Case Report

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Joubert's syndrome: a case report

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ABSTRACT

Joubert syndrome is an autosomal recessive genetic disorder that affects the area of the brain that controls balance and coordination. This syndrome is difficult to diagnose clinically because of its variable phenotype. Signs and symptoms commonly include hypotonia abnormal breathing patterns; abnormal eye movements; ataxia; distinctive facial features; and intellectual disability. Various other abnormalities may also be present. This condition is characterized by a specific finding on an magnetic resonance imaging (MRI) called a "molar tooth sign" in which the cerebellar vermis of the brain is absent or underdeveloped and the brain stem is abnormal. The exact diagnosis is often not made for several years after birth. We present a case of Joubert syndrome in a thirteen year old male with developmental delay, ataxia, mild hypotonia, nystagmus and molar tooth sign on MRI. Awareness of the characteristic clinical and radiological findings in Joubert syndrome will help in early diagnosis, appropriate counselling and proper rehabilitation.

Keywords: Ataxia, Joubert syndrome, Molar tooth sign, Nystagmus

INTRODUCTION

Joubert syndrome (JS) is a rare autosomal recessive disorder. This clinical entity is under-reported with a prevalence of less than 1 in 100,000. It is characterized by hypotonia, abnormal breathing (hyperpnea), sleep apnea and abnormal eye movements; nystagmus and including oculomotor apraxia, developmental retardation with evidence neuropathologic abnormalities of cerebellum and brainstem.¹ It may be present with dysmorphic features like hypertelorism, small ear lobes, broad forehead, arched eyebrows, broad mouth with intermittent tongue protrusion, ptosis and anteverted nostrils and hypotonia is important only if associated with other features. Molar tooth appearance is a specific finding for the diagnosis of JS. JS is an uncommon inherited condition and delayed diagnosis is usually related to its variable, non-specific presentation with a variable phenotype making it difficult to establish the exact clinical diagnostic boundaries of the syndrome. The exact diagnosis is often not made for several years after birth.² The average age at diagnosis is 33 months.³ The importance of early detection of the syndrome is stressed so that suitable measures can be started as early as possible.

CASE REPORT

A 13-year-old male case of developmental delay presented to the pediatric outpatient clinic with increase in episodes of fall while walking noticed since 1-year, ataxic gait and nystagmus. The child was born to non-consanguineous parents with uncomplicated pregnancy via spontaneous vaginal delivery at term with no perinatal asphyxia. There was no history of seizure, trauma, abnormal breathing pattern .There was no history of similar illness in any of the relatives or sibling.

Parents noticed delayed developmental at two and half year-gross motor and language delay for which physiotherapy and occupational therapy was given. He achieved neck holding at 10 month, was able to sit without support by the age of 2 years walking with support at 2.5 years and he could walk without support by the age of 3.5. Speech could be understood clearly when he was of 5 years. On presentation child had minimal motor disability and moderate impaired mental development. Intelligence quotient (IQ) testing was also done at 10 year suggested of below average intelligence.

On examination vitals were within normal range, mild facial dysmorphism in form of prominent forehead, large ears, triangular mouth, desquamation of soles was also noted. Ear, nose and throat (ENT) evaluations was normal. Neurological examination revealed normal cranial nerves and fundus, nystagmus was present. Cognitive impairment with below average IQ. Motor examination revealed mild hypotonia with normal tendon reflexes. Ataxic gait and Romberg's test positive. Ophthalmological evaluation was suggestive of refractory error. Other systemic examination were normal. Ultrasonography (USG) abdomen were done which were normal.

Magnetic resonance images on axial T1-weighted and T2-weighted showed molar tooth configuration with hypoplasia of vermis, elongated superior cerebellar peduncle. Thus based on clinical and magnetic resonance imaging (MRI) finding diagnosis of JS was made. Parents were counselled and patients were advised to continue physiotherapy and occupational therapy.



Figure 1: T1 axial- molar tooth with hypoplasia of vermis.

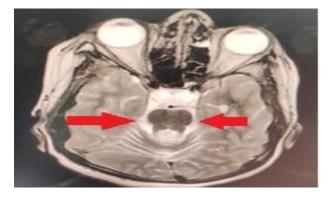


Figure 2: T2 axial-molar tooth sign (arrow).



Figure 3: T1 sagittal-cerebellar vermis hypoplasia.

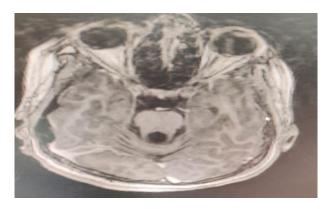


Figure 4: Post contrast.

DISCUSSION

Marie Joubert, a French neurologist, was the first to report this syndrome in five patients who presented breathing disorders and abnormal eye movements, ataxia, mental retardation associated with agenesis of the cerebellar vermis. JS is a rare autosomal recessive disorder characteristic characterized by clinical and neuroradiological findings. Although the diagnostic criteria for JS have not been established, the clinical features frequently mentioned as essential for the diagnosis of classic JS comprise: hypotonia in infancy, developmental delay/mental retardation, and one or both of the following (not absolutely required but helpful for the diagnosis) - irregular breathing pattern in infancy (intermittent tachypnea and/or apnea) and abnormal eye movements.2,4-6

Associated findings include polydactyly (8%), ocular coloboma (4%), and hamartomas of the tongue (2%), dysmorphic facies, microcephaly, tongue protrusion, multicystic kidney disease, congenital heart disease, unsegmented midbrain tectum, retinal dystrophy and agenesis of the corpus callosum. In our case the patient had developmental delay, ataxia, nystagmus, with hypotonia associated with dysmorphic features.

Key neuroimaging features of JS include deep interpeduncular fossa, narrow isthmus (the pontomesencephalic junction), lack of decussation of superior

cerebellar peduncles, fourth ventricle giving "bat wing" appearance, thick vertical superior cerebellar peduncles, rostral deviation of fastigium of fourth ventricle, wide foramen of Magendie and dysplastic vermis. The brain stem, predominantly the medulla and upper cervical spinal cord, tends to be small. "Molar tooth sign" encompasses deeper than normal posterior interpeduncular fossa, prominent or thickened superior cerebellar peduncles, and vermian hypoplasia or dysplasia. Associated supratentorial anomalies are uncommon, but cerebral cortical dysplasia and gray matter heterotopias have been reported. Moderate lateral ventricular enlargement due to atrophy has been described in 6-20% of cases. 7.8

This syndrome is classified into two groups on the basis of presence or absence of retinal dystrophy. Patients with retinal dystrophy have a higher prevalence of multicystic renal disease and these patients also appear to have decreased survival rates compared with those of patients without retinal dystrophy.⁵ Our patient has no retinal dystrophy thus decreasing the morbidity associated with it. In patients with retinal anomalies, the renal function should be monitored regularly and ultrasonography should be done to detect cystic renal disease.

JS can include a broad range of additional signs and symptoms. Other clinical features define the subtypes of JS termed as Joubert syndrome and related disorders (JSRD). JSRD are categorized into six phenotypic subgroups: Pure JS, JS with ocular defect, JS with renal defect, JS with oculo-renal defects, JS with hepatic defect, and JS with orofaciodigital defects. Now, however, any instances that involve the molar tooth sign, including those with these additional signs and symptoms, are usually considered JS.

Developmental outcome in JS is variable and can be divided into three courses: first, children who die young; second, patients who survive but are severely developmentally delayed and have a variety of visual and motor handicaps; and third, patients whose developmental quotients fall within the mildly delayed range (70-80).

With the exception of rare x-linked recessive cases, JSRD follow autosomal recessive inheritance and are genetically heterogeneous with one locus pointing to chromosome 9q. In addition, consanguinity has been documented in a few cases. While mutations in many genes are known to be associated with JS, they are only identified in about 50% of affected people who have genetic testing. Therefore, genetic testing is not required for a diagnosis of JS or JSRD.⁹

Once a diagnosis of JS is made in one neonate or an infant, the diagnosis of this syndrome can be made by looking for the specific imaging findings at ultrasound during a subsequent pregnancy. Ultrasound examination from the 20th or 21st week of gestation can detect hypoplasia of the cerebellar vermis, foetal MRI will confirm the diagnosis. ¹⁰

The diagnosis of "classic" or "pure" JS is based on the presence of the following three primary criteria: the molar tooth sign on MRI, hypotonia (weak muscle tone) in infancy with later development of ataxia and developmental delays/intellectual disability. Our patient satisfies all the above criteria is this diagnosed as classical IS

Finally, the diagnosis is important for future procedures that require anesthesia. These patients are sensitive to respiratory depressant effects of anesthetic agents like opiates and nitrous oxide. Hence, the use of these anesthetic agents should be avoided in these patients.

CONCLUSION

JS is an uncommon inherited condition. Delayed diagnosis is usually related to its variable, nonspecific presentation. Awareness of the characteristic clinical and radiological findings in JS will help in early diagnosis, appropriate counselling and proper rehabilitation and anaesthetic precautions.

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