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RESEARCH ARTICLE

JOUBERT SYNDROME: CLINICAL PRESENTATION AND NEUROIMAGING FINDINGS IN AN ADULT PATIENT - A CASE REPORT

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Abstract

Joubert Syndrome (JS) is a rare genetic disorder that affects the cerebellum and the brain stem characterized by a distinctive midbrain-hindbrain malformation, leading to a variety of neurological symptoms. This case report aims to present the clinical features and neuroimaging findings of a 35 patient diagnosed with Joubert Syndrome. This case report contributes to the understanding of the disease's variability and progression in later stages of life. Increased awareness of JS in adults is crucial for timely diagnosis, appropriate management, and genetic counseling for affected individuals and their families. Further research is needed to unravel the underlying genetic mechanisms and explore potential therapeutic interventions for this complex neurodevelopmental disorder.

Introduction:-

Joubert Syndrome (JS) is a rare autosomal recessive genetic disorder characterized by autosomal recessive transmission and congenital malformation of the brainstem, as well as agenesis or hypoplasia of the cerebellar vermis known as the "molar tooth" sign on neuroimaging[1]. It is a part of a heterogeneous group of ciliopathies characterized by primary ciliary dyskinesia and multiple organ involvement. The syndrome is characterized by early cerebellar symptoms, such as hypotonia and oculomotor apraxia, which may be accompanied by neonatal respiratory disorders. In adulthood, patients most often present with ataxia, and, inconstantly, an intellectual disability of varying severity[2]. This case report aims to present a detailed clinical description of a 35-year-old patient diagnosed with Joubert syndrome, highlighting the clinical manifestations and neuroimaging findings. The report also discusses the importance of early recognition and multidisciplinary management for patients with Joubert syndrome to optimize their overall care and quality of life.

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Case report

Our case is a 35-year-old male with a history of developmental delay and intellectual disability,and motor abnormalities,who underwent evaluation. Clinical examination revealed ataxia,intellectual disability, autism spectrum disorder, myoclonus, and walking apraxia with extrapyramidal signs .No deficit or any other associated sign, Osteotendinous reflexes were present and symmetrical.

Cerebral MRI revealed hypoplasia of the cerebellar vermis, characterized by the horizontalization of the upper cerebellar peduncles and the hollowing of the interpeduncular fossa, resulting in the characteristic "molar tooth" sign.

Additionally, there was a bat-wing appearance of the 4th ventricle. Upon comparison with the clinical data, the diagnosis of Joubert syndrome was confirmed.

Discussion:-

Joubert syndrome is a rare autosomal recessive disorder with a prevalence of approximately 1 in 80,000 live births. It was initially described in 1968 in four siblings presenting with agenesis of the cerebellar vermis, alongside episodic hyperpnoea, abnormal eye movements, ataxia, and intellectual disability , several years later, the distinctive midbrain-hindbrain malformation known as the "molar tooth sign" was first identified in JS , and later recognized in several other conditions that were previously considered as separate entities[3].

Joubert syndromeis characterized by developmental abnormalities of the cerebellar vermis and brainstem. It belongs to a group of ciliopathies, genetic conditions caused by defects in cilia-related genes crucial for cellular processes and signaling pathways during embryogenesis. The classical triad of JS includes hypotonia, developmental delay, and the aforementioned characteristic brainstem and cerebellar malformation, although not all patients may exhibit this triad.[3]

The clinical presentation of JS is highly variable, with neurological and systemic manifestations that may differ among affected individuals. The hallmark triad includes hypotonia, developmental delay, and the characteristic midbrain-hindbrain malformation [4] However, not all patients exhibit this classical triad, making the diagnosis challenging and requiring a high index of suspicion.

Cerebral MRI proved crucial in confirming the diagnosis of Joubert syndrome. The imaging study revealed An hypo-dysplasia of the vermis of variable severity, along with a very deep interpeduncular fossa and enlarged, horizontally oriented superior cerebellar peduncles , resulting in the characteristic "molar tooth" sign.[5] Diagnosing Joubert Syndrome in adulthood can be challenging due to its rarity and overlapping clinical manifestations with other neurological disorders. Furthermore, the characteristic "molar tooth" sign, a cardinal feature of JS, may not always be evident in adult patients.[6]

In concordance with our findings, the diagnosis of Joubert syndrome relies on the synergy between clinical presentation and imaging characteristics. This synergy helps clinicians differentiate Joubert syndrome from other conditions with overlapping features and aids in initiating appropriate management strategies. The differential diagnosis for Joubert syndrome includes a spectrum of neurodevelopmental and ciliopathy-related disorders. Disorders presenting with ataxia, intellectual disability, and cerebellar malformations, such as Dandy-Walker malformation and related variants, must be considered. Additionally, other ciliopathies like Meckel-Gruber syndrome share overlapping features with Joubert syndrome[7]. The key to differentiation lies in the characteristic radiological findings of Joubert syndrome, as demonstrated by the "molar tooth" sign on cerebral MRI.

Molecular genetic testing plays a pivotal role in confirming the diagnosis of Joubert syndrome and its genetic heterogeneity[8] Genetic counseling is imperative, as an accurate genetic diagnosis not only aids in clinical management but also informs family planning decisions.

In the context of adult-onset cases, as presented in our report, the diagnosis of Joubert syndrome can be particularly challenging due to the milder phenotypes and varied clinical features. This highlights the importance of considering Joubert syndrome as a potential diagnosis in adults with a history of neurodevelopmental abnormalities.[4]

The prognosis for adult patients with Joubert Syndrome varies depending on the severity of neurological manifestations and associated complications. While JS remains a lifelong condition, early recognition and comprehensive management can significantly improve the patient's quality of life and functional independence[3].

Conclusion:-

Joubert syndrome is a rare, hereditary, autosomal recessive syndrome;this case report brings to light the diagnostic journey of an adult patient with Joubert syndrome, highlighting the necessity of considering rare neurological disorders beyond their traditionally associated age groups. The convergence of clinical findings and diagnostic imaging, culminating in the distinctive "molar tooth" sign and bat-wing appearance of the 4th ventricle, facilitated an accurate diagnosis. This case reiterates the significance of early recognition, appropriate genetic testing, and multidisciplinary care to enhance outcomes and quality of life for patients with Joubert syndrome.

Figures

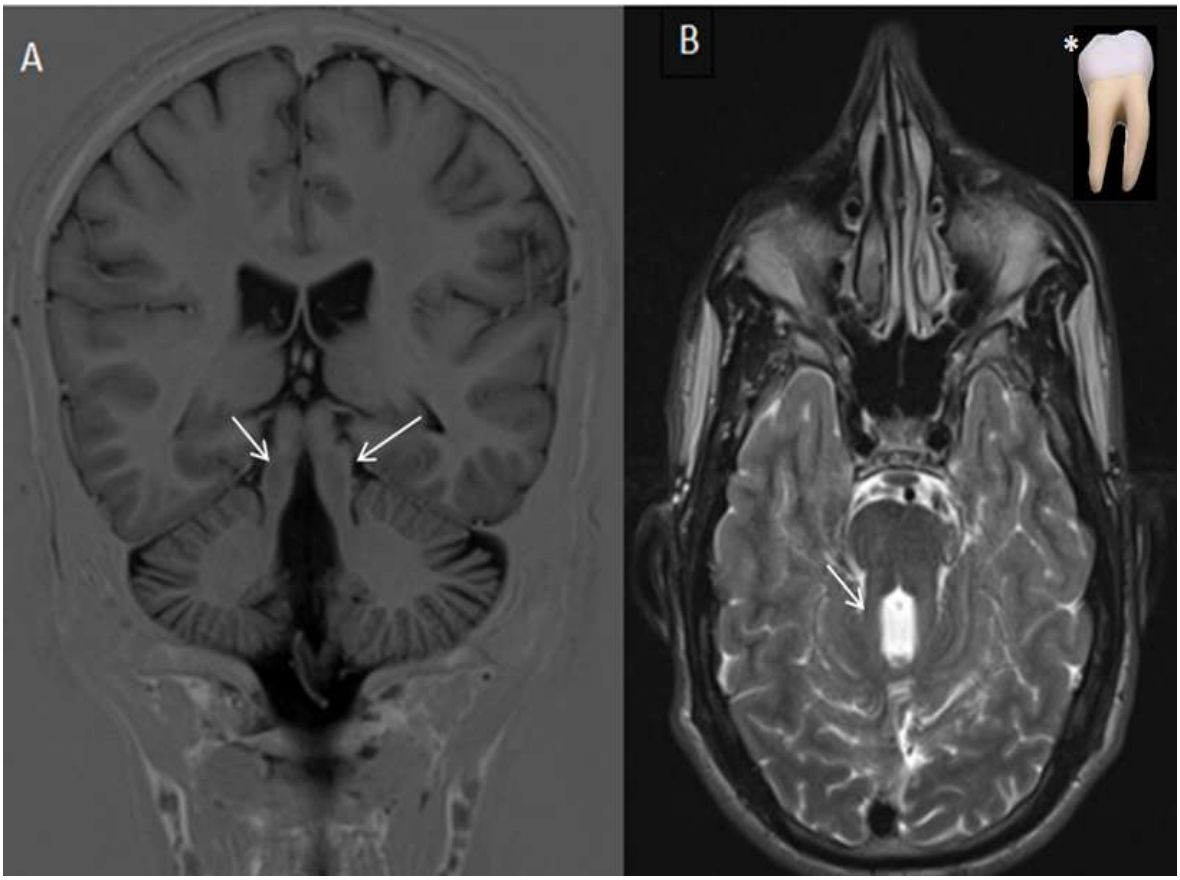

Figure 1:- The right TIR sequence Frontal View (A) and the left T2 axial image (B) shows enlargement and thickening of the superior cerebellar peduncles giving a characteristic molar tooth appearance (*).

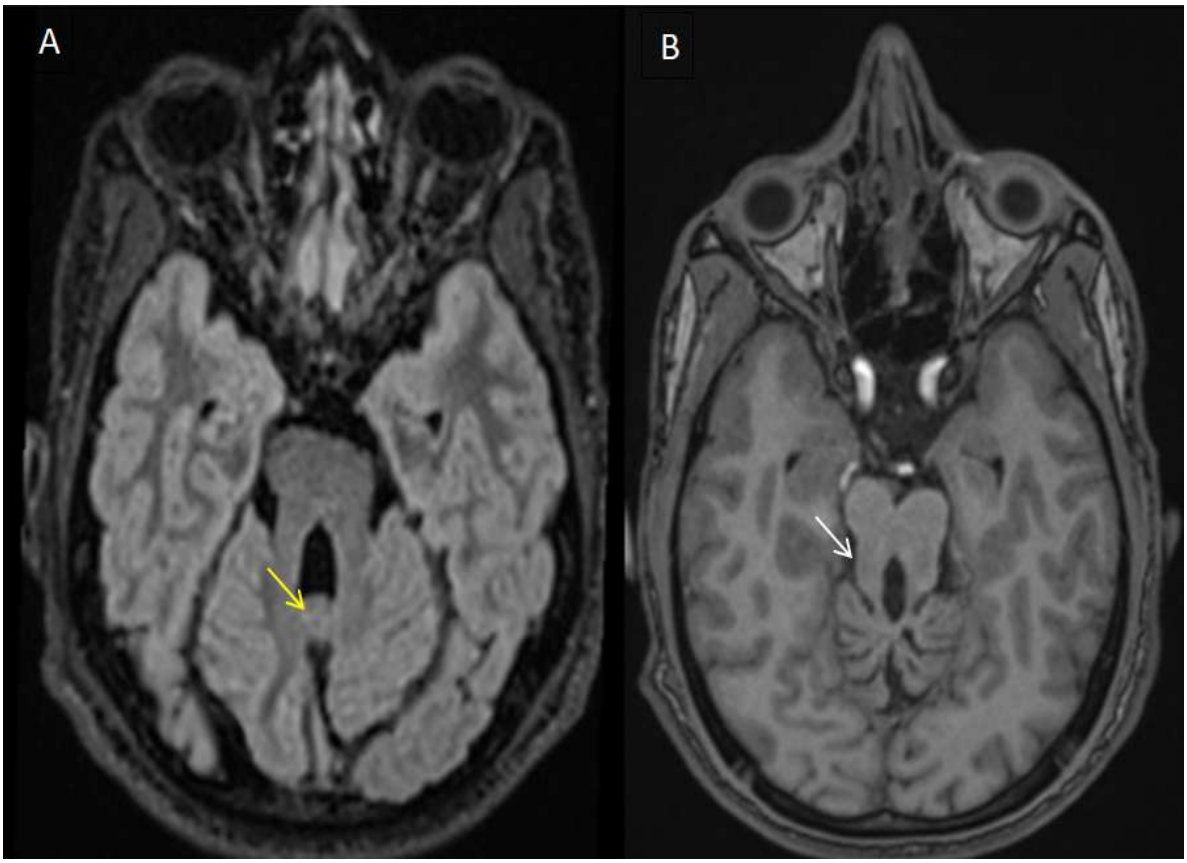

Figure 2:- The left Flair (A) and the right T1 (B) axial sequences show the thickening of the superior cerebellar peduncles in association to a small dysplasic vermis (yellow arrow).

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