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Case Report

Rare case of a floppy neonate: Joubert syndrome

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ABSTRACT

Joubert syndrome presenting during the neonatal period is very rare. We report a term neonate who presented with perinatal asphyxia followed by episodic tachypnoea interspersed with apnoea and seizures. On physical examination, baby was alert; however, on neurological evaluation, there was generalised hypotonia with panting of dog-like breathing. Magnetic resonance imaging of the brain finding revealed typical molar tooth sign suggestive of Joubert syndrome and fundus examination revealed retinal colobomas.

Keywords: Apnoea, floppy neonate, Joubert syndrome, molar tooth sign

INTRODUCTION

Joubert syndrome is a rare autosomal recessive disorder characterised by agenesis of the cerebellar vermis, clinically presenting as panting-like breathing pattern with multiorgan involvement. Magnetic resonance imaging (MRI) of the brain exhibit classic 'molar tooth sign' involving deep posterior interpeduncular fossa, with thick and elongated superior cerebellar peduncles and hypoplastic or aplastic superior cerebellar vermis.

CASE REPORT

An early term male baby was born at 38-week to non-consanguineous parents by caesarean section. He did not cry immediately after birth, required positive pressure ventilation for 1 min and APGAR scores were 5 and 7 at 1 min and 5 min, respectively. On examination, the baby had generalised hypotonia with extended posture. Initially, he was supported on non-invasive ventilation and was weaned off to room air over 48 h. At 50 h, the baby had subtle seizures with intermittent tonic posturing for which anticonvulsant therapy was started. Baby remained stable and was discharged on the day 6th of life. He was readmitted on the 9th day of life with complaints of abnormal breathing pattern and intermittent cyanosis. On examination, the baby was alert but had intermittent episodes of hyperpnea with jerky breathing, like 'panting of dog' followed by apnoea. Laboratory investigations revealed normal sepsis screen along with normal metabolic workup. To rule out central nervous system malformation, MRI of the brain was done that showed cerebellar hypoplasia with thickened elongated superior cerebellar peduncles with typical 'molar tooth sign' [Figure 1] suggestive of Joubert syndrome. Fundus examination revealed retinal colobomas. Parents were counselled about need for genetic workup; however, they were not very keen for it.

DISCUSSION

Joubert syndrome is an autosomal recessive and rarely X-linked recessive disorder. It is a rare disorder and

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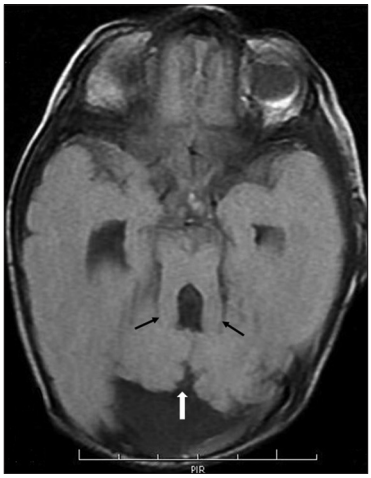

Figure 1: Magnetic resonance imaging axial image showing 'Molar tooth sign.' Thickened superior cerebellar peduncles (thin black arrow) and hypoplastic vermis (thick white arrow) are shown in the figure

characterised by agenesis of the cerebellar vermis and brainstem with a prevalence between 1 per 80,000 and 1 per 100,000 live births. Characteristic clinical features of Joubert's syndrome are hypotonia, developmental delay and at least one of the two features including irregular breathing pattern and abnormal eye movements.[1] Abnormal respirations typically seen in the neonatal period has been described as apnoeas with alternating episodic hyperpneas like a panting dog.[2] Although, this episodic panting tachypnoea is not very consistent yet a common feature and was present in about 71% of cases described by Maria *et al*.[3] It usually sets off during handling of an infant and has been reported to improve with age. Ocular abnormalities such as nystagmus, strabismus, oculomotor apraxia, congenital retinal dystrophy, pigmentary retinopathy, chorioretinal colobomas and ptosis are often present.[4] This baby had generalised hypotonia with extended posture and episodes of effortless tachypnoea alternating with apnoea which were consistent with the diagnosis of Joubert syndrome. Baby's eye examination revealed retinal colobomas further supporting the diagnosis.

Classical radiological finding described by Maria *et al*. of molar tooth sign on MRI is the hallmark feature and key to the diagnosis. Molar tooth sign comprises of deep posterior interpenduncular fossa, prominent and thickened superior cerebellar peduncles and hypoplasia or dysplasia of cerebellar vermis.[2,4] In this baby, MRI findings were consistent with molar tooth appearance that confirmed the diagnosis of Joubert's syndrome. Molar tooth sign is seen in other syndromes such as COACH, Varadi-Papp, Dekaban-Arima, Senior Loken, Joubert with polymicrogyria and Malta. However, as these syndromes have classic features of Joubert's syndrome with other supplementary prominent features it was later classified as Joubert syndrome and related disorders (JSRDs). Some physical abnormalities associated with JSRD include hepatic fibrosis, renal calcifications, cystic dysplastic kidneys, cortical renal cysts, encephalocele, polydactyly, cleft lip or palate and retinal dysplasia. However, more recently, Joubert syndrome has become the accepted term to describe all forms of Joubert's syndrome.[4-6] In this baby, abdominal ultrasounds, renal and liver functions tests, metabolic workup and urinalysis done were normal.

Various facial features described with Joubert's syndrome are high arched eyebrows, ptosis, prominent nasal bridge with anteverted nostrils, triangular shaped mouth, macrocephaly, frontal bossing, hypertelorism, high arched palate, protruded tongue and micrognathia.[4] This baby did not have any features suggestive of facial dysmorphism.

A significant number of cases of Joubert's syndrome has been reported till date in the literature. Despite this data cases reported in neonates are quite few in number. Earlier average age of diagnosis was 33 months,[3] but later many cases have been reported in infancy. A case was reported by Salva *et al*. in a 24-day-old baby who presented as nystagmus and later had developmental delay.[1] Another case was reported by Akcakus *et al*. in a 4-day-old neonate who presented with facial dysmorphism, abnormal respiratory pattern and hypotonia.[6] Solomon *et al*. reported their case in a 12-h neonate with abnormal breathing pattern, hypotonia and abnormal eye movement.[7] All three cases had molar tooth appearance on MRI brain and molecular diagnosis through gene sequencing was reported in only one case described by Salva *et al*.

As per literature till date, pathogenic variants of 34 genes have been identified to cause Joubert's syndrome that encodes proteins localising to the primary cilium or basal body. Out of these, 33 are autosomal and one is X-linked.[4] Genetic diagnosis can be established in about 62%–94% of cases with clinical diagnosis.[8,9] In this case, genetic testing could not be performed due to parental refusal. Once the genetic cause has been identified, prenatal testing can be offered to the family for planning pregnancy in the future. In few cases, serial prenatal ultrasound and foetal MRI has been used to diagnose Joubert's syndrome as early as 22 weeks. However, its sensitivity and specificity have not been evaluated yet.[4]

Clinical and radiological finding consistent with Joubert's syndrome remains the cornerstone for the diagnosis which can be further supported by genetic testing. The prognosis depends mainly on associated systemic abnormalities and on cerebellar vermis whether absent or partially developed.[10]

Steinlin *et al*. described a variable course for developmental outcome with some patients dying early in infancy, some having severe developmental disability and others surviving with mild developmental delay.[11] In view of variability of clinical outcome, early recognition and diagnosis of Joubert's syndrome will help in early institution of supportive measures and rehabilitation.

CONCLUSION

Knowledge of the characteristic clinical and radiological findings in Joubert syndrome will help in the early diagnosis and appropriate counselling.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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