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Juvenile-onset bulbospinal muscular atrophy with deafness: Vialetta-van Laere syndrome or Madras-type motor neuron disease?

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Summary. A girl with rapid-onset, bulbospinal muscular atrophy and deafness is described. The patient's mother and brother showed EMG features consistent with subclinical involvement. This bulbospinal form of spinal muscular atrophy associated with deafness described by Vialetto and van Laere closely resembles the Madras type of motor neuron disease, also associated with deafness, described by Jagganathan and colleagues.

Key words: Bulbospinal muscular atrophy – Juvenile onset – Deafness – Vialetto-van Laere syndrome – Motor neuron disease, Madras type

Introduction

Bulbospinal muscular atrophy of juvenile onset, associated with sensorineural deafness, is a rare progressive disorder thought to be inherited as an autosomal recessive trait [3, 5, 7, 13]. In 3 patients and in 17 additional cases from the literature Gallai et al. [5] noted that deafness preceded the development of neurogenic muscular atrophy. Deafness is not generally associated with other anterior horn cell degenerations, but in Southern India a sporadic form of juvenile onset motor neuron disease is associated with deafness in about a third of cases [6, 10]. In this paper we report a patient with bulbospinal muscular atrophy of subacute onset, in whom muscular weakness preceded the development of deafness and in whom there was EMG evidence of a familial cause. The clinical and pathological features and this case suggest that the Madras form of anterior horn cell disease and the van Laere type of bulbospinal muscular atrophy may be related. A later-onset X-linked bulbospinal amyotrophy with loss of anterior horn cells, but not associated with deafness, has also been recognised [11].

Case report

At the age of 12 years this Caucasian girl developed difficulty climbing onto the upper level of a bunk bed. Shortly after this she complained of intermittent vertigo, lasting up to 10 min, particularly in the morning. Six months later, following an upper respiratory tract infection, her speech became nasal. At the age of 13 years, a year after the onset of the disorder, it was realised that she could not use the telephone because of deafness. Her writing deteriorated and she developed difficulty fastening buttons and picking up small objects. She lost weight and became physically weaker than previously.

On examination at the age of 14 years, she was thin, weighing only 37 kg. There was nasal speech, a weak cough, palatal weakness and mild bilateral sensorineural deafness. Her face was atrophic with flattening of the nasolabial folds and slight bilateral ptosis. There was mild weakness of neck flexors. In the arms there was marked distal weakness with wasting of the small hand muscles. In the proximal upper limb muscles there was mild symmetrical weakness and atrophy. There was moderate weakness of trunk muscles. In the legs there was mild proximal weakness with more severe weakness of knee flexion, but distal muscles in the legs were of normal strength and bulk. The tendon reflexes were symmetrical and the plantar responses were flexor. Results of sensory examination were normal. There was not ataxia or nystagmus.

Investigation revealed no abnormality in the routine haematological and biochemical investigations. No urinary porphyrins were detected. The blood creatine kinase was 121 IU/l (normal 25–150 IU/l). The CSF protein was 70 mg/l; no oligoclonal bands were detected. A CT brain scan was normal. Audiometry showed bilateral cochlear deafness. Brainstem auditory evoked responses were absent. The visual evoked response latencies were 125 ms bilaterally (normal < 120 ms). Findings from lung function tests were abnormal. Spirometry showed a forced vital capacity of 1.67 l (predicted 3.52 l), with FEV^1 1.63 l (predicted 3.16 l). There was diaphragmatic weakness. A polysomnographic study of respiration showed that expiration was jerky and prolonged, and benzodiazepine premedication for a muscle biopsy induced apneustic breathing. Oxygen saturation in the waking state was normal, but when the patient was asleep this fell to a mean saturation of 94% and to a minimum of 91% (normal mean saturation greater than 96%, minimum saturation greater than 94%). Assay of white blood cells for hexosaminidase, galactosidase, galactocerebrosidase, aryl-sulphatase, alphafucosidase and plasma glucuronidase was normal. The blood lead was 0.3 μmol/l (normal less than 1.2 μmol/l).

EMG studies showed chronic partial denervation in biceps brachii, extensor digitorum communis, first dorsal interosseus and tibialis anterior muscles. There was an increased proportion of polyphasic motor unit action potentials in these muscles, but giant potentials were not recorded. No fasciculation potentials were recorded. Single-fibre EMG (SFEMG) showed an increased fibre density in the extensor digitorum communis muscle (3.0, normal < 1.7), with increased neuromuscular jitter and some blocking potentials. Motor and sensory nerve conduction velocities were normal, but the com-

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pound motor action potential in the abductor pollicis brevis was of reduced amplitude (2 mV). A muscle biopsy specimen was taken from the right triceps muscle. This revealed atrophy of all fibre types with clusters of small pointed fibres but without fibre-type grouping.

During a period of 2 years' follow-up there has been progression neither of the neuromuscular disorder nor of the deafness.

Family studies

Although there were no definite clinical abnormalities, her mother's musculature appeared poorly developed. The mother and the patient's two brothers were studied by EMG. In her mother and in the younger of her two brothers, there was an increased proportion of polyphasic motor unit action potentials, of increased duration, in the muscles sampled. In her mother the SFEMG fibre density was increased (2.1) in the extensor digitorum communis muscle, but the neuromuscular jitter was normal and there was no blocking. The finding of EMG studies in her older brother were normal. Motor and sensory nerve conduction velocity studies showed no abnormalities. Brain-stem auditory evoked responses could not be arranged in these family members, but the mother's audiogram was normal.

Discussion

In the previously reported cases reviewed by Gallai et al. [5] a variable clinical course has been noted. In some patients the disease appears to have pursued a progressive course, sometimes leading to an arrested phase [7, 8, 13] and in others phases of episodes worsening were superimposed on a slowly progressing course. In our case, the disorder began relatively rapidly and, during a 2-year period of observation, has not so far progressed further. In all the previously reported cases the deafness preceded the onset of muscular symptoms [5] but in our patient deafness was first noticed about a year after the onset of muscular weakness. This combination of sensorineural deafness with neurogenic muscular atrophy of bulbospinal distribution is consistent with the syndrome of bulbospinal muscular atrophy of Vialetto-van Laere type. Several previously reported cases [5, 7, 13] have shown familial involvement affecting either siblings or parents. In our patient there was no known familial involvement, but clinical examination suggested subclinical disease in the mother and this was confirmed by EMG examination. There was also EMG evidence of neurogenic change in the limb muscles of the patient's younger brother, but another brother was clinically and electromyographically normal. There was no deafness in these relatives, but auditory evoked responses were not studied. Of the 20 patients reviewed by Gallai et al. [5], 16 were girls, which is an unusual feature in inherited disease.

In the juvenile-onset form of motor neuron disease prevalent in Madras, 10 of 14 patients described by Jagganathan [6] were male; of the 5 patients in this series in whom the neuromuscular disorder was associated with sensorineural deafness, 3 were female. Only 2 of the 10 boys in this series were deaf, but 3 of the 4 girls were deaf. It is uncertain from the data available whether the Madras form of juvenile-onset motor neuron disease is identical to that described by Vialetto and van Laere, but the clinical features of these two disorders clearly overlap and it is thus possible that they represent related disorders.

Vialetto-van Laere syndrome has been described in a number of ethnic groups. Ben Hamida and Hentati [2] noted 4 patients with features suggestive of Vialetto-van Laere syndrome among 20 cases of juvenile-onset anterior horn cell disease in Tunisia, and the original cases were Portuguese. Only two cases of bulbospinal muscular atrophy associated with sensorineural deafness have come to autopsy [4, 5]. In these two cases there was loss of anterior horn cells and of motor nuclei in the brain-stem with gliosis and loss of motor axons in the anterior roots. The cochlear nuclei showed loss of neurons and there was also loss of myelinated fibres in the spinocerebellar and pyramidal tracts as well as, to a lesser extent, in the gracile columns [4]. Our patient showed striking involvement of the respiratory musculature, a feature that may cause death in this disorder, and there was involvement of the bulbar musculature. However, the pelvic sphincter musculature was spared. This pattern of selective sparing of motor neuron pools is characteristic of other forms of spinal muscular atrophy and of the acquired form of motor neuron disease [9].

The familial incidence of the disease is difficult to estimate from other recorded clinical observations. In our case, clinically unexpected evidence of involvement of the patient's mother and younger brother was found by EMG studies, a feature suggesting dominant inheritance with varying penetrance rather than autosomal recessive inheritance [3, 5, 7, 13]. Vestibular testing in another family, consisting of two sisters and a brother, could also be used to provide evidence of subclinical involvement. Of the two sisters and brother reported by Tavares and De Mattos [12], the asymptomatic younger sister showed abnormalities on cochlear vestibular tests. The brother, although deaf with cochlear vestibular abnormalities, had no neuromuscular disorder and the other sister showed the disease in a relatively advanced form.

No autopsy studies of Madras-type motor neuron disease with deafness have been reported. Sensory deafness is associated with a large number of different heredofamilial neurological disorders but is not associated with the common forms of anterior horn cell disease. Nonetheless Vialetto-van Laere syndrome and Madras-type motor neuron disease appear to be distinctive and perhaps related syndromes, and they may be important in understanding other anterior horn cell disorders.

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