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Case Report

Motor neuron disease in a young female, Madras pattern or Brown-Vialetto Van Laere syndrome? - A diagnostic dilemma

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ABSTRACT

We report a case of a 14 year old female patient with progressive ponto-bulbar palsy, bilateral deafness and distal muscle weakness with wasting. This pattern is seen in Brown-Vialetto-Van Laere which is an extremely rare neurological disorder of unknown etiology with less than 80 cases being reported till date. The syndrome was first described in 1894 by Brown and subsequently by Vialetto in 1936 and Van Laere in 1966. A similar pattern is noted in the Madras form of motor neuron disease which is seen in South India. With the available literature and data it's difficult to differentiate between these entities.

Keywords: BVVL syndrome, Madras motor neuron disease

INTRODUCTION

Brown-Vialetto-Van Laere syndrome (BVVLS) or progressive pontobulbar palsy with deafness is a rare degenerative disorder characterized by slow or rapid onset progressive bilateral deafness and cranial nerve involvement, usually motor components of the 7, 9, 10, 11 and 12. Spinal motor nerves and less commonly upper motor neuron may be involved. The female to male ratio is approximately 3:1. The age of presentation varies from infancy to the third decade.[1]

The Madras Motor Neuron Disease (MMND) was first described in the 1970's which has a similar type of presentation to the BVVL syndrome except that MMND occurred in a sporadic way and has a more benign clinical course while the BVVL syndrome has evidence of hereditary transmission and BVVL is a severe and often fatal disorder.[2]

CASE REPORT

A 14 year old girl from Andhra Pradesh presented to the hospital with c/o progressive bilateral hearing loss, motor weakness, wasting and hand-clawing in the upper extremities. The deafness and limb weakness were of insidious onset, progressing over a period of approximately 2 years. Her writing deteriorated and she developed difficulty in mixing her food and holding objects. She developed difficulty in swallowing in the last one month, more to liquids compared to solids. She was born to a 2nd degree consanguineous marriage, her parents and younger sister were normal but according to the patient's mother, the patient's maternal aunt developed deafness, weakness, difficulty in swallowing in her 2nd decade and died of a respiratory infection 4-5 years after she first developed neurological complaints.

The patient's higher mental functions were normal, she had dysarthria on examination. On cranial nerves examination her pupils were equal sized and reacting to

light and fundus was normal. Patient had a brisk jaw jerk, there was bilateral facial muscle weakness, (Figure 2, 3) bilateral sensorineural deafness, decreased gag reflex, fasciculation and atrophy of the tongue. There was bilateral symmetrical distal muscle weakness (3/5) with wasting of the small hand muscles (Figure 1). There was weakness of the trunk and leg muscles, but bulk of the leg muscles was normal. The tendon reflexes in the upper limbs and lower limbs were feeble. The plantar responses were flexor. The sensory and cerebellar examination was normal. She had a high stepping gait and was unable to do tandem walking.

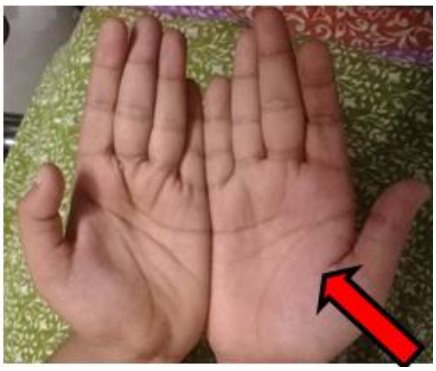

Figure 1: B/L thenar and hypothenar wasting.

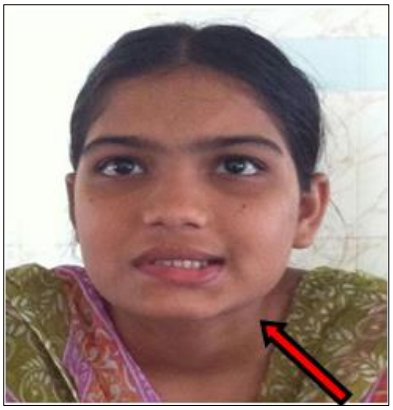

Figure 2: Mouth deviated to left.

Figure 3: Unable to close eyes completely.

Patient's haematological and biochemical parameters including thyroid profile, CK, LDH were normal, her CSF analysis showed slightly elevated proteins with normal glucose and cell count. Her ECG and 2D echo were normal. Her pure tone audiometry testing showed B/L severe sensorineural hearing loss. Her MRI- brain and cervical spine MRI showed a normal study (Figure 4, 5). Her nerve conduction studies showed reduced compound motor action potential for median, ulnar and distal nerves. There was a mild delay in the motor conduction velocities but her sensory nerve conduction velocities were normal. Respiratory function test could not be assessed because of the patient's inability which shows a possible reduced vital capacity. A provisional diagnosis of Brown Vialetto Van Laerre was made and the patient was started on oral Riboflavin 10 mg/kg/day and gradually within weeks patient's hearing and power in the limbs improved considerably, patient's ability to do her daily activities without any support was restored.

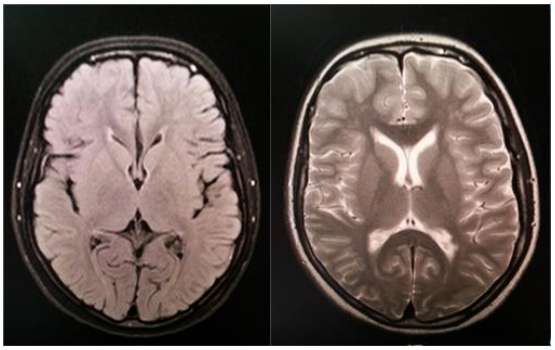

Figure 4: MRI brain T2W & T2W flair.

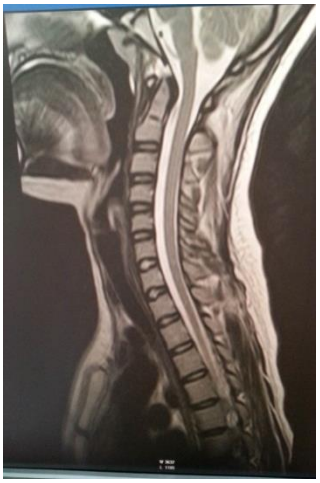

Figure 5: MRI cervical spine.

DISCUSSION

It would be unrealistic to diagnose a case as BVVL when the patient initially presents with bilateral sensorineural hearing loss, the involvement of the other lower cranial nerves in conjunction with limb weakness would likely point the diagnosis to BVVL. Sathasivam provided a

diagnostic algorithm to aid in the diagnosis of this rare neurological disorder (Figure 6).[1] The closest related entity to our case of progressive bulbar paralysis would be the Fazio-Londe syndrome but the presence of sensorineural deafness rules out this entity. The juvenile age of presentation and lack of UMN limb signs is against the diagnosis of Amyotrophic lateral sclerosis although they have been a few cases of juvenile onset ALS.[3]

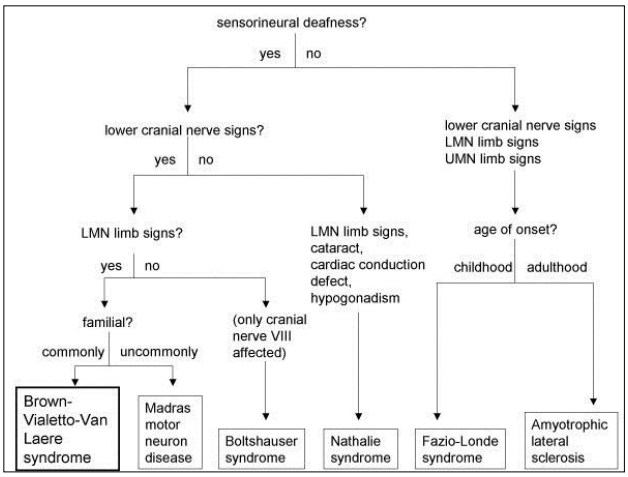

Figure 6: Diagnostic algorithm to aid in the diagnosis of rare neurological disorder provided by Sathasivam.

One more rare condition matched to our case is the Nathalie syndrome which has bilateral hearing loss, LMN limb signs in conjunction with hypogonadism, cataracts, cardiac conduction abnormalities, the lack of these abnormalities rules out this syndrome in our patient.

The juvenile onset bulbospinal muscular atrophy associated with deafness is closely related to Madras Motor Neuron Disease (MMND). The clinical features between the two syndromes resemble each other so much that it was postulated by Summers that they are related.[4] However, there are a few subtle differences between the two entities, MMND has a male predominance compared to the BVVL syndrome which has a female predominance.[5] MMND is mostly a sporadic disease which is limited to parts of Southern India but 15% of the MMND can have a familial inheritance compared to the BVVL syndrome which demonstrate autosomal recessive inheritance, although autosomal dominant and X-linked inheritance have been suggested in a few families.[5,6] MMND is considered a benign disease compared to the BVVL syndrome which has a downhill course and often fatal when left untreated.[2]

The interesting aspect in our case is that the patient is from Southern India where the MMND manifests, but the history of similar complaints which were progressive and ultimately resulted in death of the patient's maternal aunt made us think we might be dealing with a case of BVVL syndrome. The patient being a female and the rapidity of progression of symptoms consolidated our diagnosis. In 2010 Green et al. demonstrated that in some patients the disease is caused by mutations in the SLC52A3 gene, Bosch et al. demonstrated that this gene encodes the intestinal (hRFT2) riboflavin transporter and that in these patients riboflavin deficiency is the cause of the BVVL/FL syndrome.[7-10] A review of literature showed that riboflavin supplementation proved to be a life-saving treatment in 8 of the 13 patients treated with it.[2] We started the patient on 10 mg/kg/day of riboflavin and there has been a considerable improvement in the patient's motor activity and marked improvement in her hearing.

CONCLUSION

We conclude that when there is a dilemma if the case is MMND or BVVL syndrome due to the unavailability of genetic testing, the sex of the patient, presence of family history and rapidity of progression of symptoms helps in the diagnosis of BVVL syndrome and the patient can be started on riboflavin supplementation to see if there is a clinical improvement.

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