ABSTRACT: A Caucasian girl developed slowly progressive sensory neural deafness and bulbar and spinal muscle weakness typical of the Vialetto-Van Laere syndrome. As the condition progressed the major disabilities became dysphagia, respiratory muscle weakness and postural hypotension. Treatment with gastrostomy feedings, oxygen and flu­drocortisone acetate produced worthwhile functional improvement.


Bulbo-pontine Paralysis with Deafness: the Vialetto-Van Laere Syndrome

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Chronic, progressive bulbo-pontine paralysis associated with sensory neural deafness is a rare disorder also called the Vialetto-Van Laere syndrome. The syndrome is considered to be hereditary and has been reported in 25 patients. Most of the reported cases have come from Europe and North Africa (especially Mediterranean countries such as Portugal, Spain and Tunisia) although a case occurred in a black woman in Brazil. A related syndrome has been described in India and was named the Madras form of anterior horn cell disease. In this communication we report the clinical and electrophysiological findings of a Canadian patient with Vialetto-Van Laere syndrome.

CASE HISTORY

This Caucasian girl had always been thin. At the age of 12 when riding horses she was aware of weakness of dorsiflexion of the right foot. At the age of 19 she began to have progressive bilateral hearing loss, her face felt “stiff”, her voice became nasal and she began choking on liquids. She was admitted to a neurosurgical service and found to have bilateral sensorineural deafness, and weakness of the face and bulbar muscles. Brainstem glioma and multiple sclerosis were considered. MRI scan and 4 vessel angiography were negative. A neurological consultation was requested. Some weakness of the small hand muscles was noted and the diagnosis of Vialetto-Van Laere syndrome was raised. By the age of 23 she had diffuse loss of muscle bulk (weight 37.8 kg, height 168 cm). The blood pressure supine was 80/60 (by palpation only) with a pulse rate of 78. On standing the blood pressure fell to 60/40 and then to unrecordable levels while the pulse rate increased to 120 per minute. There was normal sinus arrhythmia during deep respiration. She was alert and oriented. The visual fields were full to confrontation, the discs were pale but the acuity (corrected) was 20/20 bilaterally. There was bilateral ptosis. The left pupil was slightly smaller than the right. Facial sensation was normal and the corneal reflexes were brisk. There was weakness of the facial muscles. Her forehead was smooth and she could not elevate her eyebrows at all although she could depress them slightly. The orbicularis occuli were slightly weak. She could whistle but she could not smile or show her teeth and contraction fasciculations were seen in the levator labii superioris when she attempted this. There was bilateral neural deafness. She had a nasal voice but the palate elevated in the midline and the gag reflex was present. The tongue was wasted and showed marked contraction fasciculation but no spontaneous fasciculations. The sternomastoids were weak. Diaphragm movement, tested by percussion, was reduced. The limb muscles were all very slender but their power was within normal limits (considering their bulk) except for finger extensors (4/5) on the MRC scale and the small muscles of the hand which were wasted and had strength 4/5. Contraction fasciculations could be seen in the first dorsal interosseus and abductor pollicis brevis. In the lower limbs there was weakness of the tibialis anterior (4/5) but the other muscles had normal strength for their bulk. The extensor digitorum brevis muscles were not wasted (although prominent contraction fasciculations were noted in these muscles) and she could fan her toes. The tendon jerks were exaggerated. A few beats of clonus could be obtained at the ankles. The plantar reflexes were flexor. There was no sensory loss. Vibration thresholds (obtained with a biothesiometer [Biomedical Instrument Co., Newberry Ohio]) were normal at 0.2 microns on the fingers and 0.5 microns on the toes. Joint position, pinprick, temperature and touch were all normal.
There was a gradual deterioration in muscle strength between ages 19-23. At age 23 the major problems were postural hypotension rendering her virtually bedridden, vertigo on head movements, nausea, vomiting and dysphagia causing inanition, and respiratory distress on exertion. These were treated with fludrocortisone acetate 0.1 mg 2 x daily and added salt, dimenhydrinate 100 mg, feeding by gastrostomy tube and oxygen by nasal prongs. These interventions considerably improved her energy and sense of well being and she was able to leave the house to visit friends. She is aged 24 at the time of writing.

The clinical picture of the 25 described cases of Vialetto-Van Laere syndrome is variable but the common clinical denominators are sensorineural deafness, facial weakness and lower brainstem (10th, 11th, 12th) motor nerve palsies. Rarely, additional cranial palsies (5th, 3rd and 6th) have been described. Lower motoneuron deficits of skeletal muscles producing weakness, atrophy and fasciculations have been described in 10 patients. Upper motoneuron signs such as increased deep tendon reflexes and clonus in the lower limbs were described in 5 patients but extensor plantar responses occurred only in one. None of the patients had sensory loss. Respiratory difficulties, probably due to intercostal and diaphragmatic muscle weakness, have been reported in 5 patients of whom 2 had documented restrictive lung disease. Additional features included optic atrophy (1 patient), retinitis pigmentosa (1 patient) and mental retardation (2 patients). The first symptom was deafness in all the patients except for one, the onset being from infancy to 31 years. The other cranial motor nerve deficits appeared at the same time as the deafness in 6 patients and followed the deafness, by 1-9 years, in the remaining 21. The course of the syndrome was a progressive deterioration in 6 patients, progression with periods of arrest in 10 patients, and deterioration in a series of exacerbations in 7 patients. The patients described in the literature were 11 to 47 years old when last seen (mean 24 years).

Electrophysiological studies\textsuperscript{11,14} show normal sensory action potentials and motor nerve conduction velocities. Electromyography shows evidence of chronic partial denervation. Large amplitude H and F waves observed in 2 patients have been considered to be evidence for an upper motor neuron lesion.\textsuperscript{11}

Muscle biopsies show scattered atrophic fibers suggestive of chronic denervation.\textsuperscript{11,14} A sural nerve biopsy in a 15 year old girl\textsuperscript{11} showed only slight depletion of nerve fibers.

Autopsies have been carried out on 3 cases: a 25 year old woman,\textsuperscript{9} a 27 year old woman\textsuperscript{10} and a 2 year old boy.\textsuperscript{11} The 8th nerve showed loss of axons and the ventral cochlear nucleus loss of neurons and glialis. There was loss of motoneurons in the nuclei of the 7th and 10th and 12th cranial nerves and, in the adult patients, in the nuclei of the 3rd, 5th and 6th cranial nerves as well. Lombaert et al.\textsuperscript{9} reported loss of spinal anterior horn cells. In this case\textsuperscript{9} there were abnormalities in the substantia nigra, locus coeruleus, dorsal column nuclei and degeneration of the lateral leminiscus, medial longitudinal fasciculus and trapezoid body and some gliosis of the optic pathways. In the case reported by Alberca et al.\textsuperscript{10} there was degeneration in spino-cerebellar and pyramidal tracts.
In four families there were 2 or more affected siblings. Subclinical neurological abnormalities were found in relatives of two other cases: the mother and brother of the patient reported by Summers et al.\textsuperscript{14} were found to have electromyographic abnormalities consistent with denervation, and the brother and sister of the patient reported by Tavares et al.,\textsuperscript{13} had audiometric evidence of sensorineural loss. The remainder of the cases were considered to be sporadic. Although the syndrome has been considered to be autosomal recessive the high proportion of female patients 918/22) is unusual for this type transmission. Genetic disease occurring only or largely in females may be compatible with X linked dominance or with other yet unknown non mendelian inheritance.\textsuperscript{18} For example hyperuricemia, ataxia and deafness (30720 in McKusick catalogue) is one of the diseases with female predominance, compatible with X-linked dominance.\textsuperscript{19}

A sporadic form of anterior horn cell disease has been described in South India. In one series\textsuperscript{15} bilateral 8th nerve deficit with dysfunction of 10th, 11th, and 12th nerves occurred in 3 out of 32 patients and bilateral facial palsy occurred in 1 of 32 patients. The male/female ratio in the 7 patients with bulbar symptoms was 4/3. In another series of 14 patients from the same region,\textsuperscript{16} 10/14 showed bilateral sensorineural deafness, motor bulbo pontine involvement, and pyramidal tract signs. The label of "Madras pattern of motoneuron disease" was given to the members of this group. The male/female ratio was 2/3. From the point of view of the female preponderance, it seems that there is a difference between the Vialetto-Van Laere syndrome and the Madras pattern of motor neuron disease.

Our patient developed simultaneous sensorineural deafness and bulbar weakness with progressive deterioration. The involved cranial nerves included 3rd, 7th, 8th, 10th and 12th. Spinal motoneurons and possibly upper motor neurons were involved. The electrophysiological findings showed denervation of the bulbar and limb muscles with low amplitude muscle evoked motor responses indicating loss of motor axons. The present case appears to be compatible with the diagnosis of Vialetto-Van Laere syndrome and to our knowledge is the first reported case in Canada. Postural hypotension has not been previously described in this condition. It was probably too pronounced to be attributed simply to inanition and inactivity. The reduced catecholamine levels imply a failure of the peripheral sympathetic efferent system. The piosis described in several reports and the loss of catecholamine neurons in the brainstem in one autopsied case\textsuperscript{10} may be further evidence of autonomic involvement. Treatment with gastrostomy feeding, fludrocortisone acetate and oxygen produced a worthwhile symptomatic improvement.

\textbf{Note added in proof}

The GM1 antibody titres, kindly estimated by Dr. Alan Petstronk, Washington University School of Medicine, St. Louis, were negative.

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\textbf{REFERENCES}