Joubert Syndrome – A Case Report with Classical MRI Features

Sumantro Mondal, Sumit Chakrabarty[1], Debanjali Sinha, Tony Ete, Arijit Nag, Atanu Chakraborty, Amod Prasad[2]

Departments of Medicine, [1]Radiology and Imaging, Institute of Post Graduate Medical Education and Research, [2]R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India

Correspondence: Dr. Sumantro Mondal, Doctor's Hostel. 242 A, J. C Bose Road, Kolkata - 700 020, West Bengal, India. E-mail: drmsumantro@gmail.com

ABSTRACT

Joubert syndrome a rare disorder characterized by malformation of the mid- and hindbrain. Here we report a classical case of Joubert syndrome in a 2-year-old boy who presented with respiratory irregularities, hypotonia, and developmental delays. Magnetic Resonance Imaging (MRI) of the brain showed the "molar tooth sign" with "bat wing" appearance of fourth ventricle.

Key words: India; Joubert syndrome; molar tooth sign

Introduction

Joubert syndrome (JS) is a rare autosomal recessive disorder classically manifested by hypotonia, impaired motor development, oculomotor apraxia, and breathing abnormalities. Wider spectrum of anomalies involving eye, kidney, and liver characterize the term Joubert syndrome and related disorder (JSRD). The primary anatomic defect is a congenital malformation of mid- and hindbrain. In axial magnetic resonance imaging (MRI) of brain, these anomalies produce the characteristic "molar tooth sign" (MTS), which is an essential component for diagnosis of JS and JSRD. We report a case of JS along with its classical neuroimaging features.

Case Report

A 2-year-old boy was taken to the emergency department with sudden onset tachypnea. The boy has a history of similar episodes of respiratory irregularities in the past along with flabbiness and developmental delays. His birth history was normal with a full term normal delivery and a birth weight of 2.4 kg. His early postnatal period was uneventful apart from occasional episodes of irregular respiration with spontaneous correction. As his age increased, his family members noticed delay in developmental milestones, both motor and intellectual. Examination revealed gross hypotonia. There was also inability to follow moving objects, a finding known as oculomotor apraxia. His intellectual development was also sub normal for his age. A clinical impression of JS was considered based on these presentation and clinical findings. MRI of the brain was advised to confirm or rule out this disorder. MRI of the brain was performed with a 3 Tesla GE machine. Axial T2-weighted MRI of the brain at the level of midbrain showed thinning of midbrain with deepened inter peduncular fossa along with thickened superior cerebellar peduncle – the "MTS" [Figure 1]. Vermian agenesis with "bat wing" shaped fourth ventricle was also noted in axial FLAIR sequence [Figure 2]. Rest of the cerebellar hemisphere, supra tentorial structures, and ventricular systems were normal. Characteristic MRI features including the classical "MTS" established the final diagnosis of JS.

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Discussion

JS is an autosomal recessive disorder. It was first described in four siblings with features of oculomotor apraxia, episodic hyperapnea, ataxia, and cognitive impairment.[1] The disease is very rare with a prevalence of 1 in 100,000.[2] This disorder is characterized by specific congenital malformation of the hindbrain and other phenotypic findings. In our patient, the phenotypic features were very similar to JS and later on characteristic hindbrain malformations were observed in neuroimaging. A defect in the structure or function of cilium is the pathogenic basis of JS as all the culprit six genes identified till date regulate the function of primary cilium.[3] AH1 gene is one of the identified gene, which encodes

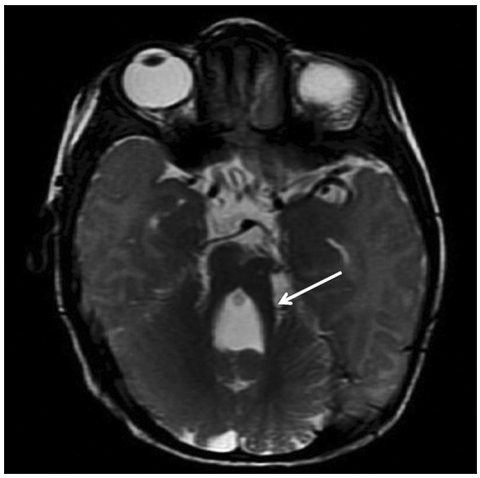

Figure 1: Axial T2-weighted MRI of brain at the level of midbrain showing the "molar tooth sign" (White arrow)

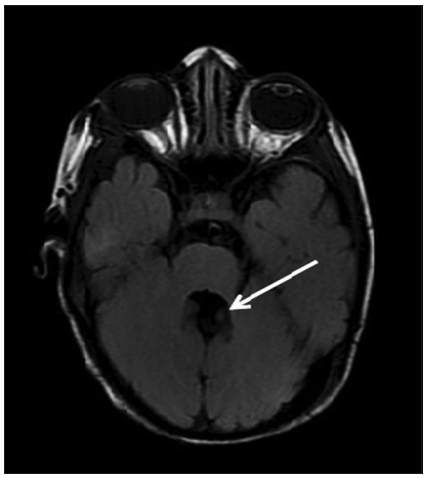

Figure 2: Axial FLAIR MRI of brain at the level of fourth ventricle showing "bat wing" appearance (White arrow)

Jouberin protein. This gene is required for cerebellar and cortical development in humans. Mutation of AH1 gene has been found in a subset of JS patients.[4]

Classic JS consists of (1) The MTS on axial cranial MRI, (2) decreased muscle tone, (3) intellectual impairment or developmental delay, (4) one or both of the following (supportive): Irregular breathing pattern in infancy and abnormal eye movements (oculomotor apraxia, nystagmus). In our patient, all of these features of classic JS was present. Other features like facial dysmorphism (ptosis, hypertelorism, and broad forehead) may also be present.[3] Polydactyly may be seen in some patients.[5] Currently, wider spectrum of involvement of other organs characterizes a new entity known as JSRD. JSRD includes other central nervous system features (callosal agenesis and occipital encephalocele), ocular coloboma, cystic dysplasia of kidney, nephronophthisis and hepatic fibrosis. Combination of various organ involvements is known as various syndromes. In cerebello-oculo-renal syndromes (CORS), ocular and renal systems are involved and another syndrome better known by its acronym is COACH syndrome (Coloboma, Oligophrenia/developmental delay, Ataxia, Cerebellar vermis hypoplasia, Hepatic fibrosis).[6] In this case, facial dysmorphism or polydactyly was absent and there was no evidence of renal or hepatic involvement. The disease presents with varying degree of clinical features and organ involvement, so the disease outcome also varies from patient to patient. Most of the infants and children of JS survive the neonatal period and there may be improvement in muscle tone, respiratory function, and feeding behaviors.

MRI of brain renders an important position in diagnosis of JS and JSRD. The "MTS" in MRI is an essential component of the diagnostic criteria of JS. This sign is seen in the axial MRI of brain at the level of midbrain. The mechanism of genesis of this sign is due to lack of decussation of fibers of superior cerebellar peduncle, which leads to peduncular enlargement. Additionally, the peduncles follow a more horizontal course. Lack of crossing fibers reduces the anterior posterior diameter of the midbrain and deepens the interpeduncular fossa.[7] In our patient, the horizontal orientation of cerebellar peduncle and deepening of interpeduncular fossa was clearly evident in brain MRI. In a patient with JS, thickening and reorientation of the superior cerebellar peduncles, vermian hypoplasia, and fourth ventricle deformity are the primary neuroimaging findings and these features are seen in almost all cases.[8] "MTS", the pathognomonic feature of JS is seen in up to 85% of patients.[9] Indeed "MTS" is an important criteria for the diagnosis of classic JS. Presence of this MRI feature in our patient consolidated the diagnosis of JS. Vermian agenesis produces a midline cleft between the cerebellar hemispheres, resulting in a "bat wing" appearance of the fourth ventricle on axial MRI images.[10] In addition to "MTS", Vermian agenesis was also evident in our patient. Poretti *et al*. found marked infra tentorial abnormalities in patients of JS. In all the patients, verminal remnants were dysplastic with enlarged, distorted fourth ventricle. Marked verminan hypoplasia was observed in 53% of patients. Hippocampal malrotation, corpus callosal dysgenesis, and absent septum pellucidum were the supra tentorial findings.[11]

In this patient, the clinical features were highly suggestive of JS and the classical MRI of brain features confirmed the final diagnosis. This report is concerned with the description of a rare disease entity along with its classical MRI features.

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