a muscle and a primary muscle disease.

In chronic denervation there is variation of fibre size. This is basically determined by measuring the shortest diameter of the fibres, which have been magnified and produced on a black and white photograph, and then plotted against the number of fibres corresponding to that diameter. In denervation due to anterior horn cell disease, there is usually a large number of hypertrophied muscle fibres not seen in other types of denervation.

## **DISCUSSION**

Many cases of juvenile spinal muscular atrophy have been wrongly diagnosed as muscular dystrophy just on their clinical findings. Clinically the second patient resembled a Becker's type of muscular dystrophy. With the advent of electromyography, the differentiation between myopathies and neurogenic atrophies was made possible. Since then, there have been reports of variants of spinal muscular atrophy in the literature but only three case reports with calf hypertrophy<sup>(1-3)</sup>.

The interest lies in the association of muscle hypertrophy in denervation. Calf hypertrophy with denervation has been described with trauma to peripheral nerves, polyneuritis, recovery from polio and in chronic S1 radiculopathy<sup>(7-11)</sup>.

Pearn and Hudgson reported five cases and thought of them as being clinically benign and the inheritance in their patients being X linked recessive<sup>(1,4)</sup>. This linkage could not be established in our patients. One of our patients is a female and she was not the product of a consanguineous marriage.

The main interest in this article is the denervation hypertrophy of the calves and in our two patients, this has been caused by anterior horn cell denervation. These two patients demonstrated actual hypertrophy of the muscle fibres without accompanying increase in the connective tissue and fat. Ricker, Rohkamm and Moxley<sup>(7)</sup> reported that in calf hypertrophy with S1 radiculopathy, the muscle biopsy showed a significant increase in the connective tissue and fat without hypertrophy of

a majority of the muscle fibres. They concluded on this basis that the relative contributions of muscle and connective tissues that account for the total amount of calf enlargement may vary within the same patient at different points in time. Laminectomy did not halt the progression of the calf hypertrophy, thus indicating that the denervation of the S1 root alone may not be contributing to the hypertrophy. Other factors obviously must play a part but these need to be evaluated by further pathophysiologic studies.

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