The management of Joubert Syndrome in Physical Medicine and Rehabilitation department

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Abstract

Since Joubert et al. first described a familial syndrome comprised of agenesis of the cerebellar vermis, episodic hyperpnea and apnea, abnormal eye movements, ataxia, and retardation associated with genesis of the cerebellar vermis, several additional cases have been reported from various parts of the world. Other abnormalities have been associated with Joubert syndrome, such as an occipital meningocele, polydactyly, facial asymmetry, and chorioretinal coloboma. We report the case of a 4-year-old male, referred to our rehabilitation department with a history of hypotonia and delayed psychomotor development. Cerebral magnetic resonance imaging (MRI) led to the clinical diagnosis of Joubert Syndrome.

Keywords: Joubert Syndrome, Cerebral MRI, Molar tooth sign.

INTRODUCTION

Joubert syndrome is a relatively rare autosomal recessive congenital disorder, whose locus is on chromosome 9q; it is characterized by cerebellar vermis hypoplasia or aplasia [1]. Some cases also possessed anomaly of the brainstem [2]. Other commonly found central nervous system abnormalities extending beyond the cerebellum have also described, including a cortical atrophy, delayed myelination, and an enlarged fourth ventricle [3]. Characteristic clinical symptoms and signs include motor and respiratory abnormalities [4]. It is currently included in the malformation spectrum of cerebello-oculo-renal syndromes [1]. An image known as a “molar tooth sign” is typically observed in cerebral MRI [5].

CASE REPORT

This This boy was the second child of a healthy related couple with a second degree of consanguinity. He had been a preterm infant (34 weeks), born after an uncomplicated pregnancy and delivery. His birth weight was 2500 grams. Only a macrocephaly was evident at birth and he has a regular breathing pattern.

Soon after birth, the infant was hypotonic, with little spontaneous movement. When examined at 4 years of age, he was emaciated. Head circumference showed a macrocephaly. All aspects of his development were delayed. He could roll over, but could not hold his head upright or sit unsupported. He smiled but didn’t react to auditory stimuli and didn’t speak. Ocular examinations revealed a bilateral divergent squint and inability to track objects with eyes. Funduscopic examination was normal. He had a generalized hypotonia but deep tendon reflexes were normal. There was an important negative findings included: Regular breathing pattern, no organomegaly and no polydactyly or syndactyly.

The audiogram revealed a bilateral sensorineural hearing loss. Numerous laboratory studies were normal including: hemoglobin, blood glucose, serum electrolytes, blood urea nitrogen, serum GOT and GPT, blood gas analyses, blood lactate and pyruvate, urinalysis, and cerebrospinal fluid. Electrocardiography and electroencephalography were also normal. No cystic lesions of the kidneys were seen by ultrasonography.

With these findings, a cerebral MRI was requested, which showed the classic “molar tooth sign”, by hypoplasia of cerebellar vermis, and led to the clinical diagnosis of Joubert Syndrome. We have

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prescribed a stander and hearing aid. A rehabilitation program was started consisting of: joint mobilization, muscle strengthening, occupational and speech therapy.

**Figure 1:** Macrocephaly and bilateral divergent squint  
**Figure 2:** Cerebral MRI showing agenesis of cerebellar vermis causing the “molar tooth sign”

**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 [6].

Reliable epidemiological data for Joubert syndrome are scarce. A prevalence of between 1 per 80 000 and 1 per 100 000 livebirths is reported by many investigators, but this is probably an underestimate that is indicative of the low awareness of the molar tooth sign in historical texts [7,8].

Clinical criteria of Joubert syndrome comprise cerebellar vermis hypoplasia/aplasia, hypotonia, developmental delay, and at least one of two additional manifestations including respiratory dysfunction (episodic hyperpnea and apnea) and abnormal eye movement [9,10]. This syndrome shows an autosomal recessive heredity, and various complications involving neurological and physical anomalies, including cystic kidney, polydactyly, meningocele, colobomas and soft tissue tumors of the tongue are known [11]. This syndrome is heterogenous with several chromosomal loci, and recent findings have implicated specific genes [12].

Patients with Joubert syndrome need to enter a diagnostic workflow and undergo regular follow-up examinations to ensure proper assessment and management of multiorgan complications [13]. In neonates and infants, particular care should be taken to manage episodes of abnormal breathing since prolonged episodes of apnoea can be life threatening and need assisted ventilation. Respiratory defects tend to improve spontaneously and sometimes disappear with age, although sleep-related breathing disorders can persist beyond childhood in some patients [4].

Nephrological assessment is particularly important, especially in young children. About 20–30% of patients with Joubert syndrome might develop juvenile nephronophthisis, and it can remain asymptomatic for several years, until acute or chronic renal insufficiency manifests in the late first or early second decade, eventually necessitating dialysis or kidney transplant [8].

Renal ultrasound might reveal small cysts and loss of cortico-medullary differentiation, or can remain negative. Thus, monitoring of defects in urinary concentration ability in young children (first morning void urine analysis, polydipsia, polyuria, or a combination of these), which generally precede impairment of renal function, is important [14].

Congenital liver fibrosis might be suspected in the presence of hepatomegaly, raised concentrations of liver serum enzymes, or abnormal liver echogenicity [15].

Our case was particular by the presence of a hearing loss that has only been reported once in the literature [16]. Most Joubert syndrome case reports, however, concern young children who could still develop sensorineural hearing loss (SNHL) later in life. Their often severe mental retardation and frequent absence of speech may inhibit easy detection of hearing loss, especially when it only affects specific frequencies [17].

The “molar tooth sign” is observed in axial neuroimaging cuts, such as cerebral CT and MRI, and is characterised by a deep posterior interpeduncular fossa, thickened and elongated superior cerebellar peduncles, as well as hypoplasia or agenesis of the cerebellar vermis [11].

In fetuses with Joubert syndrome, ultrasound examination from the 20th or 21st week of gestation can detect hypoplasia of the cerebellar vermis, which can be associated, in a subset of foetuses, with polydactyly, occipital encephalocele, or both. If a cerebellar malformation is suspected, foetal MRI will confirm the diagnosis, often allowing recognition of the molar tooth sign [18].

In families with a genetic diagnosis of Joubert syndrome in a previously affected child, prenatal diagnosis becomes possible in the first trimester of pregnancy based on genetic testing of a chorionic villous sample [13].

The prognosis of these patients is poor, with a five-year survival rate of only 50% [19]. Genetic counseling for this syndrome is necessary because there is a 25% risk of recurrence for each subsequent pregnancy [20].

Finally, appropriate rehabilitation protocols can help young patients to overcome delays in the acquisition of developmental milestones and cognition.

**CONCLUSIONS**

Joubert syndrome is a rare autosomal recessive disorder, characterized by ataxia, psychomotor retardation, ocular and respiratory abnormalities related to dysgenesis of cerebellar vermis and mesencephalon. The confrontation of the clinical data with the radiological image typically observed in cerebral MRI “molar tooth sign” led to the clinical diagnosis only guarantor of genetic counseling and prenatal diagnosis.

**Conflict of interests**

The authors have none to declare.

**Informed consent**

Was obtained from the parents.

**REFERENCES**


