International Journal of Contemporary Pediatrics
Singh H et al. Int J Contemp Pediatr. 2024 Sep;11(9):1304-1306
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20242346

Case Report

Joubert syndrome: a rare cause of hypotonia with developmental delay

Himanshu Singh[1], Prasun Bhattacharjee[1]*, Pranay Trivedi[1], Keeranmayee Mishra[2], Ashwani Parashar[1]

[1]Department of Pediatrics, Ananta Institute of Medical Science and Research, Rajsamand, Rajasthan, India
[2]Department of Obstetrics and Gynaecology, Banas Medical College and Research Centre, Rajsamand, Rajasthan, India

Received: 18 July 2024
Revised: 16 August 2024
Accepted: 21 August 2024

***Correspondence:**
Dr. Prasun Bhattacharjee,
E-mail: prasunpedia@gmail.com

ABSTRACT

Joubert syndrome is a rare autosomal recessive disorder. It is characterized by congenital ataxia, hypotonia, developmental delay, and at least one of the following features: neonatal respiratory disturbances and abnormal eye movements; including nystagmus and oculomotor apraxia. Molar tooth appearance is an essential finding for the diagnosis of Joubert syndrome. Here we presented a case of an 18-month-old male who presented with developmental delay and marked hypotonia. The main purposes of the case report were to highlight the benefit of a multidisciplinary rehabilitation team approach and describe the clinical features associated with Joubert syndrome. Brain magnetic resonance imaging showed a thick, elongated, and abnormally oriented superior cerebellar peduncle showing a molar tooth appearance with elongated bat-wing-shaped 4th ventricle and hypoplasia of the vermis suggestive of JS. Hypotonia during infancy and developmental delay with or without learning disability, associated with abnormal breathing patterns and abnormal eye movements (nystagmus) along with the radiological presence of a molar tooth sign on the brain MRI is an essential component to confirm the diagnosis.

Keywords: Hypotonia, Molar tooth sign, Developmental delay, Ciliopathy, Joubert syndrome

INTRODUCTION

Joubert syndrome (JS) is a rare autosomal recessive neurodevelopmental disorder (ciliopathy). It is characterized by ataxia, hypotonia, developmental delay, intellectual disability, and at least one feature like breathing dysregulation in newborn age and abnormal eye movements like nystagmus, strabismus, and ptosis.[1,2] This can be associated with other multi-systemic features including progressive retinal dysplasia, CHD, microcystic kidney disease, and liver fibrosis. On radiological findings, molar tooth appearance is the hallmark for the diagnosis of Joubert syndrome. Genetic counseling has been recommended to prevent Joubert syndrome. Early diagnosis by characteristic clinical and radiological findings will help in multi-disciplinary management and appropriate counseling.

CASE REPORT

An 18-month-old male born to a non-consanguineous marriage was referred to our department for evaluation of global developmental delay, cognitive impairment, and hypotonia. The child was born term via vaginal delivery. There was no history of adverse antenatal or perinatal events. There was a history of intermittent fast breathing since the neonatal age group. The diagnosis of JS was made based on a brain MRI, which showed a thick, elongated, and abnormally oriented superior cerebellar peduncle showing a molar tooth appearance with elongated bat-wing-shaped 4th ventricle and hypoplasia of the vermis (Figure 1).

JS can be classified into 6 subtypes: pure JS, JS with ocular defect (JS-O), JS with renal defect (JS-R), JS with

oculo-renal defects (JS-OR), JS with hepatic defect (JS-H), and JS with orofacial digital defects. In our case, on clinical examination, the patient had frontal bossing and nystagmus with no facial dysmorphism or digital anomaly (Figure 2).

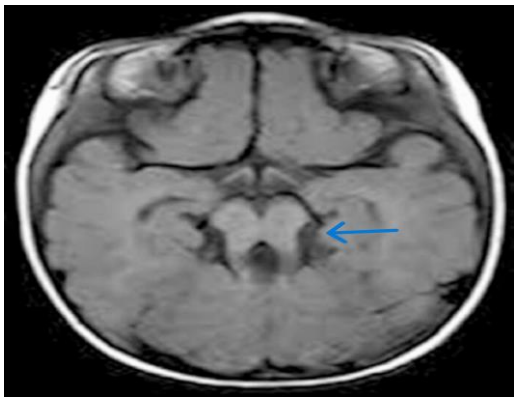

Figure 1: MRI of brain T1 image showing molar tooth malformation (the blue arrow marks the molar tooth malformation).

A neurological exam revealed marked hypotonia. There is no report of retinopathy and associated eye disorders. Moreover, the child has no pathological features of suspected renal disorders and neurocutaneous markers. The rest of the systemic examination was normal. Laboratory investigations, including complete blood count, blood sugar, electrolytes, C-reactive protein, liver enzymes, urea and creatinine, TSH, and free T4 and T3, were all normal. The initial goals and interventions were decided with the multidisciplinary team, and rehabilitation was initiated in a full-fledged manner

Figure 2: Frontal bossing can be observed in the patient.

DISCUSSION

JS is a rare autosomal recessive condition, first described by Marie Joubert. In 1969 four siblings of a French-Canadian family three males and one female, all had agenesis of the cerebellar vermis.[1,2] Hypotonia during infancy and developmental delay with or without mental retardation, associated with abnormal breathing patterns and abnormal eye movements (nystagmus), are the most important clinical signs and symptoms to suspect in the case of JS.[3] However, the radiological presence of a molar tooth sign on the brain MRI is essential to confirm the diagnosis. The present case had all the clinical symptoms except for nystagmus and mental retardation which may have been overlooked. The clinical manifestations usually start in the neonatal period, but the correct diagnosis is often delayed months or years after birth because of its variable phenotypes.[4] JS is classified into two main types, pure JS and JSRD. The term JSRD refers to a group of disorders presenting the pathognomonic features of JS in association with multiple systemic congenital abnormalities. The main findings from cranial MRI studies are cerebellar vermis hypoplasia, deepened interpeduncular fossa, and thick and horizontal enlarged superior cerebellar peduncles.[4] However, cerebellar vermis hypoplasia had been reported as a component of other disorders like trisomy 21, occipital encephalocele and Dandy-Walker malformation.[5]

Other associated clinical features than the major findings could be seen in JS like polydactyly, renal cyst, ptosis, liver anomalies, congenital heart defects, duodenal atresia, ocular fibrosis, retinal dysplasia, choanal atresia, mental retardation, soft tissue tumor of the tongue.[6,7]

Prenatal diagnosis of JS is feasible through chorionic villus sampling at about 11 weeks of gestation and genetic counseling has been recommended as one of the important measures to prevent JS.[8,9] Foetal USG may be useful to diagnose high-risk pregnancies as it showed increased nuchal translucency. The prognosis of JS cases is not bad when diagnosed and managed in early childhood through the implementation of a multidisciplinary intervention program for patients including physical therapy, special education, occupational, and speech therapy. The early intervention has shown benefits in the advancement of developmental milestones for patients with JS.[10]

In general, the prognosis of JS is poor.[11] It largely depends on the severity of the involvement of different organ systems.[12] Steinlin et al described a variable course for developmental outcome in JS: some patients die early in infancy, some have severe developmental handicaps and others survive with mild developmental delay.[13] The 5-year survival rate is 50%. Death is usually due to feeding difficulties and respiratory infections.[14] The recurrence risk for JS is 25%. The diagnosis is important for future procedures that require anesthesia because

these patients are sensitive to the respiratory depressant effects of anesthetic agents like opiates and nitrous oxide. Hence, use of these anesthetic agents should be avoided in these patients.[15]

CONCLUSION

Hypotonia in infancy and developmental delays, which may include learning disabilities, are linked to abnormal breathing patterns and eye movements (nystagmus). These symptoms, coupled with the radiological identification of a molar tooth sign on a brain MRI, are critical for confirming a diagnosis of JS. A high level of clinical suspicion and a thorough clinical examination are crucial for making the correct diagnosis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Pellegrino JE, Lensch MW, Muenke M, Chance PF. Clinical and molecular analysis in Joubert syndrome. Am J Med Genet. 1997;72:1-59.
2. Satran D, Pierpont ME, Dobyns WB. Cerebello-oculo-renal syndromes including Arima, Senior-Löken and COACH syndromes: more than just variants of Joubert syndrome. Am J Med Genet. 1999;86:459-69.
3. Parisi MA, Doherty D, Chance PF, Glass IA. Joubert syndrome (and related disorders). OMIM 213300). Eur J Hum Genet. 2007;15:511-21.
4. Akcakus M, Gunes T, Kumandas S, Kurtoglu S, Coskun A. Joubert syndrome: report of a neonatal case. Paediatr Child Health. 2003;8:499-502.
5. Boltshauser E, Isler W. Joubert syndrome: episodic hyperpnea, abnormal eye movements, retardation and ataxia, associated with dysplasia of the cerebellar vermis. Neuropadiatrie. 1977;8(1):57-66.
6. Aslan H, Ulker V, Gulcan EM. prenatal diagnosis of Joubert syndrome: A case report. Prenat Diagn. 2002;22:13-6.
7. Haug K, Khan S, Fuchs S. OFD II, OFD VI, and Joubert syndrome manifestations in 2 sibs. Am J Med Genet. 2000;91(2):135-7.
8. Brancati F, Dallapiccola B, Valente EM. Joubert syndrome and related disorders. Orphanet J Rare Dis. 2010;5:20.
9. Saraiva JM, Baraitser M. Joubert syndrome: a review. Am J Med Genet. 1992;43:726-31.
10. Parisi MA. Clinical and molecular features of Joubert syndrome and related disorders. Am J Med Genet C. 2009;151:326-40.
11. Choh SA, Choh NA, Bhat SA, Jehangir M. MRI findings in Joubert syndrome. Indian J Pediatr. 2009;76:231-5.
12. Incecik F, Herguner MO, Altunbasak S, Gleeson JG. Joubert syndrome: report of 11 cases. Turk J Pediatr. 2012;54:605-11.
13. Steinlin M, Schmid M, Landau K, Boltshauser E. Follow-up in children with Joubert syndrome. Neuropediatrics. 1997;28:204-11.
14. Alorainy IA, Sabir S, Seidahmed MZ, Farooqu HA, Salih MA. Brain stem and cerebellar findings in Joubert syndrome. J Comput Assist Tomogr. 2006;30:116-21.
15. Singh P, Goraya JS, Saggar K, Ahluwalia A. A report of Joubert syndrome inan infant, with literature review. J Pediatr Neurosci. 2011;6:44-7.

Cite this article as: Singh H, Bhattacharjee P, Trivedi P, Mishra K, Parashar A. Joubert syndrome: a rare cause of hypotonia with developmental delay. Int J Contemp Pediatr 2024;11:1304-6.