Scholars LITERATURE

Neurological Sciences and Neurosurgery

Case Report

DOI: https://doi.org/10.47275/2692-093X-131
Volume 4 Issue 1

Joubert Syndrome in 10-Year-Old with Renal Involvement: A Case Study

Sagar Dabbara[1]*, Arya P[2] and Laxmi Poojita AN[3]

[1]Sri Venkateswara Medical College, Andhra Pradesh, India
[2]Ramaiah Medical College, Bengaluru, India
[3]Kurnool Medical College, Andhra Pradesh, India

Abstract

Joubert syndrome (JS) is a rare recessive autosomal disorder in infants and children. JS is a ciliopathy with defects in the primary cilium. JS has mid brain-hind brain malformation which includes: (i) cerebellar vermis hypoplasia, (ii) abnormal deep interpeduncular fossa at Isthmus and Pons, and (iii) Horizontally thickened and elongated Superior Cerebellar Peduncles. Diagnostic symptoms include hypotonia, ataxia, abnormal breathing patterns, atypical eye movements, and intellectual disability. Molar tooth sign on axial sections of MRI (magnetic resonance imaging) is a primary diagnostic criterion. Here we report a case of a 10-year-old female intellectually disabled child who was noted to have developmental delay and vision problems soon after 5 to 6 months of birth. The patient was diagnosed with JS based on an MRI brain finding of Molar tooth appearance.

Keywords: Hyperkalemia; Joubert syndrome; Classification; MRI brain

Correspondence to: Sagar Dabbara, Sri Venkateswara Medical College and Hospital, Andhra Pradesh, India; E-mail: dabbarasagar@gmail.com

Citation: Sagar Dabbara, Arya P, Laxmi Poojita AN (2023) Joubert Syndrome in 10-Year-Old with Renal Involvement: A Case Study. Neurol Sci Neurosurg, Volume 4:1. 131. DOI: https://doi.org/10.47275/2692-093X-131

Received: January 31, 2023; **Accepted:** March 02, 2023; **Published:** March 07, 2023

Introduction

The JS is an autosomal recessive disorder first described by Dr. Marie Joubert in 1969 is associated with agenesis of the cerebellar vermis characterised by hypotonia, ataxia, developmental retardation, oculomotor findings, and abnormal respiratory findings [1]. Joubert Syndrome and related disorders (JSRD) is the classification used to describe the disorders w that present with molar tooth signs on MRI brain and extra-central nervous system involvement. JSRD is classified into six phenotypic presentations (Table 1) [2]. JSRDs can be determined through the extra-central nervous system involvement, such as midline facial defects, polydactyly, hepatic fibrosis, nephronophthisis or cystic dysplastic kidneys, and retinopathy- each with its own set of symptoms and signs [3]. The spectrum of JS ranges from a mild form with minimal motor disability and normal mental development to severe motor disability and moderate mental retardation. Treatment of JS is symptomatic and supportive. JS is also associated with other syndromes like Dekaban-Arima syndrome, COACH syndrome, Varadi-Papp syndrome, and Senior-Loken syndrome (Table 1) [3, 4].

Case Report

A 10-year-old intellectually disabled female child presented to the hospital with chief complaints of decreased food intake and 1 - 2 episodes per day of vomiting for the past 15 days. She was drinking only coconut water (on a liquid diet) for many days. They consulted a nearby clinic and took supportive measures for gastric problems. She had 1 - 2 episodes/ day of vomiting consisting of food particles initially, then watery. Therefore, supportive measures for gastric problems were given in a nearby clinic. Later, she developed rashes on both her upper and lower limbs (one week back). In view of persistent vomiting and rashes, they again consulted a nearby clinic and started on oral cefixime. On the day of admission, she has 3 episodes of vomiting followed by cardiac arrest in the clinic. She was resuscitated and was further evaluated and started treatment.

History: Second child of second-degree consanguineous marriage. Pregnancy was an uneventful and normal vaginal delivery. The child needed resuscitation for 3 minutes after which she cried. No history of NICU stay. The child was noted to have developmental delay and vision problems soon after 5 - 6 months of birth but was not evaluated for the same. MRI done after 1 year of birth suggested JS (molar tooth appearance) (Figure 1). The patient lost to follow-up after that. She was noted to have polyuria and polydipsia for 3 - 4 months before hospitalization.

She was admitted with the above-mentioned complaints. At the time of admission, the child was drowsy with GCS 12/15 with acidotic breathing; immediate VBG was sent from the ER which was suggestive

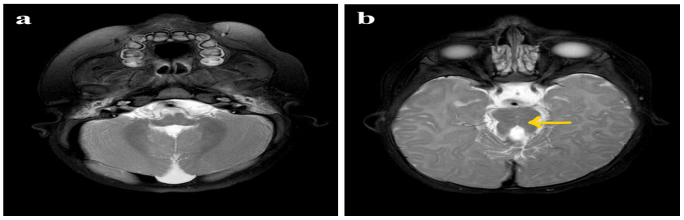

Figure 1: MRI brain scan (a) Axial T2 weighted image showing opposition of cerebellar hemispheres in the middle with absent cerebellar vermis and (b) Axial T2 weighted image showing classical molar tooth appearance in the midbrain.

Table 1: JS classification based on clinical characteristics [2].

Type(s)	Abbreviation	Characteristic(s)	Associated gene(s)
Pure JS	JS	Molar tooth sign	Several gene mutations
JS with ocular defect	JS-O	Molar tooth sign Retinal dystrophy Leber congenital amaurosis	AH1
JS with renal defect	JS-R	Molar tooth sign Nephronophthisis	NPHP1 and RPGRIP1L
JS with oculorenal defects	JS-OR	Molar tooth sign Retinal dystrophy Nephronophthisis	CEP290
JS with hepatic defect	JS-H	Molar tooth sign Congenital hepatic fibrosis	TMEM67
JS with orofaciadigital defect	JS-OFD	Molar tooth sign Polydactyly Lobulated/bifid tongue (including hamartomas)	TMEM216

of severe acidosis with hyperkalemia (8.5 mg/dl). Peripheries were cold with feeble peripheral pulsations and BP was (85/45 mm Hg).

Examination

The patient was moderately built and nourished. She weighed 38 kg (75th percentile). She was pale and tachycardic with a heart rate of 188 bpm, cold extremities, and feeble peripheral pulsations with a BP 0f 90/60 mm Hg. She had no icterus/ cyanosis/ clubbing/ edema, Temp - 98.6 ^{o}F, respiration rate - 24/min, SpO_2 - 96% at room air, GRBS - 168 mg/dl, CVS - S1 S2 heard (no murmurs), RS - B/L normal vesicular breath sounds present, the acidotic pattern of breathing observed. The abdomen was soft, non-tender, and bowel sounds present. CNS - The child was drowsy, responsive to a painful stimulus, and making faint incomprehensible sounds. Higher mental functions - Child conscious, but intellectually disabled (only said mother's and father's name), memory, and orientation could not be assessed further. Cranial nerve examination with evident squint noted and other cranial nerves were normal. Motor examination showed hypotonia and hyporeflexia. Power: Grade 4/5 all muscle groups.

She was given fluid boluses and started on potassium correction in the ER itself (salbutamol nebulisation, glucose with insulin bolus, and calcium gluconate). Bicarbonate correction was also given in view of acidosis. The child was immediately shifted to PICU. Relevant blood investigations showed severe metabolic acidosis with hyperkalemia with a severely deranged renal profile (BUN-150 mg/dl and creatinine values of 12 mg/dl). Ophthalmology evaluation showed exotropia in both eyes and no retinitis pigmentosa. Ultrasound abdomen showed nephronophthisis. In view of the above findings and the child's history diagnosis of JS with renal involvement with acute on chronic renal failure was made and haemodialysis was started. Fluid restriction was done along with correction of vitamin D and calcium and haematinics were also initiated in view of anaemia. After 3 cycles of haemodialysis, hyperkalaemia settled, BUN and creatinine values came down. In view of anaemia, a blood transfusion was also given.

Discussion

JS is a rare disorder with a prevalence of 1 in 1,00,000. JS is a rare autosomal recessive disorder characterized by neuropathologic abnormalities of the cerebellum and brainstem, with hypoplasia or aplasia of the vermis [1]. JS is characterised by hyperpnoea episodes, hypotonia, ataxia, renal involvement hepatic involvement [3]. The main clinical signs of JS are intellectual disability ranging from near-normal intellect to profound mental retardation, hypotonia, ataxia, abnormal eye movements, and alternating tachypnea-apnea during the first few months of life [5]. The majority of JS patients have hypotonia and intellectual disability. Respiratory symptoms start in the neonatal period and gradually diminish with age. Eye involvement is characterised by nystagmus and oculomotor apraxia. Since the exact location of the disorder's affected gene has not been determined, JS must be diagnosed using clinical and radiological symptoms [1].

Diagnostic criteria of JS include hypotonia, global development disorder, ataxia, and neurological finding of molar tooth syndrome on MRI brain [6]. JSRD is a spectrum of disorders that have "molar tooth sign" on MRI brain. JSRD is a disorder of cilia grouped as "ciliopathies". Defects in the transport or arrangement of cilia-centrosomal proteins have an adverse effect on a variety of the critical developmental signaling pathways which are essential for cellular development, such as sonic hedgehog, Wnt signalling, planar cell polarity, and directional movement [7]. Multi-organ involvement can occur due to ciliary dysfunction. The renal disease affects nearly one-fourth of patients with JS [1]. The most common renal presentation is nephronophthisis. It is characterised by tubulointerstitial disorder with the irregular, thickened basal membrane of the tubular epithelium and interstitial fibrosis. The end-stage renal disease develops usually by the end of the second decade [3].

Ordinarily, the superior medullary velum, which is in the fourth ventricle's roof, is where the superior cerebellar peduncles ascend. They are noticeable and extend horizontally toward the midbrain in JS. The trans-axial slices of the Ponto mesencephalic junction have a molar teeth appearance due to the deep midline fissure and the horizontal superior cerebellar peduncles [8].

The primary features of JS on MRI are (i) aplastic or dysplastic cerebellar vermis, (ii) absence of decussation of fibers in the superior cerebellar peduncles and the cerebellar tracts, (iii) abnormal inferior olivary nucleus, and (iv) dysplastic and heterotrophic cerebellar nuclei. Management of JS is mainly supportive treatment. Rehabilitative strategies are needed for cognitive defects and specific management is required for individual system involvement.

Conclusion

In conclusion, JS is a rare inherited condition. Variable and nonspecific presentation leads to delayed diagnosis. Prenatal diagnosis is essential for genetic counselling in cases with confirmed gene mutation.

References

1. Malaki M, Nemati M, Shoaran M (2012) Joubert syndrome presenting as unilateral dysplastic kidney, hypotonia, and respiratory problem. Saudi J Kidney Dis Transpl 23: 325-329.

2. Brancati F, Dallapiccola B, Valente EM (2010) Joubert Syndrome and related disorders. Orphanet J Rare Dis 5: 20. https://doi.org/10.1186/1750-1172-5-20

3. Sattar S, Gleeson JG (2011) The ciliopathies in neuronal development: a clinical approach to investigation of Joubert syndrome and Joubert syndrome-related disorders. Dev Med Child Neurol 53: 793-798. https://doi.org/10.1111/j.1469-8749.2011.04021.x

4. Satran D, Pierpont MEM, Dobyns WB (1999) Cerebello-oculo-renal syndromes including Arima, Senior-Löken and COACH syndromes: more than just variants of Joubert syndrome. Am J Med Genet 86: 459-469. https://doi.org/10.1002/(SICI)1096-8628(19991029)86:5<459::AID-AJMG12>3.0.CO;2-C

5. Joubert M, Eisenring JJ, Robb JP, Andermann F (1969) Familial agenesis of the cerebellar vermis. A syndrome of episodic hyperpnea, abnormal eye movements, ataxia, and retardation. Neurology 19: 813-825. https://doi.org/10.1212/wnl.19.9.813

6. Gleeson JG, Keeler LC, Parisi MA, Marsh SE, Chance PF, et al. (2004) Molar tooth sign of the midbrain–hindbrain junction: occurrence in multiple distinct syndromes. Am J Med Genet A 125: 125-134. https://doi.org/10.1002/ajmg.a.20437

7. Maria BL, Quisling RG, Rosainz LC, Yachnis AT, Gitten J, et al. (1999) Molar tooth sign in Joubert syndrome: clinical, radiologic, and pathologic significance. J Child Neurol 14: 368-376. https://doi.org/10.1177/088307389901400605

8. Sztriha L, Al-Gazali LI, Aithala GR, Nork M (1999) Joubert's syndrome: new cases and review of clinicopathologic correlation. Pediatr Neurol 20: 274-281. https://doi.org/10.1016/s0887-8994(98)00154-4