Joubert Syndrome: A Rare Radiological Case

Dr Ali Akhtar, Clinical Fellow in Neurosciences

University Hospital Coventry & Warwickshire NHS Trust

Abstract

Joubert syndrome (JS) is a rare autosomal recessive neurodevelopmental disease characterized by abnormal breathing patterns composed of episodic tachypnea/apnea, hypotonia, ataxia, developmental delay, intellectual impairment, ocular impairment, renal cysts, and hepatic fibrosis.

Introduction

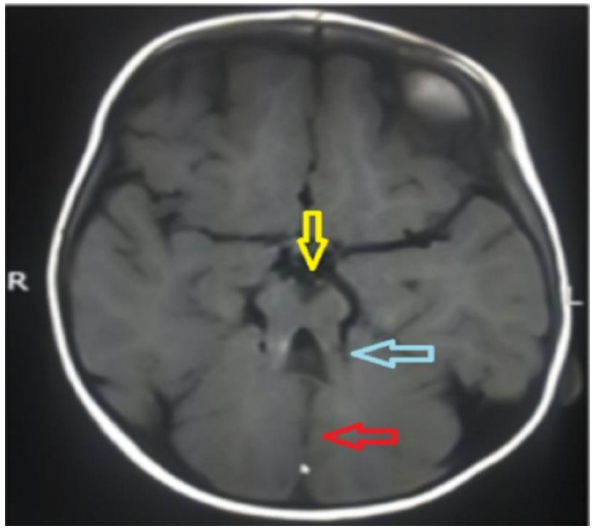
- Classic JS is characterized by the triad of hypotonia, developmental delays, and pathognomic brainstem and cerebellar malformation called the molar tooth sign (MTS) [1].
- **The average age at diagnosis is 33 months.**

Case History

We report the case of a 4-year-old boy who presented with global developmental delay, bilateral nystagmus, and gaze instability with difficulty walking and maintaining an upright posture.

Examination

Examination revealed facial dysmorphic features with a depressed nasal bridge and deepened orbital sockets, hypotonia, gait ataxia, and bilateral horizontal pendular nystagmus.



MRI Imaging shows deep interpeduncular fossa (yellow arrow) with thick and elongated superior cerebellar peduncles (blue arrow) imparting molar tooth appearance and aplasia of the cerebellar vermis with cerebellar hemispheres (red arrow).

Discussion

- A defect in genes encoding for **cilium proteins** results in the clinicopathological manifestations of JS and JSRD [1].
- Joubert syndrome-related disorders (JSRD) describe previously distinct pathological entities with the neuroradiological feature of MTS while involving other organ systems. Based on organ involvement, JSRD is classified into six phenotypes [1].

Clinical Subtype	Clinical Features
Pure JS	Hypotonia, ataxia, developmental delay, molar tooth sign
	No retinal or liver involvement
	No major gene associated with the phenotype
JS with ocular defect	Molar tooth sign, neurological features
	Retinal dystrophy and Leber's congenital amaurosis
	AHI1 gene most commonly mutated (20% of cases)
JS with renal defect	Molar tooth sign
	Nephronophthisis
	Absence of retinal involvement
	NPHP1 and RPGRIP1L genes commonly mutated
JS with hepatic defect	JS features
	Congenital hepatic fibrosis, chorioretinal or optic nerve colobomas, and nephronophthisis
	TMEM67 gene mutated in 70% of cases
JS with oculorenal defects	Neurological signs
	Retinal dystrophy, nephronophthisis
	CEP290 gene mutated in 50% of cases
JS with oro-facio-digital defects	Neurological features of JS
	Lobulated tongue, multiple oral frenula, mesoaxial polydactyly with y-shaped metacarpals, cleft lip/palate
	Hypothalamic hamartoma or congenital absence of the pituitary gland

Conclusion

Prototypical MRI finding is a molar tooth appearance with concomitant cerebellar vermis hypoplasia and a batwing configuration of the fourth ventricle. Management of such cases includes easing respiratory and feeding difficulties, along with rehabilitation for cognitive and behavioral difficulties.

1. Joubert syndrome and related disorders. Brancati F, Dallapiccola B, Valente EM. Orphanet J Rare Dis. 2010;5:20