Case Report

Joubert Syndrome- A Case Presentation

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Abstract

Joubert syndrome is an autosomal recessive disorder characterized by partial or complete agenesis of the cerebellar vermis. Clinical features include attacks of tachypnea alternating with respiratory pauses, abnormal ocular movements, severe psychomotor retardation and ataxia. A 12 year-old male patient was diagnosed as Joubert syndrome by clinical and radiological findings. After 10 years follow up, his ataxic symptoms improved to be enough to supply self care. Our case was interesting because of his good prognosis which is rare for this condition.

Keywords: Joubert Syndrome, ataxia, prognosis, MRI, cerebellar

INTRODUCTION

Joubert syndrome (JS) is an autosomal recessive neurodevelopmental disorder which is characterized by the molar tooth malformation (MTM), a complex brainstem malformation that reflects aplasia or marked hypoplasia of the cerebellar vermis, thickened and elongated superior cerebellar peduncles and a deepened interpeduncular fossa17,15.

There is no clear data about its prevalence but in the consecutive evaluation of 3000 cranial MR imaging and CT examination of pediatric patients, Şener found 10 patients with Joubert syndrome23. Genetic studies related to disease have shown different features and locus in different populations7.

We present clinical and MR imaging features of our case who was followed during 10 years.
CASE PRESENTATION
A 12 year-old male patient was admitted to the ophthalmology clinic because of his complaints involved with gaze abnormalities. Perinatal anoxia and early developmental delay (he walked when he was three years old and he spoke in the same time.) were present in history. There was no infection history or drug use during pregnancy but her mother had four abortus with unknown causes previously. He had prominent gait ataxia since he walked, but no marked limb ataxia. His mother stated that he had hyperventilation episodes especially when he was nervous. When he began to school, his abnormal eye movements and ataxia was recognized by his teachers. His school success was low. These all complaints did not show marked progression, furthermore, he showed some improvement.

There was no consanguinity and no person who had similar symptoms in the family. In neurological examination, he had deviation to the right of the left eye in neutral position. There was horizontal nystagmus during gaze to left in both eyes. In the conjugate gaze to the right, there was limitation of the right eye. Occasionally, gaze apraxia or incoordination of eye movement were also observed. Fundoscopic examination revealed mild optic atrophy. He had no motor weakness of the limbs. Deep tendon reflexes were hyperactive in all extremities. Plantar responses were flexor. There was mild dysmetria and disturbed rapid alternating movements. He had severe gait ataxia. Romberg sign was negative and no sensory abnormality was found. He had borderline intelligence (IQ: 70 in Porteus test).

His routine hematological and biochemical tests were normal. ECG and telecardiography were normal. In cranial MRI; The axial T2-weighted MR images showed dysplasia of the superior cerebellar peduncles that resulted in a molar tooth configuration (Figure 1). The more caudal T2-weighted transverse MR image showed the fourth ventricle shaped like a bat wing (Figure 2). The T2-weighted transverse MR images showed severe hypoplasia of the vermis (Figure 3). Furthermore, there was evidence of severe vermian hypoplasia that involved the superior and inferior vermes, with an open communication between the fourth ventricle and the extracerebellar subarachnoid space.

![Figure 1: The axial T2-weighted MR image shows dysplasia of the superior cerebellar peduncles that resulted in a molar tooth configuration.](image1)

![Figure 2: The more caudal T2-weighted transverse MR image shows the fourth ventricle shaped like a bat wing.](image2)
In our patient, after ten years follow up, significant improvement was observed especially in truncal and limb ataxia. Occasionally tachipnea and tachicardia episodes were observed but he did not need any treatment. He was able to graduated from high school and started to work in an information office.

**DISCUSSION**

According to Patel and Barkovich’ classification (classification scheme for cerebellar malformations) Joubert syndrome (molar tooth malformations - associated with brain stem dysplasia) was classified as in focal cerebellar dysplasia (17).

Classic JS is associated with neonatal hypotonia, ataxia, developmental delay, mental retardation, and often neonatal apnea/hyperpnea (irregular breathing) and/or ocular motor apraxia (3,9,12,14,15,23). The syndrome has been reported as associated with various conditions (retinal coloboma and retinal dystrophy in approximately 50%, tongue protrusion in more than 30%, multicystic kidney disease in 30% of patients with retinal dysplastic features, and polydactyly in up to 15% of patients) (7,10,11,13,15,22).

Autistic features have also been reported as a relatively common component of JS (8). Our case had clinical features with the cases reported as classic Joubert syndrome. He had marked eye movement abnormalities, ataxia, respiratory abnormality and mental retardation.

The biochemical and genetic basis of the Joubert syndrome is very complex. The recent discoveries found that Joubert Syndrome Related Disease (JSRD) can be due to mutations in CEP290 (19,25), mutations in NPHP1 (5,16), RPGRIP1L (1,6,27), and TMEM67 (a.k.a. MKS3) (2) which previously implicated in ciliary function and this have further strengthened the hypothesis that JS related disease is due to defective ciliary function (4).

Mutations were identified in ARL13B in two families with the classical form of JS (4).

It was found associated with some other malformations (8% polydactyly, 4% colobomas, 2% renal cysts, 2% soft tissue tumors of the tongue) (18). Necropsy findings consisted of an almost total aplasia of vermis, dysplasias and numerous heterotopias of cerebellar nuclei and almost total absence of pyramidal decussation and anomalies in the structure of the inferior olivary nuclei, descending trigeminal tract, solitary fascicle and of the dorsal column nuclei (20).

The TWI of MRI of cases showed characteristic MRI features of Joubert syndrome including dilatation of the fourth ventricle with some appearance of bat-wing shaped, elongation and stretching of the superior cerebellar peduncles, dysphasia of the vermis, widening of the foramen of magendi and posterior cistern. It was suggested that MRI can provide characteristic findings of Joubert syndrome confirm the clinical diagnosis (21). Beside characteristic findings, the MRI finding of the patients revealed thinned optic tracts,
enlarged temporal horns, hig signal of the cerebral periventricular white matter abnormal signal in the decussation of the superior cerebellar peduncles, abnormal embryonic vessels associated with the dysplastic folia of cerebellar hemispheres\(^{(15)}\). As a result of midbrain, vermic and cerebellar peduncle abnormalities, axial neuroimaging showed a unique “molar tooth” appearance of these structures\(^{(24)}\). The brain MR imaging of our case was consistent with reported imaging features of Joubert syndrome.

It has been reported that the importance of recognizing Joubert syndrome is related to the outcome, its autosomal recessive trait, and the potential complications that may develop\(^{(26)}\). A follow-up study in 19 children with Joubert syndrome showed that three children died before 3 years of age, whereas the remaining children showed neuromotor developmental retardation and various levels of reduced cognitive development\(^{(22)}\). In our patient, prognosis was not poor. There was enough improvement to supply normal daily life. The diagnosis is important for future procedures that require anesthesia\(^{(18)}\). Patients with Joubert syndrome are extremely sensitive to the respiratory depressant effects of anesthetic agents, such as opioids, and nitrous oxide. Therefore, adult patients with ataxia must be evaluated carefully for Joubert's syndrome.

Cases with cerebellar vermic abnormalities must be evaluated for Joubert syndrome and must be considered for various progresses of the disease.

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