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Van der Knaap syndrome, a case from West Bengal, India

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Abstract

Leucodystrophies are a group of white matter diseases caused by an abnormality in the formation or maintenance of one or more components of the myelin sheath. The devastating course of the disease coupled with the lack of any definitive treatment render them potentially fatal and incurable. Van der Knaap Syndrome, also known as megaloencephalic leucoencephalopathy with subcortical cyst, is a relatively new and rare entity. Although reported sporadically from Europe, Asia and the Agarwal community in India, there is practically no case report from the eastern part of India. We present a case of van der Knaap syndrome in an adult female with some atypical features.

INTRODUCTION

Leucodystrphies are rare, relentlessly progressive, chronic diseases with varied clinical manifestations and mostly affect children. Among them, Van der Knaap syndrome usually presents during the first decade of life with enlarged head, motor disabilities, seizures, learning difficulty and mental function deterioration. We are reporting a patient of this syndrome presenting first time at the age of 35 years from West Bengal, a state of eastern India. .

CASE REPORT

A 35 year old nondiabetic, nonhypertensive Hindu female born out of nonconsanguinous marriage was admitted on 24th of February, 2009 following an episode of generalized convulsion. She had a large head since birth compared to others of her age. Although her birth and developmental histories were normal, she showed learning problem since 9 years of age and hearing difficulty since 12 years of age. There was no history of fever, jaundice, skin rash, photosensitivity, sensory loss, trauma, intake of drugs, toxin exposure or similar illness in the past. Among her 3 brothers and 4 sisters, her younger sister had an enlarged head, mental retardation and difficulty in walking. General physical examination was normal except for an enlarged head (head circumference 58 cm). Mini Mental Status Examination score was 18. She had normal speech, fundi, spine, and neck height ratio. There was bilateral sensori-neural deafness. Power was 4/5 with spasticity in all 4 limbs. Deep tendon reflexes were exaggerated with bilateral extensor plantar, without any wasting or fasciculation. There was no sensory or cerebeller involvement. Gait was spastic. Other systems examination revealed no abnormality. Figure 1 showed the patient with enlarged head.

Routine blood biochemistry, chest x-ray, ECG and ultrasound of the abdomen were normal. ELISA for HIV was nonreactive. The CSF study including adenosine deaminase value was normal. There was no oligoclonal band. Titres for HSV, Japanese B and Chikungunya were negative. Electroencephalography of the brain, nerve conduction study and electromyography of all 4 limbs were normal. Visual evoked potential showed delayed P100 latencies with normal to slightly low amplitudes in the eyes suggestive of bilateral demyelinating anterior visual pathway dysfunction. Brainstem evoked response revealed bilateral sensorineural deafness.

MRI showed extensive symmetrical white matter changes appearing as hypointensity on T1 and hyperintensity on T2 and FLAIR images, associated with subcortical cysts in the fronto-temporal region with diffuse cortical atrophy and small hemorrhage in left frontal region (which may be due to her fall during convulsion). MR spectroscopy showed NAA/Creatine ratio of 1.38 and Choline/Creatine ratio of 1.26. Figure 2 shows the MRI & MR spectroscopy of brain.

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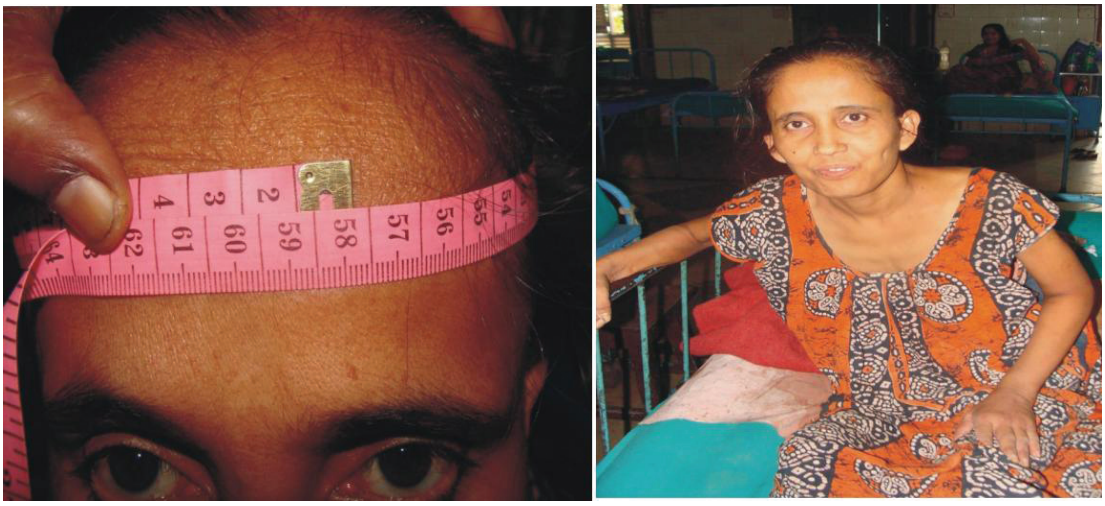

Figure 1. Picture of patient showing enlarged head

DISCUSSION

Van der Knaap syndrome is an autosomal recessive disorder with mutation of the MLCI genes in some patients, causing defect in the myelin formation or maintenance. Although scattered neuropathological cases[1-,3] were reported in the 1960's, it was in the 1990's that the disease was recognized as a distinct clinical entity.[4-6] Classical signs of the disease, appearing any time between birth and 10 years of age, include an abnormally enlarged head appearing in infancy, learning difficulties, spasticity, ataxia and seizures. The

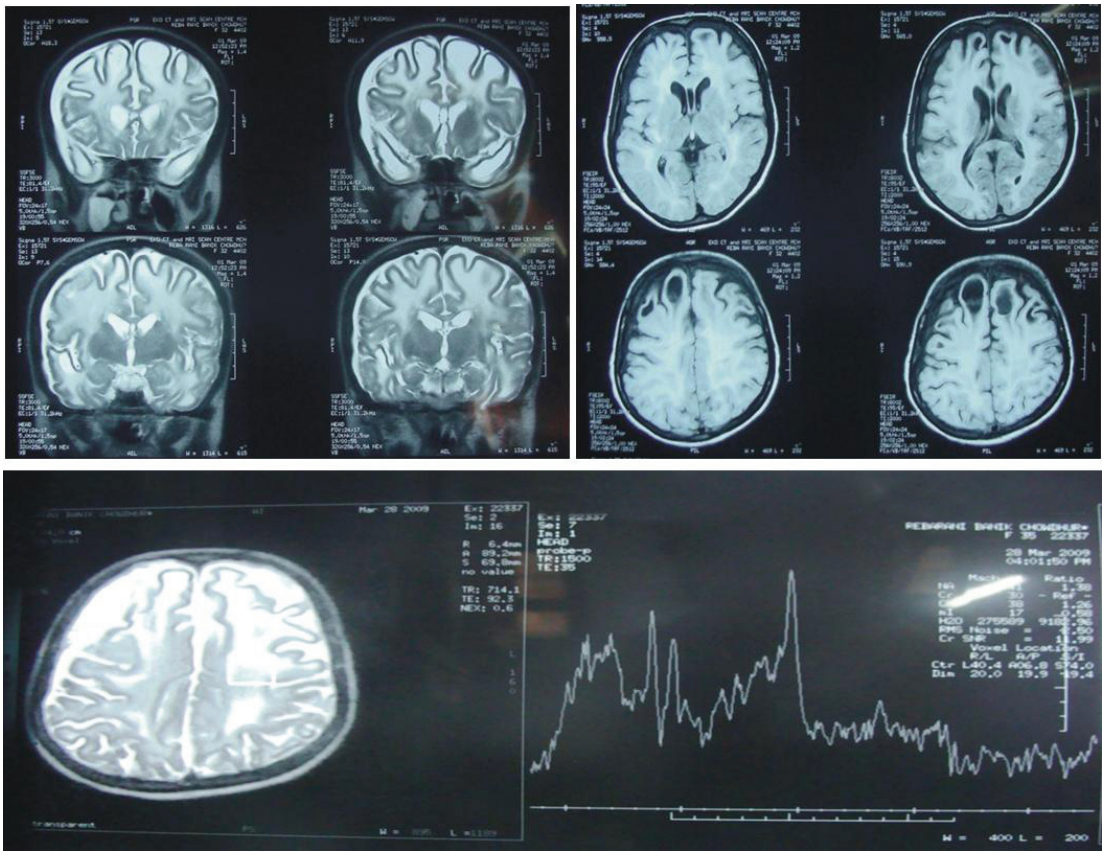

Figure 2: MRI of brain showing extensive bilateral white matter change with subcortical cysts and MR spectroscopy

hallmark imaging finding is that of the brain MRI showing megaloencephaly, extensive symmetrical white matter changes with subcortical cysts. The differential diagnoses we considered included Canavan's disease, Alexander's disease, glutaric aciduria type 1 and Tay - Sach's disease. The unique MRI finding in our patient favours the diagnosis of van der Knaap syndrome. Moreover, survival till third decade is almost impossible in these diseases.

The first case in India was reported by Singhal *et al*[7] in 1996. They found that 26 out of their 30 patients belonged to the Agarwal community of northern India. Most frequent clinical features were seizure, large head, mild to moderate cognitive defect, pyramidal signs and cerebellar signs with a protracted clinical course. Only 1 patient had visual impairment with optic atrophy. The age of onset of symptoms varied from birth to 27 years. In 2003, a case series report by Singhal *et al*[8], found 63 Agarwal patients out of 70. Our patient comes from West Bengal, a state of eastern India. Sensori-neural deafness and anterior visual pathway involvement are uncommon features in this disease. But our patient had both these features. Another interesting feature was in spite of extensive MRI change, she presented first time with seizure at the age of 35 years.

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