Case Report

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Joubert Syndrome: A Rare Case Highlighting the Significance of the Molar Tooth Sign

Radiology Section

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ABSTRACT

Joubert Syndrome (JS) is a rare autosomal recessive neurodevelopmental disorder characterised by malformation of the cerebellar vermis and brainstem, leading to a wide spectrum of neurological manifestations. Early recognition can be challenging in infancy because the presenting features are often subtle and may overlap with other causes of developmental delay. We report a case of a one-year-old male child who presented with delayed developmental milestones, particularly delayed sitting and poor truncal stability. The parents also described intermittent episodes of rapid breathing followed by brief pauses since early infancy. The child was born at term with an uneventful antenatal and perinatal history and was the first child of non-consanguineous parents. On examination, the child had generalised hypotonia and mild global developmental delay. Growth parameters showed a weight of 8.2 kg, length of 73 cm, and an increased head circumference of 51 cm. Routine laboratory investigations, including complete blood count, serum electrolytes, and liver and renal function tests, were within normal limits. Visual and hearing screening were unremarkable, and abdominal ultrasonography did not reveal renal or hepatic abnormalities. Neuroimaging was performed to further evaluate the developmental delay. Non-contrast computed tomography suggested a posterior fossa malformation, and subsequent Magnetic Resonance Imaging (MRI) demonstrated hypoplasia of the cerebellar vermis, thickened and elongated superior cerebellar peduncles, and a deepened interpeduncular fossa forming the characteristic molar tooth sign, along with mild ventriculomegaly. These findings established the diagnosis of JS. This case highlights the critical role of MRI in diagnosing JS, particularly in resource-limited settings where advanced genetic testing may not be readily available. Careful recognition of characteristic neuroimaging findings can enable timely diagnosis, appropriate counselling, and early initiation of supportive management.

Keywords: Cerebellar vermis abnormalities, Hydrocephalus, Hypotonia, Magnetic resonance imaging, Neurodevelopmental disorders

CASE REPORT

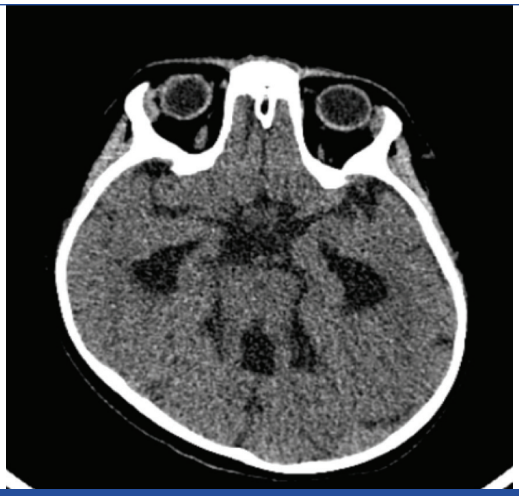
A one-year-old male infant was brought by his parents with concerns of delayed developmental milestones. He had poor head control until five months of age, was unable to sit without support, and had not yet begun to crawl. The parents also noticed intermittent rapid breathing followed by pauses, along with difficulty maintaining balance when placed in a sitting position and would often topple over.

The pregnancy and perinatal history were unremarkable. The infant was born at term via normal vaginal delivery with a birth weight of 2.6 kg with no history of NICU admission. Feeding history was normal. The child is the firstborn of non-consanguineous parents. There was no history of developmental delay or similar neurological illness in the family. No history of spontaneous abortions or previous affected siblings was noted. The child was immunised for age, and vaccination records were verified at the time of presentation. There was no history of missed doses or post-vaccination complications. There were no prior medical evaluations done.

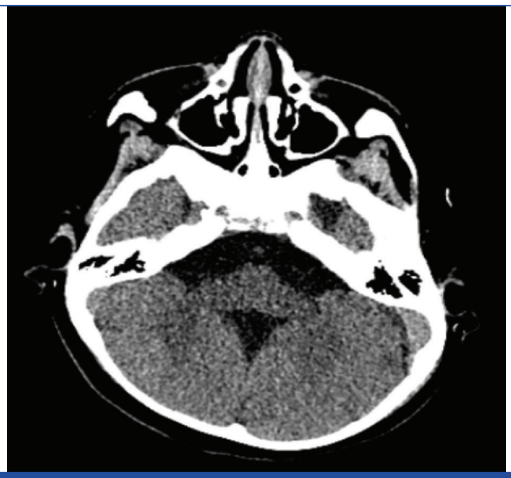
The child exhibited truncal hypotonia and reduced spontaneous movements. There were no dysmorphic facial features. Head circumference was increased, 51 cm (Normal HC for one-year-old - 46 - 47.5 cm) [1]. The child weighed 8.2 kg with a length of 73 cm. The child had intermittent episodes of rapid breathing (tachypnoea or hyperpnea) alternating with brief pauses (apnoea) with no history of seizures. Systemic examination was otherwise unremarkable. Routine blood tests including complete blood count, serum electrolytes, liver and renal function tests were within normal limits. Visual and hearing screening was normal. Retinal dystrophy and oculomotor apraxia may develop later or can be subtle and difficult to elicit in a one-year-old child. The patient was therefore referred to ophthalmology and advised sequential follow-up.

Developmental assessment at one year of age revealed mild global developmental delay. In the gross motor domain, the child was able to sit with minimal support but had not yet achieved pulling to stand, corresponding to an approximate developmental age of nine months (Developmental Quotient: 75) [2,3]. Fine motor evaluation showed an emerging pincer grasp with the ability to transfer objects between hands, consistent with a developmental age of approximately 10 months (Developmental Quotient: 83) [2,3]. In the language domain, the child produced monosyllabic vocalisations and responded to name but had not developed meaningful words, corresponding to a developmental age of nine months (Developmental Quotient: 75) [2,3]. Social and adaptive skills were relatively better preserved, with presence of social smile and imitation of simple gestures, approximating a developmental age of 10 months (Developmental Quotient: 83) [2,3]. Overall findings were suggestive of mild global developmental delay, with comparatively greater involvement of the gross motor domain.

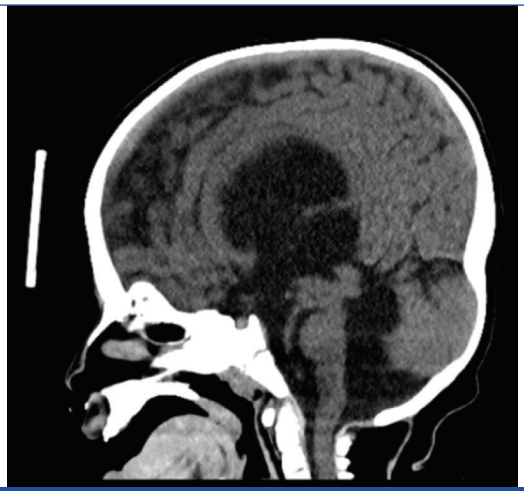
Abdominal ultrasound did not reveal any polycystic kidneys or hepatomegaly. Due to the combination of enlarged head circumference, hypotonia and developmental delay, an MRI brain was advised to evaluate posterior fossa structures. Given the non-specific clinical history, further evaluation with CT scan and MRI was crucial. Non-contrast CT brain showed the molar tooth appearance of midbrain with elongation of superior cerebellar peduncles [Table/Fig-1] and hypoplasia of the cerebellar vermis [Table/Fig-2] with dilatation of bilateral lateral ventricles, 3rd ventricle and mild dilatation of the fourth ventricle and a deepened interpeduncular fossa, [Table/Fig-3] raising suspicion of a posterior fossa malformation. However, detailed assessment of the brainstem configuration was limited on CT, and MRI was advised for further evaluation. MRI of the brain in this case, revealed hypoplastic cerebellar vermis [Table/Fig-4a,b] and prominent superior cerebellar peduncles, giving a



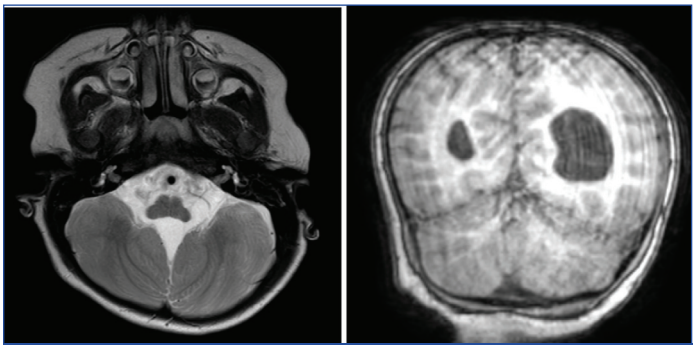
[Table/Fig-1]: Axial CT image demonstrating the classical Molar Tooth Sign (MTS) of the midbrain, characterised by elongated superior cerebellar peduncles.



[Table/Fig-2]: Hypoplasia of cerebellar vermis.

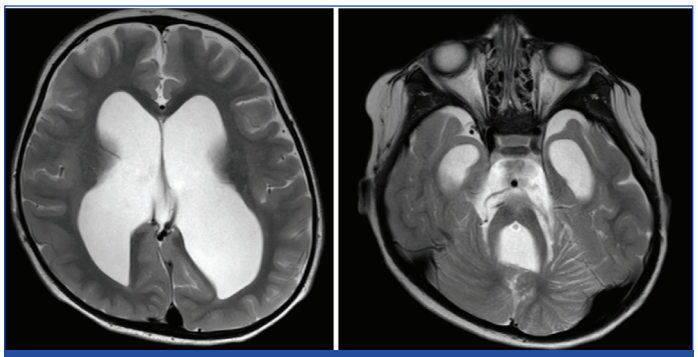


[Table/Fig-3]: Sagittal sections of the CT brain showing ventricular dilatation with enlarged posterior fossa.

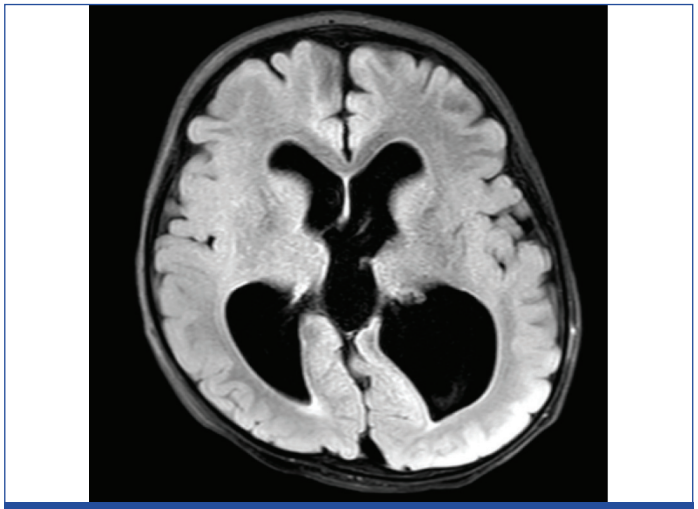


[Table/Fig-4a,b]: (Axial T2W and Coronal T1W) demonstrate hypoplasia of midline vermis.

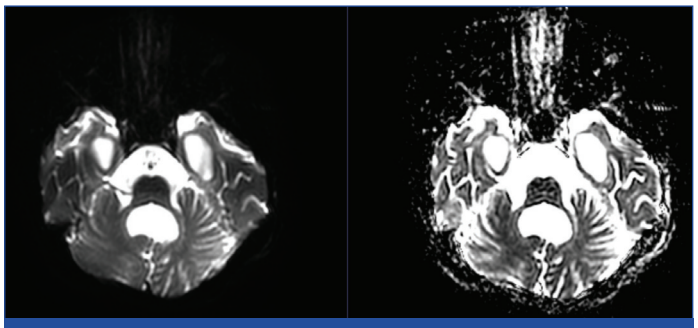
molar-tooth-like configuration on axial sections [Table/Fig-4c,d]. Deepened interpeduncular fossa noted, consistent with hindbrain malformation. Dilatation of bilateral lateral ventricles, 3rd ventricle and 4th ventricle was noted, suggestive of communicating hydrocephalus [Table/Fig-5] No evident hyperintensity noted on diffusion weighted images and corresponding Apparent Diffusion Coefficient (ADC) map [Table/Fig-6].



[Table/Fig-4c,d]: Axial T2-Weighted (T2W) sequences demonstrate symmetrical dilatation of the bilateral lateral ventricles and fourth ventricle, along with elongation of both superior cerebellar peduncles, consistent with the molar tooth appearance of the midbrain.



[Table/Fig-5]: Axial FLAIR image showing dilatation of bilateral lateral ventricles and 3rd ventricle.



[Table/Fig-6]: No evidence of any diffusion restriction on Axial DWI and ADC maps.

Genetic testing was suggested to the family for molecular confirmation and genetic counselling. However, it could not be pursued because of financial constraints and limited accessibility in the setting. In the absence of molecular testing, the diagnosis was established based on the characteristic clinical features and the pathognomonic molar tooth sign on MRI, which remains a reliable diagnostic marker for JS.

After MRI confirmed the molar tooth sign, the diagnosis was clearly explained to the parents, emphasising the role of neuroimaging. They were counselled about the genetic nature, variable outcomes, and need for long-term follow-up. A multidisciplinary plan with physiotherapy for hypotonia, developmental support, systemic screening, and genetic counselling was advised.

DISCUSSION

The JS is a rare autosomal recessive neurodevelopmental ciliopathy characterised by a complex midbrain-hindbrain malformation with a pathognomonic molar tooth sign on MRI. The syndrome classically presents with global developmental delay, hypotonia, abnormal eye movements, and breathing dysregulation in infancy, although the clinical phenotype is highly variable across cases [4,5]. In the index case, MRI demonstrated the characteristic features of JS with hypoplasia of the cerebellar vermis, thickened and abnormally oriented superior cerebellar peduncles, and a deepened interpeduncular fossa creating the classic molar tooth appearance. Additionally, the fourth ventricle exhibited a bat-wing configuration, a common associated finding reflecting vermian hypoplasia [6].

In infants around one year of age, clinical examination may not always reveal classical neurological signs, and cooperation can be limited. Many features of JS - such as abnormal extraocular movements or specific breathing patterns - may be intermittent or subtle and easily missed during a short Outpatient Department (OPD) visit [6,7]. Although molecular confirmation is recommended for definitive diagnosis and subtype classification in JS, comprehensive genetic testing may not be feasible in resource-constrained settings because of limited availability, cost considerations, and infrastructural barriers. Hence, neuro-imaging often becomes the key to diagnosis [8].

These findings align closely with previously published cases. For instance, a comparable classic MRI pattern has been described by Singh P et al., in a seven-month-old infant presenting with developmental delay and abnormal eye movements, wherein imaging demonstrated the characteristic molar tooth configuration due to thickened, elongated superior cerebellar peduncles, along with a bat-wing shaped fourth ventricle and associated vermian hypoplasia on T2-weighted sequences [9]. A large case series by Poretti A et al., demonstrated that the molar tooth sign is present in nearly all genetically confirmed cases, but the severity of vermian hypoplasia and accompanying supratentorial findings may vary substantially between individuals [10]. Similarly, Brancati F et al., reported significant phenotypic variability, with imaging findings ranging from isolated molar tooth sign to additional hindbrain anomalies, renal cystic changes, and subtle cortical dysplasia [4].

Infancy presentations documented in the literature further highlight this variability. Alam S et al., described a nine-month-old female with global developmental delay, hypotonia, and molar tooth sign on MRI without significant systemic involvement, similar to this case [11]. In contrast, Chettiankandi S et al., reported an infant with ocular anomalies including coloboma and retrobulbar cysts in association with JS, emphasising that additional structural abnormalities can be present on imaging [12]. Neonatal series by Choudhary R et al., have underscored the importance of prompt neuroimaging in infants with nonspecific delays, where CT may suggest posterior fossa malformation and MRI confirms the diagnosis [13].

Comparative imaging studies also elucidate the range of radiological presentations. Poretti A et al., analysed 75 patients with JS and noted that a subset displayed mild fourth ventricle prominence, cortical atrophy, or asymmetrical cerebellar hemispheres, underscoring that strict textbook descriptions do not capture the full spectrum [10]. Glass IA et al., noted that detailed neuroimaging evaluation, particularly identification of the molar tooth sign, is critical for distinguishing JS from other posterior fossa malformations such as Dandy-Walker malformation and other conditions associated with cerebellar vermis hypoplasia [14]. Other published cases highlight the phenotypic heterogeneity of JS and related disorders (JS-related disorders) with extra-CNS involvement. For instance, cases with concurrent renal anomalies (e.g., nephronophthisis or polycystic kidney changes) and audiovisual impairment have been reported, broadening the clinical spectrum beyond isolated neurodevelopmental delay. These multisystem manifestations underscore the importance of detailed systemic evaluation in JS, even when initial presentation is limited to developmental symptoms [4,7].

The JS demonstrates marked genetic heterogeneity, with multiple causative genes identified, most encoding proteins related to primary cilium function. Although advances in molecular sequencing have improved genetic diagnosis, neuroimaging-particularly recognition of the molar tooth sign-remains crucial for establishing a presumptive diagnosis, especially in settings where genetic testing is not readily available [6]. Notably, genotype-phenotype correlations remain imprecise: large imaging cohorts have not demonstrated consistent linkage between specific neuroimaging features and underlying mutations, although the severity of vermian hypoplasia may correlate with the degree of neurodevelopmental impairment. Thus, while molecular confirmation enhances diagnostic precision and informs genetic counselling, the absence of gene profiling does not preclude an accurate clinical-radiologic diagnosis [6]. Key differentials such as Dandy-Walker malformation and rhombencephalon synapsis also present with vermian abnormalities; careful MRI assessment is critical to differentiate these entities. Dandy-Walker malformation typically shows cystic dilatation of the fourth ventricle with upward displacement of cerebellar vermis, whereas JS shows the signature molar tooth sign with horizontally oriented superior cerebellar peduncles [15].

Published literature suggests that neurodevelopmental outcomes in JS are heterogeneous, ranging from severe delay to milder deficits, potentially modulated by the degree of infratentorial dysplasia and presence of supratentorial or systemic anomalies. Longitudinal follow-up, which was not available for this patient, remains essential to monitor developmental trajectory and identify late-onset complications such as retinal dystrophy or renal impairment that may emerge in childhood [6].

CONCLUSION(S)

This case highlights that JS can present in infancy with subtle and nonspecific features such as mild developmental delay, making early clinical diagnosis difficult. MRI plays a crucial role by demonstrating the characteristic molar tooth sign, enabling definitive diagnosis even when classical symptoms are absent or evolving. The presence of mild ventriculomegaly in this case also suggests that associated hydrocephalus may coexist and should be carefully assessed. Thus, recognition of key neuroimaging findings is essential for early diagnosis, timely intervention, and appropriate counselling, particularly in resource-limited settings.

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