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# Joubert Syndrome and Related Disorders (JSRD) with Molar Tooth Sign -A Case Report

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**Abstract:** Joubert syndrome and related disorders (JSRD) are group of multiple congenital anomalies syndrome with the characteristic molar tooth sign, a midbrain-hindbrain malformation visible on brain imaging. Since it has variable phenotypes it is difficult to diagnose clinically and thus underreported. Awareness needs to be created among clinicians for its early diagnosis .We report JSRD in a10 year old male child.
**Keywords:** Joubert syndrome, molar tooth sign, brain imaging, midbrain – hindbrain malformation.

## INTRODUCTION

Joubert Syndrome and Related Disorders (JSRD) are group of disorders which are genetically and clinically heterogeneous with varied multi organ involvement mainly retina, kidneys, liver and skeleton. They follow autosomal recessive inheritance with the exception of rare X-linked recessive cases [1]. In JSRD , neuroradiological finding of Molar Tooth Sign (MTS) is obligatory [2,3].Presence of abnormally deep interpeduncular fossa ; elongated, thick, and mal-oriented superior cerebellar peduncles; and absent or hypoplastic cerebellar vermis gives the appearance of a "molar tooth" on axial brain MRI through the junction of the midbrain and hindbrain (isthmus region)[4].Cardinal neurological signs of JSRD are hypotonia evolving to ataxia, developmental delay, ocular motor apraxia, and breathing dysregulation which are present from the neonatal period. The exact diagnosis is often not made for several years after birth. This clinical entity is underreported with a prevalence of less than 1 in 100,000. Only about 200 cases have been reported worldwide [5].The average age at diagnosis is 33 months [6].

## CASE REPORT

A 10 years old male child presented to Pediatric outpatient clinic with abnormal eye movements, unsteady gait and developmental delay. The child was delivered at term gestation out of a product of a first degree consanguineous marriage and was first in birth order. Within few days after birth the child had episodic rapid movements of the eye balls with deviations to lateral extremes of gaze which were present throughout the day. The child was unable to visually fixate and follow objects. There was history of breathing problems in infancy in the form of episodic tachypnea. No treatment was taken for the same and the child gradually outgrew this problem .There is no history of seizures or feeding difficulty in the past. His development quotient corresponded to 5 years of age. The child had flat forehead, hyperteleorism (fig-1) and retractile testes with no neurocutaneous markers .On anthropometry, height was 121 cm (<3$^{rd}$percentile), weight 25 kg (3$^{rd}$percentile) and head circumference 53.5 cm (50$^{th}$percentile), BMI was 17( 50$^{th}$percentile) according to the WHO growth charts. On examination ataxic gait was present with normal reflexes .The cranial nerves and other systemic examination was also normal. On Ophthalmic evaluation, the child had decreased visual acuity in both eyes. There was bilateral macular dystrophy and choroidemia suggestive of retinal involvement.

Complete haemogram, renal function tests, serum electrolytes, liver function tests, urine osmolality (earliest marker of nephronophtisis), ultrasonography of abdomen were normal. T2 weighted axial images revealed deepened inter peduncular fossa with elongated superior cerebellar peduncles oriented perpendicular to pons, hypoplastic vermis with prominent cerebellar follicles giving a molar tooth appearance suggestive of Joubert Syndrome (fig-2).

**Figure 1: Child showing flat forehead, hyperteleorism, wide based gait**

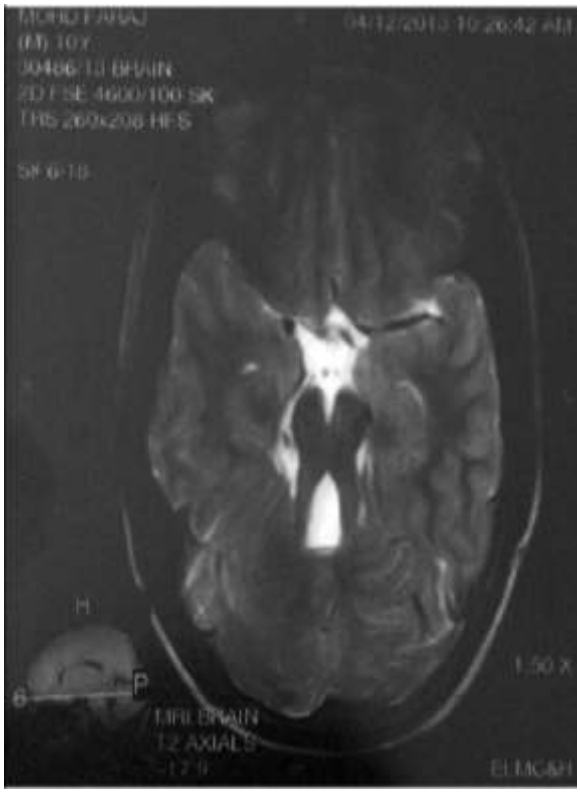

**Figure 2: T2 Weighted Axial Image showing molar tooth sign**

Supportive therapy was started and the patient was referred to the opthalmology department for management of visual impairment.Need of regular follow ups was stressed so as to identify early renal or hepatic involvement.

## DISCUSSION

JSRD are classified in six phenotypic subgroups: Pure JS; JS with ocular defect; JS with renal defect; JS with oculorenal defects; JS with hepatic defect and JS with orofaciodigital defects [7]. Pure Joubert syndrome has three primary diagnostic criteria (a) The molar tooth sign (b) Hypotonia in infancy with later development of ataxia (c) Developmental delays/intellectual disability [3].

These findings are accompanied by episodic tachypnea or apnea and/or atypical eye movements, breathing abnormalities, which improve with age. Our patient had all the above features with a history of breathing abnormalities in infancy. In JSRD, retina is one of the organs most frequently involved in the form of retinal dystrophy, due to progressive degeneration of photoreceptor cells. The clinical spectrum can range from congenital retinal blindness (Leber congenital amaurosis (LCA) to retinal dystrophy [8] .Ocular Colobomas may be present can be unilateral or bilateral, and mostly affect the posterior segment of the eye [2].

Our patient did not have coloboma and had retinal disease on opthalmological examination.He had features of Classic JS with ocular defects.

Being an autosomal recessive inheritance, risk of JSRD for a couple with an affected child is 25% i.e. one in four. Prenatal diagnosis is feasible through chorionic villus sampling. In at-risk pregnancies, fetal ultrasound may detect hypoplasia of the cerebellar vermis. Recently, fetal MRI has been acknowledged as the method of choice to delineate posterior fossa malformations, facilitating the diagnosis of the disease before 24 weeks of gestation [8].

Cerebellar vermin anomalies are reported with other disorders, such as the Dandy-Walker syndrome and rhomboence- phalosynapsis. In the Dandy-Walker syndrome, a large cystic abnormality of the posterior fossa is seen and the cerebellar hemispheres are fused in rhomboence- phalosynapsis, [9, 10].hence can be easily distinguished from Joubert syndrome.

Rehabilitation strategies must be planned for cognitive and visual impairment. Retinal impairment is progressive in nature and renal and hepatic

complications are a major cause of death in JSRD patients hence should be timely diagnosed and managed .Our patient did not have renal and hepatic involvement at present hence need for regular follow-ups were stressed.

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