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

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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.

RÉSUMÉ: Paralysie bulboprotubérantielle avec surdité: syndrome de Vialetto-Van Laere. Nous décrivons le cas d'une fille de race caucasienne qui a développé une surdité neurale lentement progressive et une faiblesse musculaire bulbaire et spinale typique du syndrome de Vialetto-Van Laere. Avec la progression de la maladie, la dysphagie, la faiblesse des muscles respiratoires et l'hypotension posturale ont été les signes les plus invalidants. L'alimentation par gastrostomie, l'administration d'oxygène et d'acétate de fludrocortisone ont entraîné des améliorations fonctionnelles significatives.

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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.[1-14]

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.[13] A related syndrome has been described in India and was named the Madras form of anterior horn cell disease.[15,16] 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 21 she had developed drooping of her eyelids and had to tilt her head back in order to see when driving. She now had more obvious weakness of the facial muscles and small muscles of the hand. At age 22 she developed shortness of breath on exertion, postural hypotension, vertigo with sudden head movements and began to spend most of her time in a horizontal posture. There was no family history of neurological disorders and her parents were not related.

On examination at the age of 23 she had diffuse loss of muscle bulk (weight 37.8 kg, height 168 cm). The blood pressure supine was 80/? (by palpation only) with a pulse rate of 78. On standing the blood pressure fell to 60/? 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[17] and the small muscles of the hand which were wasted and had strength 4/5. Contraction fasciculations could be seen in the first dorsal interosseous 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.

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Investigations

MRI scans of the brain and brainstem at ages 19, 20 and 22 and 4 vessel angiograms age 19 were normal. The CSF protein was 0.55 G/L (normal 0.2 - 0.4 G/L). All routine biochemical and hematological studies were normal. Audiograms at the age of 20 showed bilateral neural deafness. Brainstem evoked responses showed only the first component. The electroretinograms were normal but there was evidence for subclinical involvement of the optic system. Pattern reversal visual evoked potentials were recorded from each eye (with corrective glasses). The P100 potentials were of low amplitude and replicated poorly. The latencies were prolonged (right = 122 ms; left = 120 ms; normal = 89-114 ms).

Peripheral neuromuscular system

Extensive EMG studies were not possible because of her intolerance of the discomfort. At age 19 the sensory nerve action potential amplitudes, distal latencies and conduction velocities were normal for the right median, ulnar, and sural nerves. Motor nerve conduction velocities, distal latencies, amplitudes, and f waves were normal for the right median ulnar, peroneal, and posterior tibial nerves. Normal sympathetic skin responses were recorded from the hands and feet following a sharp inspiration or stimulation of the median nerve at the wrist. There was fibrillation (scored from 0 to 4+) in the frontalis muscles (3+), orbicularis oris (2+), the tongue muscles (1+) and tibialis anterior (1+). There was no motor units under voluntary control in the frontalis muscle and a reduced number in orbicularis oris.

By age 20 the amplitude of the compound action potential of the right abductor pollicis brevis had fallen to 1.8 mV (normal greater 4 mv) but sensory and motor nerve conductions were otherwise normal. There was a marked reduction in the number of motor units in the right first dorsal interosseous and tibialis anterior and there were large amplitude polyphasic potentials in both of these muscles. Fibrillation (1+) was detected in the tibialis anterior.

By age 22 the nerve conductions had not changed. Limited EMG studies showed no fibrillation in the frontalis or zygomaticus muscles but there was a marked reduction in the number of motor units in the first dorsal interosseous and tibialis anterior.

Respiratory Function

The physical examination finding of reduced diaphragmatic excursion was confirmed by fluoroscopy which showed inspiratory descent of 1.1 cm on the right and 0.7 cm on the left. Formal pulmonary function testing showed a moderate restrictive ventilatory defect with forced vital capacity of 2.71 L or 65% of the predicted value and a pattern of lung volume changes compatible with respiratory muscle weakness. Maximal inspiratory mouth pressure was moderately reduced to 44% of the predicted value but expiratory pressure was better preserved at 72% of predicted. Arterial blood gases drawn while she breathed room air while at rest were within normal limits with no evidence of hypoventilation or hypoxemia and oximetric monitoring overnight revealed no sleep related desaturation. However, with minimal exertion (slow walking) there was prompt desaturation to 84%.

Cardiovascular System

Postural hypotension became a major problem from age 22 onwards. The electrocardiogram and echocardiogram were normal. The recumbent renin (0.6 ng/L/sec) and aldosterone (251 pmol/L) were normal and rose (1.1 ng/L/sec, 1141 pmol/L respectively) with the upright posture indicating a normal response to changes in renal blood flow. The resting cortisol was raised to 783 and 1015 nmol/L on the two occasions it was tested (normal 170-660 nmol/L). This was attributed to "stress". Serum cortisol increased further following a synthetic ACTH injection suggesting that the adrenal axis was normal. The recumbent plasma epinephrine was reduced at 0.10 nmol/l (normal 0.17-0.52 nmol/l) and plasma norepinephrine was reduced at 1.1 nmol/l (normal 1.27-2.80 nmol/l). These values did not rise with the upright posture. This suggests that the release of norepinephrine from sympathetic nerve endings was reduced. Thus the postural hypotension appeared to be due to sympathetic dysfunction. If so, the prominent tachycardia on standing must have been due to withdrawal of vagal action or sparing of sympathetic efferents to the heart.

Course

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.

Discussion

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 motor 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 limb 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 remainder. 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[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.[11]

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

Autopsies have been carried out on 3 cases: a 25 year old woman,[9] a 27 year old woman[10] and a 2 year old boy.[11] The 8th nerve showed loss of axons and the ventral cochlear nucleus loss of neurons and gliosis. 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.[9] reported loss of spinal anterior horn cells. In this case[9] there were abnormalities in the substantia nigra, locus coerulus, dorsal column nuclei and degeneration of the lateral leminisci, medial longitudinal fasiculus and trapezoid body and some gliosis of the optic pathways. In the case reported by Alberca et al.[10] there was degeneration in spino-cerebellar and pyramidal tracts.

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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.[14] were found to have electromyographic abnormalities consistent with denervation, and the brother and sister of the patient reported by Tavares et al.,[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.[18] For example hyperuricemia, ataxia and deafness (30720 in McKusick catalogue) is one of the diseases with female predominance, compatible with X-linked dominance.[19]

A sporadic form of anterior horn cell disease has been described in South India. In one series[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,[16] 10/14 showed bilateral sensorineural deafness, motor bulbopontine 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 uppermotor 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 ptosis described in several reports and the loss of catecholamine neurons in the brainstem in one autopsied case[10] may be further evidence of autonomic involvement. Treatment with gastrostomy feeding, fludrocortisone acetate and oxygen produced a worthwhile symptomatic improvement.

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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References

1. Brown CH. Infantile amytrophic lateral sclerosis of the family type. J Nerv Ment Dis 1894; 21: 707-716.
2. Vialetto E. Contributo alla forma ereditaria della paralisi bulbare progressiva. Riv sper Freniat 1936; 40: 1-24.
3. Van Laere J. Paralysie bulbo-pontine chronique progressive familiale avec surdité. Un case de syndrome de Klippel-Trenaunay dans la meme fratrie: Problèmes diagnostiques et génétiques. Rev Neurol 1966; 115: 289-295.
4. Van Laere J. Un nouveau cas de paralysie bulbo-pontine chronique progressive avec surdité. Rev Neurol 1977; 133: 119-124.
5. Arnuold G, Tirdon P, Laxenaire M, et al. Paralysie bulbo-pontine chronique progressive avec surdité. À propose d'une observation de de Fazio-Lonnde. Rev Oto-neurol-ophthal 1968; 40: 158-161.
6. Trillet M, Girard PF, Schott B, et al. La paralysie bulbo pontine progressive avec surdité. À propos d'une observation clinique. Lyon Med 1970; 223: 145-153.
7. Boudin G, Pépin B, Vernant JC, et al. Cas familial de paralysie bulbo-pontine chronique progressive avec surdité. Rev Neurol 1971; 124: 90-92.
8. Serratrice G, Gastaut JL. Amyotrophies dégénératives et lésions du neurone moteur (à propos de 32 observations). Marseille Med 1972; 109: 821-840.
9. Lombaert A, Dom R, Carton H, et al. Progressive ponto bulbar palsy with deafness. A clinico-pathological study. Acta Neurol Belg 1976; 76: 309-314.
10. Alberca R, Montero C, Ibanez et al. Progressive bulbar paralysis associated with neural deafness. A nosological entity. Arch Neurol (Chic) 1980) 37: 214-216.
11. Gallai V, Hockaday JM, Hughes JT, et al. Ponto bulbar palsy with deafness (Brown-Vialetto-Van Laere syndrome). A report on three cases. J Neurol Sci 1981; 50: 259-275.
12. Ben Hamida M, Hentati F. Maladie de Charcot et sclérose lateral amyotrophique juvenile. Rev Neurol 1984; 140: 202-206.
13. Tavares CCA, De Mattos JP, De Amorim AC. Données cochléo-vestibulaires dans la sclérose laterale amyotrophique (forme de Van Laere). Rev Laryngol Otol Rhinol 1985; 106: 375-378.
14. Summers BA, Swash M, Schwartz MS, et al. Juvenile onset bulbospinal muscular atrophy with deafness: Vialetto-Van Laere syndrome or Madras-type motor neuron disease? J Neurol 1987; 234: 440-442.
15. Sayeed ZA. Velmurugendran CU, Arjundas G, et al. Anterior horn cell disease seen in south India. J Neurol Sci 1975; 26: 489-498.
16. Meenakshisundaram E, Jaganathan K, Ramamurthi B. Clinical patterns of motor neurone disease seen in young age group in Madras. Neurology (India). Neurology 1970; 18: 109-112.
17. Medical Research Council Memorandum No. 45. Aids to the examination of the peripheral nervous system. British Stationery Office. 1976.
18. Johnson EG. Mendelian and non-Mendelian inheritance. *In:* Rowland LP, Woods DS, Scon EA, DiMauro S. eds. Molecular genetics in diseases of brain and nerve and muscle. Oxford University Press. New York and Oxford, 1989: 24-35.
19. McKusick VA. Mendelian inheritance in man. 7th Edition. Baltimore, The John Hopkins University Press, 1986.

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