

Case reports

Brown-Vialetto-van Laere syndrome ; the first turkish case

Ömer Faruk AYDIN^a, Dilek ÖZÇELIKEL^b, Nesrin ŞENBİL^a, Y. K. YAVUZ GÜRER^a

^aDepartment of Pediatric Neurology, Dr. Sami Ulus Children's Hospital, Ankara, Turkey

^bAnkara Numune Hospital, Department of Neurology, Ankara, Turkey

Abstract

We describe a 14-year-old female patient with progressive ponto-bulbar palsy and deafness. The first symptom was present at the age of 9 as a difficulty in walking and then she was stable with mild clumsy walking till 14 year-old. It was noticed that she had rapidly progression gait disorder, hearing loss, difficulty in swallowing and speaking in a period of 2.5 months. Clinically, there were bilateral facial weakness, atrophic tongue with fasciculations, poor gag reflex, deafness, axial and appendicular hypotonia, severe muscular weakness involving muscles of neck, shoulder, and upper arms, hands with thenar and hypothenar amyotrophy. Hearing loss was documented by brainstem auditory evoked potentials. Other laboratory investigations, screening tests and imaging studies were normal. These clinical features are consistent with the Brown-Vialetto-van Laere syndrome.

Key words : Brown-Vialetto-van Laere Syndrome ; pontobulbar palsy ; deafness ; motor neuron disease.

Introduction

The Brown-Vialetto-van Laere syndrome (BVVLS) is characterized by bilateral sensorineural deafness with slow or rapid onset and progressive cranial nerve palsies, usually involving the motor components of 7th and 9th to 12th (more rarely the 3rd, 5th, and 6th) cranial nerves (1, 2). In addition, anterior horn cell and upper motor neuron involvement is well described, often occurring together (3, 4, 5). The other neurological features have been reported including ataxia, optic atrophy, retinitis pigmentosa, epilepsy and autonomic disturbances (4, 6, 7, 8). Cognitive impairment and sensory deficit are not commonly involved in this syndrome.

The etiopathogenesis of this disease is still unknown. A moderate elevation of ganglioside GM1 antibodies was found which may suggest a possible autoimmune origin (9). Tests for mutations in the survival motor neuron and neuronal apoptosis inhibitory protein genes were normal in two patients (2, 10).

Hawkins *et al.* 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 (5). The most of familial cases are female. There is a 5:1 preponderance of females among recorded cases of BVVLS (13, 15). Fifty percent of patients are sporadic cases (2). The onset of the disease is usually in late childhood and adolescence ; however, cases with symptoms beginning within the first five years and cases with an irregularly progressive course have been reported (2, 6, 13). We report a case with this rare syndrome. To our knowledge, this will be the first case with BVVLS reported from Turkey.

Case report

The 14-year-old female patient had first gait difficulties at the age of 9 years. She was able to walk clumsily and had an improvement with mild gait difficulty as a sequela after 5 months. Before admission, the patient had had progression of gait disorder since 2.5 months. She had difficulty in speaking, hearing and swallowing for 1 month. She lost weight and became physically weaker than before. She also complained of sleepiness during the day and of shortness of breath. The parents reported that she had dysphagia for liquids and occasionally for solids. Her second degree consanguineous parents were healthy. No other family members had neurological symptoms or hearing deficit.

The patient's general appearance was that of a weak and slender girl. The neurologic examination revealed a bilateral facial weakness with poor smile and flattening of nasolabial folds, and inability to close the eyes tightly, atrophic tongue with fasciculations, poor gag reflex, deafness, axial and appendicular hypotonia. She had severe muscular weakness of neck, shoulder, and upper arms and amyotrophic thenar and hypothenar muscles. She had difficulty in swallowing and had nasal speech. There was no ptosis, no ocular movement impairment. Ophthalmologic examination was normal.

Her sensory examination seemed equally intact. The tendon reflexes were normal in the upper limbs and pathologically brisk in legs. Plantar responses were extensor. She had dysmetria on the left upper and lower extremities. There was no fasciculation in muscles except tongue but she had a mild global weakness. She seemed to be of normal intelligence. The following investigations were normal ; routine haematology and biochemistry including thyroid function, creatine kinase, serum and cerebrospinal fluid (CSF) lactate and pyruvate levels, Tandem MS, organic acid analysis of urine, lysosomal enzyme screening (sphingomyelinase, total hexosaminidase, hexosaminidase A, beta-galactosidase, alpha-galactosidase, arylsulfatase A), ANA, Anti-dsDNA, vitamin E, vitamin B12, serum alpha-feto-protein and carcinoembryonic antigen, anticardiolipin antibodies and antiphospholipid antibodies. CSF contained 4 lymphocytes/mm³, protein 58 mg/dl and glucose 51 mg/dl. Magnetic resonance imaging of brain and cervical spine were normal, as was abdominal ultrasonography and echocardiography. Brainstem auditory evoked potentials (BAEP) were completely absent. Visual evoked responses and sensory evoked responses were normal. Respiratory function tests couldn't be done because of uncooperation due to possible impaired vital capacity. Motor and sensory nerve conduction velocities revealed mild delay, but the compound motor action potentials in the median and peroneal were of reduced amplitude. No fasciculation potentials were recorded. Mild neuropathic findings were detected in needle electromyography. The muscle biopsy showed type I fibres group atrophy ; specifically there were no myopathic features and no morphological evidence of a mitochondrial myopathy.

Discussion

The clinical neurological findings of sensorineural deafness, facial diplegia, atrophy and fasciculations of tongue, and wasting neck and shoulder muscles, upper motor neurone signs in the lower limbs point to a lesion in the lower brain stem and cervical spinal cord, and this combination is consistent with the syndrome of bulbospinal muscular atrophy of BVVL type. This disease should be differentiated from structural lesions of the brainstem such as tumours, encephalitis, disorders of the cranial nerve and muscle diseases.

Clinically, Fazio-Londe disease (FLD) affects the bulbar cranial nerves of young children in a progressive fashion and ptosis also is found but deafness is not a feature (11). BVVLS is usually found in late childhood and adolescents. However, cases with symptoms beginning within the first 5 years also have been reported (2, 6, 13, 15).

The Madras form of juvenile-onset motor neuron disease (MND) is characterized by facial weak-

ness, dysphagia, dysarthria, fasciculations on tongue, limp weakness, upper motor neuron findings and juvenile onset. Sensorineural deafness was also reported as 30%. But it is a distinctive entity from that described by Brown-Vialetto and van Laere. Madras pattern MND differs in certain respects ; occasional recessive inheritance is described and the disease has a slowly progressive course. Furthermore the sex distribution is different, males outnumbering females and commonly found in South India as a sporadic (12). But the clinical features of these two disorders clearly overlap and it is thus possible that they represent related disorders (3).

Familial juvenile amyotrophic lateral sclerosis is characterized by pure motor dysfunction with both upper motor neuron and lower motor neuron involvement. Affected children develop spasticity, hyperreflexia, generalized fasciculations. Coincident deafness could be rarely (14). Half of familial cases with no recognized symptoms in their parents or other relatives, suggesting autosomal recessive inheritance (2). We couldn't do BAEP and/or examine her close relatives in neurologic aspect. Neither there was a history of deafness nor neuromuscular disease in our patient's family, but there was a second degree consanguinity which may suggest an autosomal recessive inheritance in this case.

In most cases with BVVLS, deafness was followed within a few years by lower cranial motor nerve palsies. The level of deafness is very variable, ranging from almost complete to very mild (1). Summers BA et al. reported a case whose deafness was first noticed about a year after the onset of muscular weakness (3). In our patient, hearing loss was noticed several months after the progression of gait disorder during second attack. In patients, the subsequent clinical course varied greatly from case to case. In some patients the disease appears to have pursued a progressive course, sometimes leading to an arrested phase and in others phases of episodes worsening were superimposed on a slowly progressing course (7). Our patient's first symptoms as gait difficulty had occurred at the age of 9 years. She had improvement partially with a sequela and no progression of her gait difficulty till 14 years old. She has been maintained on assisted ventilation at home using a portable ventilator at nights.

REFERENCES

1. DAVENPORT R. J., MUMFORD C. J. The Brown-Vialetto-van Laere syndrome : a case report and literature review. *Eur. J. Neurol.*, 1994, **1** : 51-54.
2. MEGARBANE A., DESGUERRES I., RIZKALLAH E., DELAGUE V., NABOUT R., BAROIS A., URTIZBEREA A. Brown-Vialetto-van Laere Syndrome in a Large Inbred Lebanese Family : Confirmation of Autosomal Recessive Inheritance ? *Am. J. Med. Genet.*, 2000, **92** : 117-121.

3. SUMMERS B. A., SWASH M., SCHWARTZ M. S., INGRAM D. A. Juvenile-onset bulbospinal muscular atrophy with deafness : Vialletto-van Laere syndrome or Madras-type motor neuron disease ? *J. Neurol.*, 1987, **234** : 440-442.
4. BRUCHER J. M., DOM R., LOMBAERT A., CARTON H. Progressive pontobulbar palsy with deafness. *Arch. Neurol.*, 1981, **38** : 186-190.
5. HAWKINS S. A., NEVIN N. C., HARDING A. E. Pontobulbar palsy and neurosensory deafness (Brown-Vialletto-van Laere syndrome) with possible autosomal dominant inheritance. *J. Med. Genet.*, 1990, **27** : 176-179.
6. ALBERCA R., MONTERO C., IBANEZ A., SEGURA D. I., MIRANDA-NIEVES G. Progressive bulbar paralysis associated with neural deafness. A nosological entity. *Arch. Neurol.*, 1980, **37** (4) : 214-216.
7. VAN LAERE J. E. A new case of chronic progressive bulbo-pontine paralysis and deafness. *Rev. Neurol.*, 1977, **133** (2) : 119-124.
8. ABARBANEL J. M., ASHBY P., MARQUEZ-JULIO A., CHAPMAN K. R. Bulbo-pontine paralysis with deafness : the Vialletto-van Laere syndrome. *Can. J. Neurol. Sci.*, 1991, **18** (3) : 349-351.
9. SZTAJZEL R., KOHLER A., REICHART M., DJIENTCHEU V. P., CHOFFLON M., MAGISTRIS M. R. Brown-Vialletto-van Laere syndrome : a case with anti-ganglioside GM1 antibodies and literature review. *Rev. Neurol. (Paris)*, 1998 Jan, **154** (1) : 51-4.
10. ORRELL R. W., HABGOOD J. J., DE BELLEROCHE J. S., LANE R. J. The relationship of spinal muscular atrophy to motor neuron disease : investigation of SMN and NAIP gene deletions in sporadic and familial ALS. *J. Neurol. Sci.*, 1997, **145** (1) : 55-61.
11. McSHANE M. A., BOYD S., HARDING B., BRETT E. M., WILSON J. Progressive bulbar paralysis of childhood. A reappraisal of Fazio-Londe disease. *Brain*, 1992, **115** (Pt 6) : 1889-1900.
12. SAYEED Z. A., VELMURUNGENDRAN C. U., ARJUNDAS G., MASARREEN M., VALMIKINATHAN K. Anterior horn cell disease seen in South India. *J. Neurol. Sci.*, 1975, **26** (4) : 489-498.
13. VOUDRIS K. A., SKARDOUTSOU A., VAGIAKOU E. A. Infantile progressive bulbar palsy with deafness. *Brain Dev.*, 2002, **24** : 732-735.
14. MITSUMOTO H. Disorders of upper and lower motor neurons. In : *Neurology in Clinical Practice*. BRADLEY W. G., DAROFF R. B., FENICHEL G. M., MARSDEN C. D. (eds). 3rd ed., Vol I, 2000, Butterworth Heinemann, MA, USA :1985-2018.
15. GALLAI V., HOCKADAY J. M., HUGHES J. T., LANE D. J., OPPENHEIMER D. R., RUSHWORTH G. Ponto-bulbar palsy with deafness (Brown-Vialletto-van Laere syndrome). A report on three cases. *J. Neurol. Sci.*, 1981, **50** (2) : 259-275.

Ömer Faruk AYDIN, M.D.
 Ümitköy Sitesi, 22.Blok No = 6,
 06530 Ankara (Turkey)
 E-mail : ofaydin@yahoo.com.