

CASE REPORTS

Distal spinal muscular atrophy with vocal cord paralysis

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Abstract

We describe a family with distal spinal muscular atrophy and vocal cord paralysis, similar to the condition reported by Young and Harper in 1980. Both pedigrees are consistent with autosomal dominant inheritance.

Dysphonia is well recognised in certain types of spinal muscular atrophy. In childhood, the best known of these is Fazio-Londe disease, also known as progressive bulbar paralysis. In this condition multiple cranial nerve palsies occur early, including bilateral facial weakness, palatal and vocal cord palsies, and tongue involvement, and in combination they contribute to dysarthria and hoarseness. These are later followed by the onset of flaccid weakness, wasting, and hyporeflexia in the upper limbs and later still in the legs.

There is another type of spinal muscular atrophy in which hoarseness, not associated with other bulbar manifestations, is a characteristic feature. There is, in addition, slowly progressive distal wasting and weakness. Young and Harper¹ described the first family in Wales in 1980, and we now describe a second unrelated Welsh family with involvement of at least three successive generations.

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The family pedigree is shown in the figure. Table 1 shows the clinical features and table 2 shows the results of electrophysiological studies.

The proband (IV.3), born in 1981, was referred to The Hospital for Sick Children at 6 years of age because of parental concern about her impaired hand function, in the context of a family history of so-called peroneal muscular atrophy affecting many family members. She had had a slightly hoarse voice from 4 years of age. A weak grip was noted later and from the age of 5 she held and manipulated a pencil and spoon with difficulty.

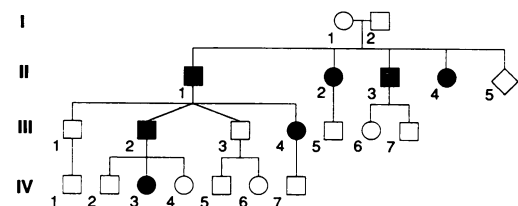
Examination showed a hoarse voice, without facial weakness, palatal palsy, tongue atrophy, or fasciculation. She had a weak grip. Tone was normal and reflexes were preserved though depressed in the arms. Her gait was normal, apart from poor heel walking. Indirect laryngoscopy showed left vocal cord paralysis.

Nerve conduction studies and electromyography were normal.

Subsequently, her voice became more hoarse and she found writing progressively difficult. Examination at 9 years of age showed mild weakness of grip, finger extension, and wrist flexion without wasting. There was bilateral pes cavus and heel walking remained poor. Tone was normal but reflexes were depressed in the arms. Sensation was normal. Nerve conduction studies were normal but electromyography showed evidence of early neurogenic change. The older brother (IV.2) and younger sister (IV.4) of IV.3 were both asymptomatic with normal examinations, at the ages of 8 years and 11 months respectively.

The father of IV.3 (III.2), born in 1955, first noticed wasting and weakness of his hands at 12 years of age when a teacher commented on his poor handwriting. Slowly progressive wasting of his hands and distal forearms followed, with weakness, particularly of the thumbs, stiffness in cold weather, and inability to straighten the fingers. Wasting of his feet and lower legs supervened, with 'floppy' feet which caught on the pavement. He believed he had always had a hoarse voice without stridor or pulmonary symptoms. Despite his disabilities, he was employed as a labourer.

Examination showed a hoarse voice but the rest of the cranial nerves were normal. He had claw hands with marked wasting of the small muscles of the hands and mild wasting of the forearms. There was severe weakness of the small hand muscles and less prominent involvement of the wrist flexors and extensors. There was mild wasting and weakness of distal leg muscles. The tendon reflexes were present with flexor plantar responses and sensation was intact. Indirect laryngoscopy showed bilateral vocal cord paralysis.



The family pedigree.

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Table 1 Clinical findings.

Subject	Sex	Age (y)	Age at onset (y)	Vocal cord changes	Upper limb involvement	Lower limb involvement
IV.3	F	6	4	Left vocal cord palsy	Present	+
III.2	M	32	12	Bilateral palsy	Present	+
III.4	F	?	21	Hoarse voice	Present	Absent
II.1	M	63	Teens	Hoarse voice	Present	++
II.3	M	60	?	?	Present	Absent
II.4	F	58	?	Absent	Present	Absent
II.2	F	62	?	Hoarse voice	?	+++

+++ = severe, ++ = moderate, + = mild.

Table 2 Electrophysiological studies.

	III.2	IV.2	IV.3	IV.4
<i>Sensory studies</i>				
Sural SAP (uV)		19	(aged 6 y) 18	(aged 9 y) 16
SCV (m/s)		57	48	51
<i>Motor studies</i>				
<i>Medial popliteal (abd hallucis)</i>				
Distal CMAP (mv)		7	11	6.0
Distal motor latency (msec)		4.2	3.5	5.0
F wave latency (msec)		32	27.5	35.5
Velocity (m/s)		52	*	53
<i>Median (abd pollicis brevis)</i>				
Distal CMAP (mv)				3.6
Distal motor latency (msec)				3.5
F wave latency (msec)				24
Velocity (m/s)				51
<i>Lateral popliteal (ext dig brevis)</i>				
Distal CMAP (mv)	2.8			
Distal motor latency (msec)	5.5			
F wave latency (msec)	52			
Velocity (m/s)	45			
<i>Electromyography</i>				
Extensor digitorum communis	*	N	*	Early NC
First dorsal interosseous	*	N	*	N
Tibialis anterior	CPD	*	*	*

CPD = chronic partial denervation. NC = neurogenic change. N = normal. * = not done.

Table 3 Comparison of clinical findings and electrophysiological studies.

Reference	Age at onset (y)	Distribution of wasting/weakness	Rate of progress	Cranial nerve palsies	Inheritance	Nerve conduction	EMG
1	Teens	Distal	Slow	VCP	AD	N	CPD
3	40	Distal/proximal	Rapid/slow	VCP/dysphagia	?	N	CPD
2	Early school age	Distal	Very slow	VCP/deafness	AD	N	CPD
Our family	4-21	Distal	Slow	VCP/hoarseness	AD	N	CPD

VCP = vocal cord paralysis. CPD = chronic partial denervation. N = normal.

Motor and sensory nerve conduction studies were normal, but there was electromyographic evidence of chronic partial denervation in distal muscles. Lung function tests showed marked variable upper airways obstruction.

The younger sister of III.2 (III.4) was said to be similarly affected, with onset of wasting and weakness of her left hand at 21 years of age. She had always had a hoarse voice.

The paternal grandfather (II.1), born in 1924, was said to be more severely affected than III.2 with a hoarse voice and marked wasting of his hands. He had wasted feet, an abnormal gait with foot drop and a tendency to trip, and recent difficulty in climbing and

descending stairs. Despite onset in his teenage years, he was still employed at 63 years.

Two sisters and one brother of II.1 were said to have similar complaints. His 61 year old brother (II.3), who was also employed, and 58 year old sister (II.4) had wasted hands not associated with hoarseness. His 62 year old sister (II.2) was the most disabled family member, having been wheelchair bound for 10 years.

Discussion

The neurological syndrome in this family comprised gradual onset of wasting and weakness of distal muscles, usually in the first or second decade. Upper limb involvement preceded lower limb symptoms and the condition was slowly progressive. All but two affected members had a hoarse voice, often from childhood. All subjects examined showed unilateral or bilateral vocal cord paralysis.

Electrophysiological findings were entirely normal in the proband at the age of 6 years, but when repeated three and a half years later electromyography showed evidence of early neurogenic change, consistent with anterior horn cell fallout given the clinical context. Her father, at 32 years, showed normal motor and sensory conduction studies but electromyography was consistent with chronic distal spinal muscular atrophy.

Table 3 compares our clinical findings and electrophysiological studies with those of other groups.¹⁻³ Our family is comparable with the Welsh family described by Young and Harper¹ in 1980. They share many clinical and electrophysiological features. Upper limb involvement preceded lower limb changes in most patients. Only one subject in the family of Young and Harper had a normal voice and indirect laryngoscopy showed unilateral or bilateral vocal cord paralysis in the hoarse subjects examined.

In 1985, Boltshauser *et al*² also described distal spinal muscular atrophy with vocal cord paralysis and the additional finding of sensorineural deafness, involving three generations in one family. Distal atrophy, more marked in the upper limbs, was apparent from early school age and proved very slowly progressive. Tendon reflexes were absent but there were no sensory changes. One subject had congenital stridor and another hoarseness.

Electromyography was consistent with chronic partial denervation. Motor conduction studies were abnormal in one case but sensory conduction studies were normal in all three subjects. Sensorineural deafness has not otherwise been described in published reports in association with distal spinal muscular atrophy.

Our family shares fewer clinical features with the case described by Serratrice *et al*³ in 1984. They reported a 59 year old man with onset of difficulty in climbing stairs at 40 years of age who, by 45 years, needed a stick to walk and had associated dysphagia and dysphonia. Subsequent progression was slow. Examination showed proximal and distal atrophy and

proximal muscle weakness. There was moderate dysphagia and vocal cord paralysis. Neurophysiological studies and muscle biopsy were consistent with a chronic spinal muscular atrophy. Lung function tests showed a restrictive abnormality. His sister was not examined but was said to have a similar condition, with a waddling gait and dysphonia.

This syndrome differs from that described here in its proximal distribution of atrophy and weakness, later onset, initial rapid progression, and associated dysphagia in addition to vocal cord paralysis.

The inheritance of the condition described by Serratrice *et al*³ is not clear, and it could be a different disorder. In our family, there are affected male and female subjects in three successive generations, one example of male to male transmission, and absence of parental consanguinity. There is also variability of phenotypic expression; for example, a sister and brother showed wasted hands only at the ages

of 58 and 60 years respectively, whereas their 62 year old sister was seriously disabled. Our pedigree is thus consistent with autosomal dominant inheritance, as are the pedigrees described by Young and Harper¹ and Boltshauser *et al*.² Although there is no direct evidence, we cannot exclude the possibility of a relationship between our family and that of Young and Harper.¹

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- 1 Young ID, Harper PS. Hereditary distal spinal muscular atrophy with vocal cord paralysis. *J Neurol Neurosurg Psychiatry* 1980;43:412-8.
- 2 Boltshauser E, Hof E, Spillman T, Hydegger H, Wehren A. Dominante Spinale Muskelatrophie mit Stimmbandlahmung und Innenohrschwerhörigkeit. *Schweiz Arch Neurol Psychiatr* 1985;136:75-87.
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