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Case Report

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Canavan disease: a rare case report

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ABSTRACT

Canavan disease is a very rare, fatal, autosomal recessive neurodegenerative disorder. It usually manifests during infancy. Mutations in the aspartoacylase (ASPA) gene (17p13.3), which code for the aspartoacylase enzyme, cause this disease. It is a leukodystrophy and affects white matter of the brain. This disease is associated with deficiency of an essential enzyme, aspartoacylase. The deficiency leads to loss of white matter in brain, leading to defective transmission of nerve signals. This disorder affects all ethnic groups, but occurs with greater frequency, in individuals of Ashkenazi Jewish descent.

Keywords: Autosomal recessive, Leukodystrophy, Aspartoacylase, N-acetyl-L-aspartic acid

INTRODUCTION

The disease occurs worldwide and the incidence of severe Canavan disease in the non-Jewish population is approximately 1:100,000 births. When both the parents are of Ashkenazi Jewish descent, the incidence is 1:6,400 to 1:13,500 births.[1,2] The clinical features in Canavan disease, varies between severe forms with leukodystrophy, macrocephaly and severe developmental delay, to a very rare mild/juvenile form characterized by mild developmental delay. These two forms of this disease are clinically indistinguishable.[3-5] Patients with severe form of the disease have severe hypotonia, developmental delay and other neurologic impairments, and a very high N-acetyl-L-aspartic acid (NAA) concentration in urine, blood and cerebrospinal fluid. The milder forms of Canavan disease, presents with mild developmental delay, speech defects or achievement at school. The urine NAA may be slightly elevated.

CASE REPORT

This female child four years old Hindu girl presented to us at rural tertiary care center in south west Bihar at Narayan Medical College and Hospital. She was 3rd in birth order, born out of a non-consanguineous marriage, at term after an uneventful pregnancy with normal vaginal delivery. She was brought to emergency in a state of status epilepticus. She had grossly delayed developmental milestones in all domains. The family history revealed that elder male sibling was also diagnosed with Canavan disease, and died at four and half years of age. She had two elder siblings. One elder sibling was 15 years old, alive and healthy.

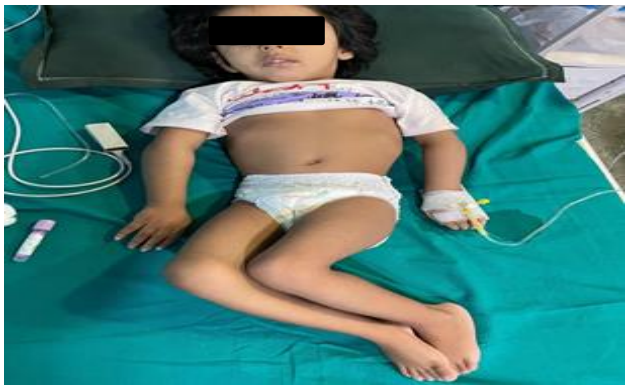

Figure 1: Child having multiple contractures at knee and ankle joint and large head.

On examination, head circumference was 52.5 cm, and consistent with macrocephaly for the age. Child had pallor and was febrile, vitals were stable. Both the pupils were equal and reacting to light. The central nervous system (CNS) examination revealed generalized spasticity with brisk deep tendon reflexes. She had horizontal nystagmus with marked contractures involving both knees and ankles in both upper and lower limbs (Figure 1). The chest and abdominal examination were unremarkable.

MRI investigations revealed symmetric hyper intensities in bilateral fronto-parietal and parieto-occipital white matter, posterior limb of internal capsule, bilateral basal ganglia and parts of thalami on T2 sequencing.

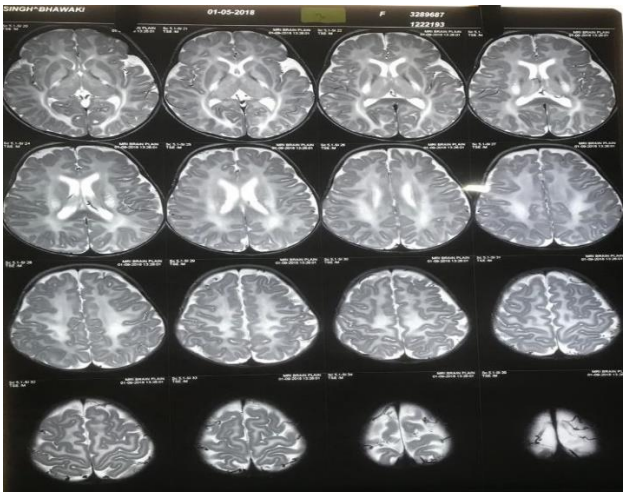

Figure 2: Symmetric hyper intensities in bilateral fronto-parietal and parieto-occipital white matter, posterior limb of internal capsule, bilateral basal ganglia and parts of thalami on T2 sequencing.

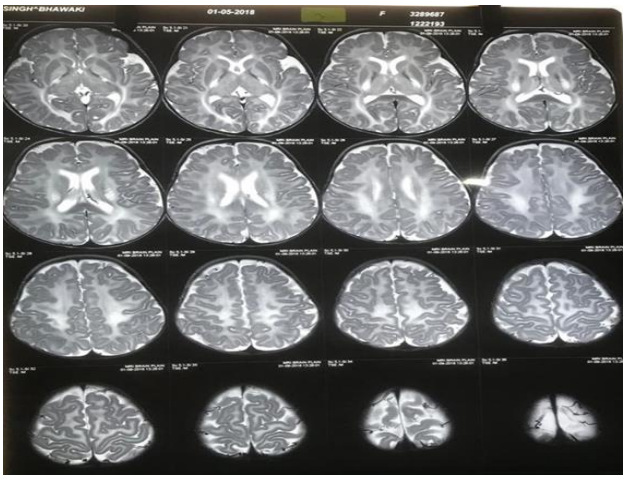

Figure 3: MRI brain showing hypo intensities on T1 sequences involving posterior parieto-occipital and adjacent temporal white matter, as well as high frontoparietal white matter, posterior limbs of both the internal capsules, bilateral globus and the thalami, extending into the brain stem, bilateral deep cerebellar white matter involving dentate nuclei.

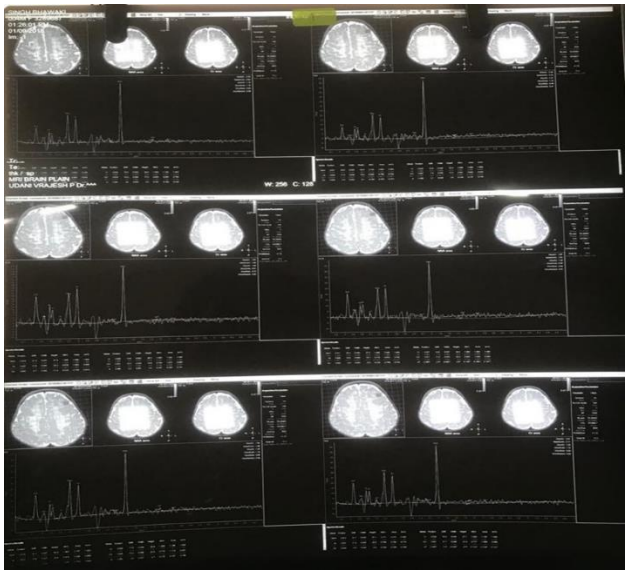

Figure 4: MR spectroscopy – large NAA peak is noted within many voxels throughout, more prominent in basal ganglia regions. The above findings are consistent with a metabolic disorder like Canavan disease.

DISCUSSION

In previous case reports, Irilouzadian et al reported a case of 14-month-old female patient who had regression of acquired milestones.[2,3] Her brain MRI reported diffuse white matter T2 hyper-intensity and T1 hypo-intensity in the periventricular, juxta-cortical, and subcortical white matter with posterior brain stem, putamen, bilateral thalami, and cerebellum white matter involvement.[2,4] In our case study, internal capsule was also involved.

Sunuwar et al had reported a case of 12-year-old girl presented with spasticity in bilateral lower limb and seizure disorder. The child had progressive psychomotor retardation, cerebellar signs, pyramidal signs, and relative megalencephaly. By the age of two years and three months, she developed head lag, macrocephaly, and hypotonia of bilateral lower and upper limbs. MRI revealed diffuse white matter changes, hypointense on T1 and hyperintense on T2, there were hyperintense signal changes in bilateral globus pallidus and anterolateral part of thalami with involvement of corpus callosum. Dilation of ventricles was also noted, and MRS showed characteristic N-acetyl-aspartate peaks suggestive of Canavan disease.[3,4]

Daraz et al reported a case of 6 months old, male infant, initially infant washaving feeding difficulties, later she developed seizure and delayed development of milestones with hypotonia.[4,5] MRI brain revealed diffuse, symmetrical white matter degeneration in the subcorticalareas, with bilateral involvement of the globus pallidus. Gas chromatography and mass spectroscopy showed increased acid N-acetyl-aspartate which

confirmed the diagnosis.[6,7] In this child there is involvement of internal capsule, thalami and cerebellum.

CONCLUSION

It is important to recognize this disease to prevent recurrence in a family, given its devastating course and non-availability of treatment. The chance of having an affected child is 25% as it is an autosomal recessive disorder. Genetic counseling and genetic testing are recommended for parents to prevent the inheritance in subsequent pregnancies. Management of these children is a nightmare most of the severe form of the disease is fatal. Management of children suffering from Canavan disease requires a team approach including pediatric neurophysician, developmental pediatrician, orthopedician, physiotherapist, occupational therapist and social worker. The main therapy is replacement of the enzyme aspartoacylase, appropriate anticonvulsants and good nutrition along with regular physiotherapy.

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