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CASE REPORT

Joubert Syndrome: A Case Report

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Abstract

Joubert syndrome (JS) is a relatively uncommon, genetic, autosomal recessive disorder. It has varied neurological manifestations like hypotonia, ataxia, global developmental delay, cognitive disability, abnormal eye movements, and abnormal neonatal breathing patterns. This case report aims to highlight the benefits of early identification and early timely intervention, which should be undertaken by a multidisciplinary rehabilitation team to treat patients of JS.

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Introduction

Joubert syndrome (JS) is a relatively uncommon, genetic, autosomal recessive disorder. This syndrome was first brought to notice in 1968.[1] It has varied neurological manifestations like hypotonia, ataxia, global developmental delay, cognitive disability, abnormal eye movements, and abnormal neonatal breathing patterns.[2] Molar tooth sign (MTS) and bat-wing appearance of the fourth ventricle, on axial magnetic resonance imaging of the brain are pathognomonic and diagnostic of JS.[2,3]

The prevalence of JS is 1:80,000 to 100,000 live births on review of literature. The number of case reports in the literature is small and hence the prevalence is underestimated.[3,4]

JS is difficult to diagnose at an early stage. It usually presents as a global developmental delay in most of the cases. It may not be diagnosed in the initial period, however, the presence of hypotonia, delayed developmental milestones, and respiratory distress may raise the possibility of JS. Radiological findings along with the clinical features and genetic study confirm the diagnosis of JS. Most children with this syndrome can reach up to adulthood. Early detection along with early multidisciplinary intervention, medical management and rehabilitation can simulate brain growth which is good for a better prognosis.

Case Report

A 12 months old male baby, was admitted to the paediatric department at a tertiary care centre with main complaints of inability to hold neck properly

along with floppiness of body, and inability to sit without support. The baby was first born to 3° consanguineous marriage without any significant antenatal history. The delivery was a full-term, normal vaginal, with breech presentation at the hospital. The baby cried soon after birth, after physical stimulation and weighted 2 kgs. The postnatal period was uneventful. On examination baby had pallor, hypotonia with minimal dysmorphism i.e. had a persistently open mouth with an arched upper lip. The infant had a perineal rash due to prolonged use of diaper and did not have any neurocutaneous markers. Investigations like ultrasound abdomen, eye examination, and laboratory investigations which included complete blood count, blood sugar, electrolytes, C- reactive protein, liver enzymes, urea and creatinine, TSH, free T4 and T3, were all within normal limits.

The brain MRI finding showed "Molar tooth sign" (Figure 1) which helped in the diagnosis of JS.

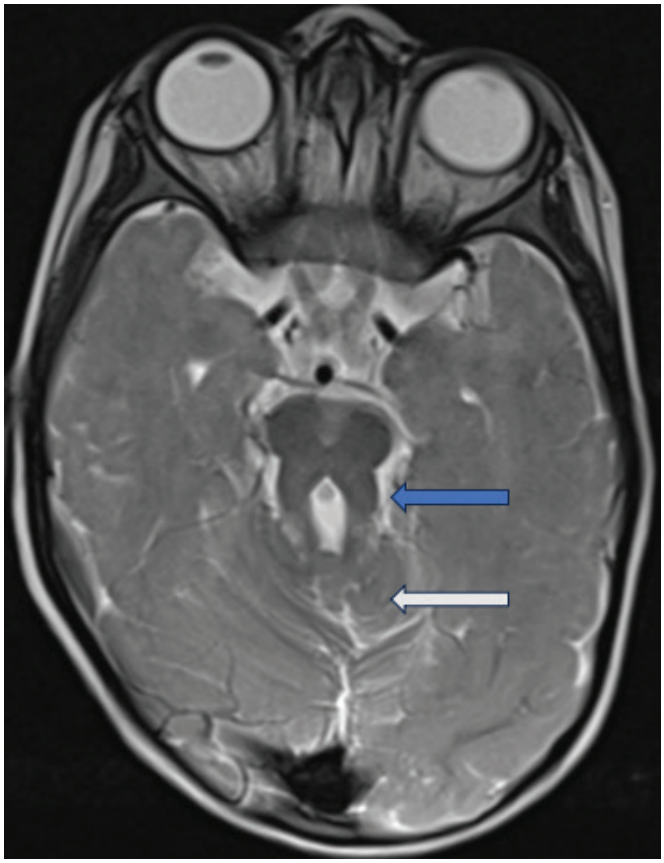

Figure 1: Axial T2W MR image showing thickened and elongated superior cerebellar peduncles - molar tooth appearance (blue arrow) and hypoplastic cerebellar vermis (white arrow).

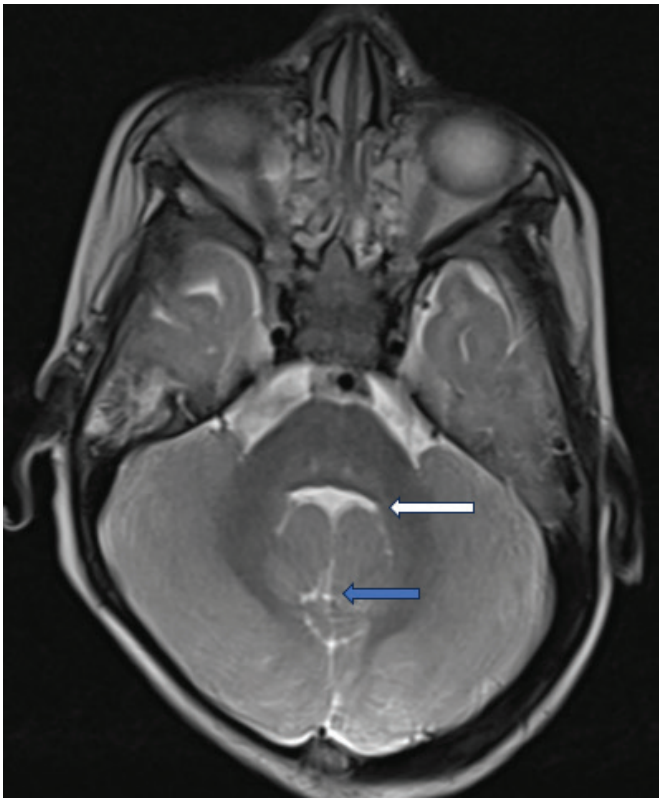

Figure 2: Axial T2W MR image showing median vermian cleft (blue arrow) and batwing appearance of fourth ventricle (white arrow).

The superior cerebellar peduncles were elongated and thickened along with widened interpeduncular fossa and hypoplastic cerebellar vermis (Figure 1). The midline cleft with the deformed contour of the fourth ventricle resembled a "Batwing appearance" (Figure 2).

Next-generation sequencing (NGS) of genes, revealed a pair of homozygous mutations in 2 genes (CEP41 and TMEM 138) which was consistent with the JS. However, this variation is reported as a variant of uncertain significance due to limited literature availability.

Discussion

JS is a rare autosomal recessive, heterogeneously inherited, congenital disorder. It is associated with agenesis of cerebellar vermis. There is failure of decussation of neural fibre in the superior cerebellar peduncles and the pyramidal tracts.[5] The thickened superior cerebellar peduncle runs a more horizontal course between the brainstem and the cerebellum. These findings appear like the MTS in the MRI. There

is a batwing appearance of the fourth ventricle on imaging. These typical MRI findings along with clinical features are characteristic of JS.

Classification of JS: There are six subtypes -

(1) Pure JS
(2) JS with ocular defect (JS-O)
(3) JS with renal defect (JS-R)
(4) JS with oculo-renal defects (JS-OR)
(5) JS with hepatic defect (JSH) and
(6) JS with Oro-fascio-digital JS defects.

Oculomotor apraxia is a common finding which is an abnormality of voluntary conjugate eye movements due to impairment of planning and organization of eye movements. The commonest eye movement abnormality in JSRD is saccades, where, the eyes rapidly change fixation from one target to another.[6]

Other systemic involvement with JS can be varied, such as coloboma, retinal dysplasia, multi-cystic dysplastic kidney, hepatic fibrosis and polydactyly.[7]

Hypotonia, global developmental delay with or without cognitive impairment, abnormal breathing patterns and abnormal eye movements (nystagmus), are the most important clinical signs and symptoms in JS. MR findings, as described in our case, are diagnostic.

Genetic counselling is recommended and is one of the most important measures to prevent and confirm JS. Prenatal diagnosis of JS can be done by chorionic villus sampling, at about 11 weeks of gestation and also by foetal ultrasound. Foetal ultrasound may show increased nuchal translucency in high-risk pregnancies.

The overall prognosis in JS is not so good. The survival rate is about 50%, at 5 years of age. There is severe cognitive and motor impairment which can lead to developmental delay. Death in these cases is usually due to feeding difficulties mainly due to aspiration and repeated chest infections.[8] The recurrence rate in future pregnancies is around 25%. The outcome in cases of JS can be better if it is diagnosed early in infancy. Early and timely interventions through a multidisciplinary approach which includes physical therapy, special education, occupational, and speech therapy, can lead to a relatively better prognosis.

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