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Brown-Vialetto-Van Laere syndrome: a rare syndrome in otology - case report and literature review

H V Prabhu, DLO, DOHNS, MRCS, M J K Brown, FRCS(Ed), FRCS(Lon)

Abstract
Brown-Vialetto-Van Laere syndrome, or pontobulbar palsy with deafness, is a rare disorder characterized by bilateral sensorineural deafness and a variety of cranial nerve disorders usually involving the motor components of the lower cranial nerves. Less commonly, spinal motor nerves and upper motor neurons are involved. Familial and sporadic cases have been reported. Based on evidences, this syndrome has been related to autosomal recessive, autosomal dominant and X-linked inheritance. Autoimmune origin has been considered as well.

In this paper, we report the case of a 38-year-old female patient who primarily presented with bilateral sensorineural hearing loss and then progressively developed Xth and VIIth cranial nerve paralysis. Brown-Vialetto-Van Laere syndrome was diagnosed with this symptom complex of sensorineural hearing loss and pontobulbar palsy.

Key words: Bulbar Palsy; Hearing Loss; Cranial Nerve Diseases

Case report

A 28-year-old woman presented originally to our outpatient department with bilateral hearing loss without any significant family history of deafness. Clinical ENT examination was normal. Pure-tone audiometry confirmed sensorineural hearing loss. On initial presentation hearing loss was more severe on the left side compared with the right. Hearing deteriorated bilaterally during the follow-up visits, as shown in the pure-tone audiograms (Figure 1). Magnetic resonance imaging (MRI) scan of the internal auditory meati was performed, which was reported to be normal. She was fitted with a digital hearing aid to overcome this disability.

The patient further developed hoarseness of voice during the next follow-up period of one year. Indirect laryngoscopy examination revealed bilateral adductor weakness of the vocal folds. A direct laryngoscopy examination confirmed the clinical findings.

Investigations were carried out to look into the cause of this problem. Thyroid profiles, Venereal Disease Research Laboratory (VDRL), *Treponema pallidum haemagglutination* (TPHA), and mitochondrial deoxyribonucleic acid (DNA) study were normal. Electronystagmography (ENG) study was normal with no evidence of generalized neuropathy. Lumbar puncture and cerebrospinal fluid (CSF) analysis were normal. Radiological investigation, which included X-ray of the chest and ultrasound scan of the thyroid, were also normal.

During the next follow-up period of one year, the patient developed difficulty in swallowing with episodes of coughing when drinking or eating solids. Apart from VIIIth and Xth cranial nerve paralysis, the rest of the neurological examination was normal. Barium swallow revealed a marked cricopharyngeal impression with no other abnormalities.

The disease was progressive which particularly affected the patient's swallowing and breathing. Tracheostomy was performed to relieve stridulous breathing and to provide nocturnal intermittent positive pressure ventilation for central nocturnal hypoventilation. She also developed a partial right upper facial weakness at the age of 35 years. Progressive involvement of the motor component of the lower cranial nerves is characteristic of this disease. The interesting fact in this case is that the facial nerve involvement has been unilateral whereas both the VIIIth and Xth cranial nerve palsies are bilateral. The patient is followed up every six months by the ENT and respiratory team to monitor the progress of the disease. Over the last three years of follow up there has been no progression in the disease.

A precise diagnosis is essential for advising the patients about their prognosis, for identifying those diseases with genetic implications, and to offer appropriate treatment.

Discussion

The Brown-Vialetto-Van Laere syndrome, or pontobulbar palsy with neural deafness, or hereditary progressive bulbar paralysis with deafness, is characterized by bilateral nerve deafness and a variety of cranial nerve disorders, usually involving the motor components of the lower cranial nerves. Spinal motor nerves and, less commonly, upper motor neurons are also affected. The onset of the disease is usually in childhood and the course is irregularly progressive.

The first case was reported by Brown in 1894. Familial cases in a pattern consistent with autosomal recessive inheritance were reported by Vialetto (1936), Van Laere (1966) and Boudin *et al.* (1971).

From the Department of ENT, Royal Gwent Hospital, Newport, UK.
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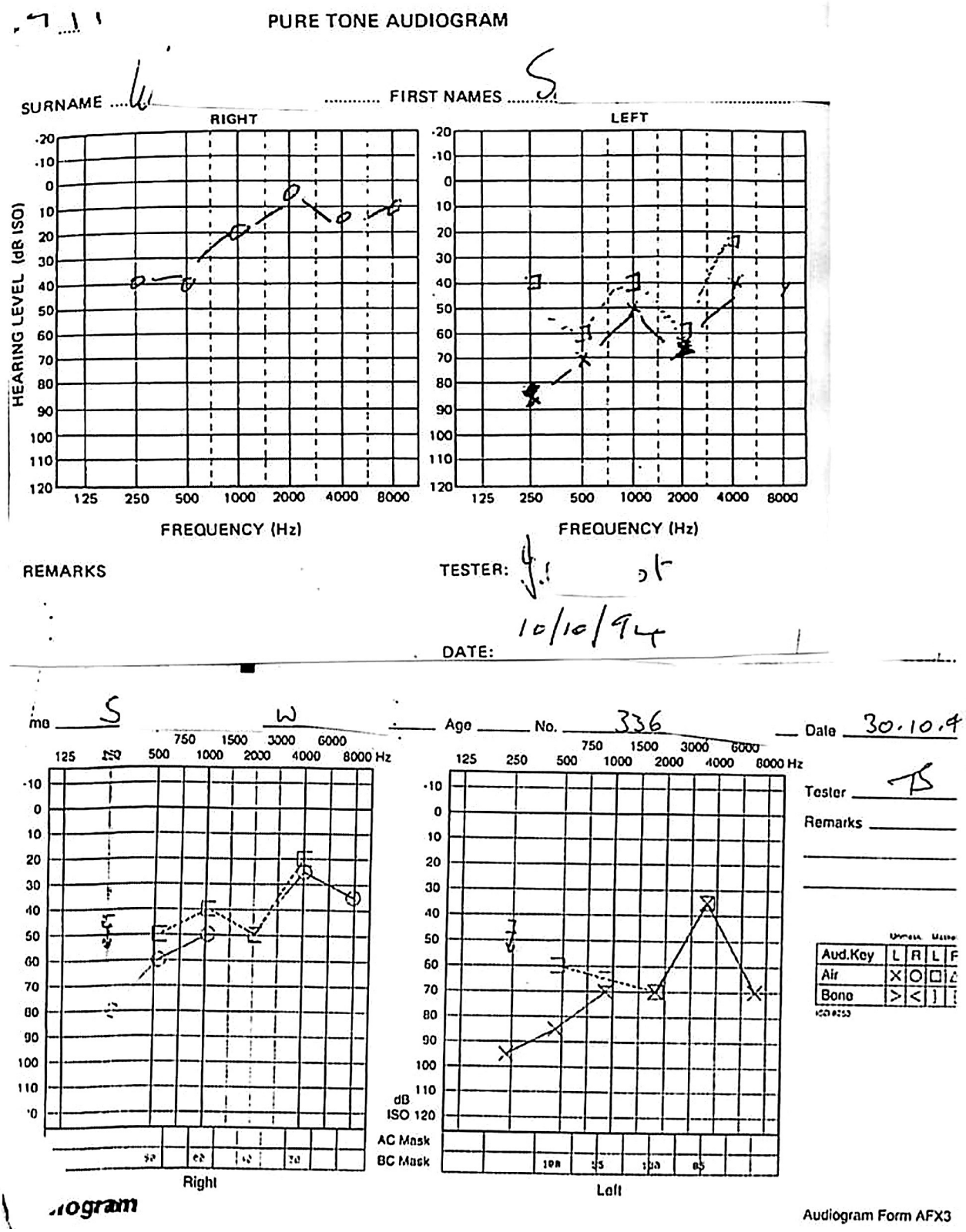

FIG. 1

Audiograms showing initial hearing loss in 1994 and recent hearing loss in 2004.

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In 1981, Gallai *et al.* described two cases and reviewed previously published ones, in which the primary symptom was sensorineural deafness of slow or rapid onset followed within a few years by lower cranial motor nerve palsies. Hawkins *et al.* (1990) suggested that the disorder may be genetically heterogeneous with autosomal recessive and autosomal dominant forms, or alternatively that it may be caused by a mutant gene on the X chromosome. [1] There are reports of this disease in a consanguineous Lebanese family as well, and was of severe variety.[2]

Since the first description by Brown in 1894, about 37 cases have been reported. Half of these are familial with no recognized symptoms in parents or relatives, suggesting autosomal recessive inheritance. In two families autosomal dominant inheritance with variable penetrance and expressivity, and alternatively X-linked inheritance, were postulated.[2] All other cases were sporadic, one of which had a moderate elevation of anti-ganglioside GM1 antibodies, also suggesting a possible autoimmune origin.

The aetiopathogenesis of this disease is still unknown. Onset of the disease is in the second decade with no abnormality in the early development. In previous reports, the sex ratio was shown to be 1:5 with female preponderance.[3] Brown-Vialetto-Van Laere syndrome has been described in a number of ethnic groups, but the original cases were from the Portuguese community.

The clinical course of the syndrome varies greatly from case to case. There were cases with progressive deterioration, progressive deterioration with periods of stabilization and deterioration with abrupt periods of exacerbation. Fifty per cent of the patients reported before the year 2000 survived more than 10 years after the onset of the first symptom, while only three survived for five years or less after the initial symptom.[3] Mortality in patients suffering from this disease has been mainly because of respiratory compromise,[3] either from infections[5] or respiratory muscle paralysis. Major features include fasciculation of the tongue, weakness of the facial and neck muscles and neurological disorders involving the cranial nerves as mentioned above.

There are very few pathological descriptions, which have reported neuronal injury and depletion in the IIIrd, Vth, VIth and VIIth to XIIth cranial nerve nuclei. Other pathological findings include loss of spinal anterior horn cells, degeneration of spinocerebellar and pyramidal tracts, degeneration of cerebellar purkinje cells and abnormalities in the substantia nigra, locus coeruleus, olives, cuneate nucleus, ambigus nucleus, dorsal nucleus of Clarke, fastigial nucleus, lateral lemnisci, medial longitudinal fasciculus, trapezoid body, optic pathways and solitary tract.[3,5] Detailed study of the auditory and vestibular pathway revealed that the cochlear nuclei were almost devoid of neurons and severely gliotic.[4]

Two cases diagnosed with the syndrome underwent autopsy. In these two cases there was similar pathology as explained above. The 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.

There are few variants of Brown-Vialetto-Van Laere syndrome described.

Fazio Londe disease,[6] which is a bulbar palsy of childhood, without deafness, and respiratory muscle involvement may lead to death within a few years. It is usually inherited as an autosomal recessive trait. Progressive muscular atrophy and spinal muscular atrophy do not show neural deafness, and present with lower motor neuron signs only.

The Nathalie syndrome, characterized by spinal muscular atrophy and sensorineural hearing loss, also includes cataracts, cardiac conduction disorders, and hypogonadism.

Boltshauser syndrome[6] is very close to this syndrome, although brain-stem signs are restricted to vocal fold paralysis and the inheritance is likely to be autosomal dominant.

- **Brown-Vialetto-Van Laere syndrome or pontobulbar palsy is a rare degenerative neurological condition characterized by bilateral sensorineural deafness and lower cranial nerve palsies**
- **In this case report the presentation, clinical course and management are discussed**

Madras disease is also very close and could be the same disorder except being sporadic in the majority of cases and showing possible environmental origin as well.

The early age of onset, deafness, early involvement of bulbar nuclei and absence of pyramidal signs distinguish it from amyotrophic lateral sclerosis. As the cause of this syndrome is not known, management of these patients is mainly supportive, like assisted ventilation and gastrostomy feeding. Steroids and intravenous immunoglobulin have been used in patients with temporary relief.

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Address for correspondence:
Mr H V Prabhu,
Senior House Officer,
Department of ENT,
Royal Gwent Hospital,
Newport NP20 2UB, UK.

E-mail: hvinodprabhu@hotmail.com

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