

Joubert's syndrome presenting as end-stage renal disease; a case report

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Abstract

Joubert's syndrome is a genetically heterogeneous and autosomal recessive inherited disorder characterized by hypotonia, ataxia, psychomotor delay, and variable occurrence of oculomotor apraxia and neonatal breathing abnormalities. Molar tooth sign and molecular diagnosis is the key diagnostic feature for this disease. However, existing diagnostics method of Joubert's syndrome is challenging, due to extremely clinically and genetically heterogeneous, overlapping with several other ciliopathies. Here we report the clinical findings and the clinical course of end-stage renal disease (ESRD) in early childhood in Joubert syndrome.

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Introduction

Marie Joubert et al in 1969 first described hypotonia, abnormal eye movements, ataxia and alternating hyperpnoea and /or apnoea in 4 French-Canadian siblings with molar tooth sign in magnetic resonance imaging (MRI) scan. Joubert's syndrome (JS) is a rare genetically heterogeneous inherited disorder characterized by congenital ataxia, hypotonia, developmental delay, abnormal eye movements including nystagmus, oculomotor apraxia, Leber congenital amaurosis, pigmentary retinopathy and hepatic abnormalities include hepatic fibrosis (1,2). Renal findings in JS are nephronophthisis and cystic renal dysplasia. It has been reported in 30% of cases in the published data. Facial dysmorphism and limb abnormalities such as polydactyly have also been described. This clinical entity is under reported with prevalence of less than 1 in 100000. Even though the clinical features are present in the new born, the exact diagnosis is made several years later (1-4).

Case Report

A 12-year-old male child presented to the department of nephrology with history of unsteadiness of gait from the age of 6 years and impaired appetite with vomiting of one month duration. The child was born of consanguineous parents with no significant history of perinatal asphyxia. There was history of delayed milestones and also found to have unsteadiness of gait from the age of 6 years

Core tip

Joubert's syndrome is a genetically heterogeneous and autosomal recessive inherited disorder characterized by hypotonia, ataxia, psychomotor delay, and variable occurrence of oculomotor apraxia and neonatal breathing abnormalities. Molar tooth sign and molecular diagnosis is the key diagnostic feature for this disease.

and it was progressively worsening. History of recurrent episodes of seizures was present in the past. The child had polyuria for the past one year. There was no history of diabetes, hypertension, recurrent urinary tract infection or surgery in the past.

On examination the child was found to have growth retardation with global developmental delay, frontal bossing, low set ears with facial dysmorphism, non-paralytic convergent squint and polydactyly. His blood pressure was 100/70 mm Hg. Neurological examination revealed normal cranial nerves, normal fundus, and hypotonia of all the limbs with sluggish reflexes. Sensory examination was normal. Bilateral cerebellar signs with truncal ataxia was present. Bladder and bowel exam was normal. Other system examination was normal.

Investigations revealed normocytic normochromic anemia with hemoglobin of 6.2 g/dL. His blood urea nitrogen and creatinine were 62 mg/dL and 6.8 mg/dL respectively. Hyperkalemia with potassium of 5.8 mmol/L was present. Urine routine examination



showed 1+ proteinuria and no active urinary sediment. Bilateral contracted kidneys were present on ultrasound examination. MRI brain showed classical molar tooth sign (Figure 1) such as hypoplasia of midline cerebellar vermis with enlarged superior cerebellar peduncle and deeper than normal posterior interpeduncular fossa that resembles the cross section through a molar tooth. In view of end-stage renal failure with severe renal failure and uremic gastrointestinal symptoms, patient was initiated on hemodialysis through central venous catheter. Later bed side continuous ambulatory peritoneal dialysis (CAPD) catheterization was done and initiated on peritoneal dialysis with 4 exchanges of 2.5% peritoneal solution. Patient had improved symptomatically.

Discussion

Joubert's syndrome was first described in four siblings in a large French-Canadian family with cognitive impairment, ataxia, episodic tachypnea, eye movement abnormalities and cerebellar vermis agenesis by Marie Joubert in 1969 (1). The incidence of this rare autosomal disorder is 1 in 100 000 live birth (2). JSs are genetically heterogeneous and all known genes encode proteins localized at or near primary cilium. Ten causative genes have been identified so far (3-5). Maria et al referred to the appearance of long, thick superior cerebellar peduncles, a deep interpeduncular fossa and vermis hypoplasia or aplasia on brain MRI as molar tooth sign (6). The following features are essential for the diagnosis of JS. First; molar tooth sign on brain MRI. Second; intellectual/developmental delay of varying degree. Third; hypotonia in infancy. Fourth; presence of one of the following for supporting the diagnosis -episodic apnea and or tachypnea and abnormal eye movements (nystagmus and or oculomotor apraxia) (7). Renal disease ranges in severity from classic nephronophthisis with onset in late childhood or later to cystic renal dysplasia (8). Failure to concentrate the urine, increased renal echogenicity and eventually renal failure occurs. Renal disease occurs in 25%-30% in the published data (3). Other findings that may occur include liver fibrosis with portal hypertension, polydactyly, scoliosis and facial dysmorphism. Our patient had global developmental delay, hypotonia of all the limbs and bilateral cerebellar signs with truncal ataxia, renal involvement leading on to end stage renal failure requiring dialysis, facial dysmorphism with low set ears, non-paralytic convergent squint and polydactyly were present. MRI brain of the child showed classical molar tooth sign. Hence the diagnosis of JS was made. As our patient had end stage renal failure with uremic gastrointestinal symptoms, hemodialysis was initiated followed by bed side CAPD catheterization and peritoneal dialysis. The importance of identifying JS is related to the outcome, its autosomal recessive type, and the potential complications that develop. This syndrome is classified into two groups on the basis of presence or absence of retinal dystrophy. Association between retinal dystrophy and multi-cystic renal disease is very high and these patients appear to have poor prognosis (3,9). Our patient did not

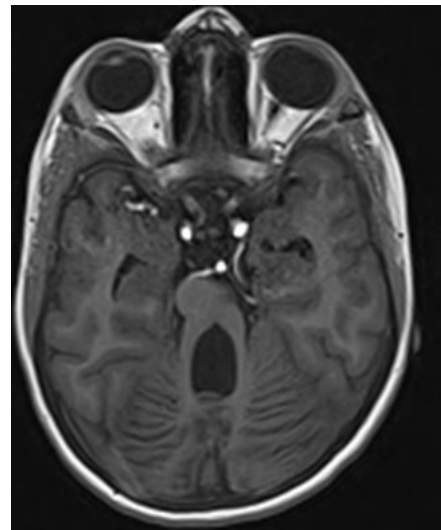


Figure 1. Axial MRI image of the cerebellum and brain stem of a child with Joubert's syndrome.

have evidence of retinal dystrophy. Hence close surveillance for retinal, renal, and hepatic involvement is necessary since the prognosis depends on the presence of these conditions (4). Also helps to diagnose antenatally by ultrasound during subsequent pregnancies if JS was identified in one child of a family (10).

Finally, the diagnosis is required for future surgical procedures requiring anesthetic agents such as opioids, and nitrous oxide as these individuals particularly sensitive to the respiratory depressant effects of such drugs. These drugs should be avoided and close perioperative respiratory monitoring is essential (11).

Conclusion

Joubert's syndrome is a rare genetic disorder with heterogeneous clinical features. Neuroimaging helps in the diagnosis. Once the diagnosis is made evaluation for the involvement of liver, kidney and eye is required. The potential complications that may develop and the avoidance of certain anesthetic drugs during surgical procedure are important once the diagnosis is made.

Authors' contribution

All authors contributed equally to the preparation of the case report.

Conflicts of interest

The authors declare no conflict of interest.

Ethical consideration

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References

- Joubert M, Eisenring JJ, Robb JP, Andermann F. Familial agenesis of the cerebellar vermis. A syndrome of episodic hyperpnea, abnormal eye movements, ataxia, and retardation. *Neurology*. 1969;19:813-25.
- Gill H, Muthusamy B, Atan D, Williams C, Ellis M. Joubert

- syndrome presenting with motor delay and oculomotor apraxia. *Case Rep Pediatr.* 2011;2011:262641.
3. Saraiva JM, Baraitser M. Joubert syndrome: a review. *Am J Med Genet.* 1992;43:726-31.
 4. Brancati F1, Dallapiccola B, Valente EM. Joubert Syndrome and related disorders. *Orphanet J Rare Dis.* 2010;5:20.
 5. Chance PF, Cavalier L, Satran D, Pellegrino JE, Koenig M, Dobyns WB. Clinical nosologic and genetic aspects of Joubert and related syndromes. *J Child Neurol.* 1999;14:660-6
 6. Maria BL, Hoang KB, Tusa RJ, Mancuso AA, Hamed LM, Quisling RG, et al. "Joubert syndrome" revisited: key ocular motor signs with magnetic resonance imaging correlation. *J Child Neurol.* 1997;12:423-30.
 7. Parisi MA. Clinical and molecular features of Joubert syndrome and related disorders. *Am J Med Genet C Semin Med Genet.* 2009;151C:326-40.
 8. Kumada S, Hayashi M, Arima K, Nakayama H, Sugai K, Sasaki M, et al. Renal disease in Arima syndrome is nephronophthisis as in other Joubert-related Cerebello-oculo-renal syndromes. *Am J Med Genet A.* 2004;131:71-6.
 9. Steinlin M, Schmid M, Landau K, Boltshauser E. Follow-up in children with Joubert syndrome. *Neuropediatrics.* 1997;28:204-11.
 10. Barkovich AJ. *Pediatric Neuroimaging.* 2nd ed. New York: Raven: 1995:249-257.
 11. Habre W, Sims C, D'Souza M. Anaesthetic management of children with Joubert syndrome. *Paediatr Anaesth.* 1997;7:251-3.