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Case Report

Fetal Corpus Callosum Agenesis Revelling a Joubert Syndrome in an Infant

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Abstract

Joubert syndrome (JS) is a recessive neurodevelopmental disorder characterized by midbrain-hindbrain malformation recognizable on axial brain magnetic resonance imaging with the so called "Molar Tooth Sign". Although the radiological hallmark of JB is neurological, the variable involvement of a spectrum of multiorgan abnormalities is also described from the neonatal period, and that include mainly the retina, kidneys, skeleton, and liver. Recent genetic research have incriminated 21 genes so far, all of which encode for proteins of the primary cilium or its apparatus.

Keywords: *Corpus Callosum Agenesis; Joubert Syndrome; Molar Tooth Sign; Magnetic Resonance Imaging*

Abbreviations

MTS: Molar Tooth Sign; MRI: Magnetic Resonance Imaging; JS: Joubert Syndrome

Introduction

Molar tooth sign on MRI is the radiological trademark of Joubert syndrome and it associative disorders. This useful "diagnostic handle" is based on a radiologic triad of thick and straight superior cerebellar peduncles, deep interpeduncular fossa, and hypoplastic/dysplastic superior cerebellar vermis. We report a 7 month old girl with Joubert syndrome in whom the MRI shows on one hand typical radiological features related to her condition and on the other a corpus callosum agenesis.

Case Report

A 7 month old girl was admitted to Ibn Sina children hospital for evaluation of her atony and developmental delay, in addition to strabismus and ptosis in both eyes. At 6 month of prenatal life, intrauterine ultrasound had revealed agenesis of the corpus callosum.

She was the only one, with notion of first degree consanguinity, born at term after a normal pregnancy, weighting 2880 kg, her psychomotor milestones were markedly delayed. At age 7 months, when she was first examined she smiled but did not fix or follow, because of lack of tone, she was unable to up her head deep tendon reflexes were normal a grasping reflex was present she was not able to track objects. She had social smile following auditive inputs on neuro ophthalmological examination she had horizontal nystagmus, ptosis on both eyes more accentuated on the left one. Neurophysiological examination were also negative, blood and urine tests excluded metabolic, infective muscular or genetic diseases, abdominal ultrasound was preteen.

Follow up MRI confirmed the ultrasound detected splenium callosal agenesis and revealed further mid and hind brain anomalies such as hypoplasia of the cerebellar vermis, abnormalities of the brain stem at the ponto-mesencephalic junction and dysmorphic fourth ventricular in addition the infamous “molar tooth sign” that sealed the Joubert syndrome diagnosis.

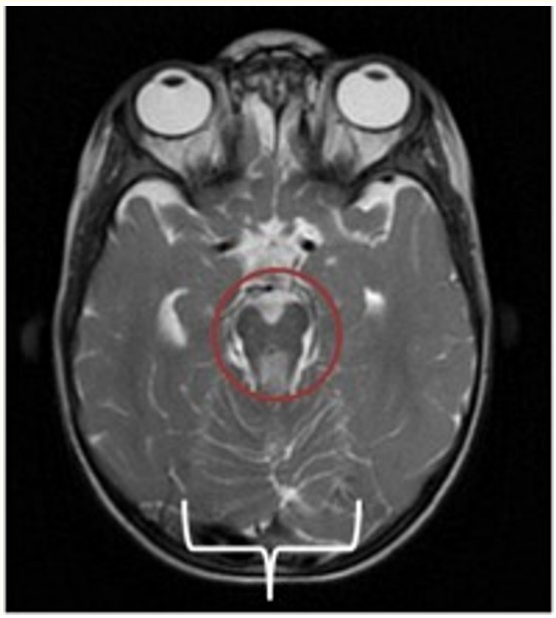

Figure 1: *T2-weighted axial image showing “molar tooth sign” (red circle):*

-Long, thick superior cerebellar peduncles and a deep interpeduncular fossa.

-Vermis hypoplasia with flanking cerebellar hemispheres (white arrow).

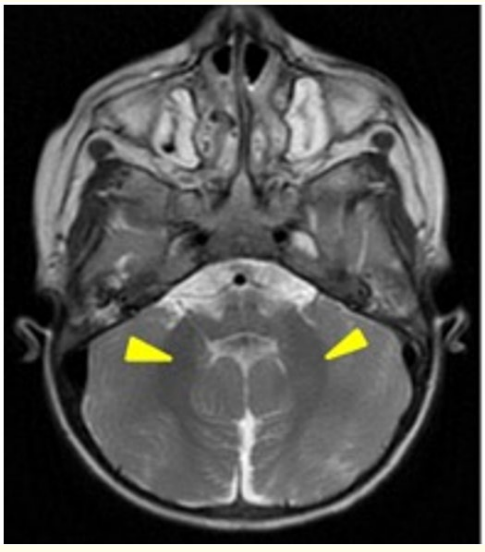

Figure 2: *T2-weighted axial image revealing the bat wing configuration of the 4th ventricle (yellow triangle).*

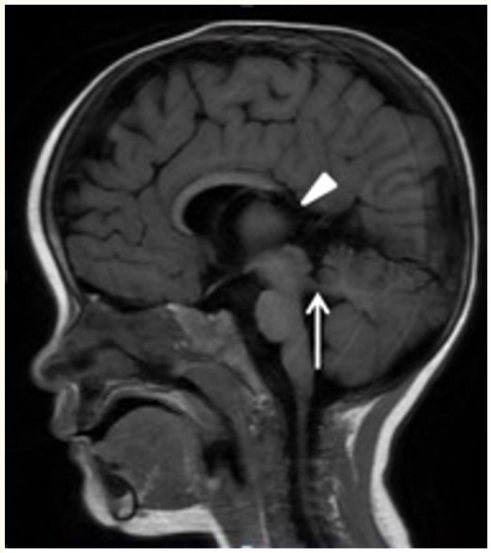

Figure 3: *T1-weighted parasagittal image showing a horizontally oriented superior cerebellar peduncle (white arrow) and partially agenesis of splenium corpus callosum (white triangle).*

Discussion

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 epidemiologists [1]. In terms of demographic distribution, the mean age of cases with JS was 2.6 ± 2.3 years. Consanguinity was observed in 56.4% cases with JS [6].

Clinically JS can be suspected from as early as the first few months of life, upon the observance of hypotonia, abnormal ocular movements and occasionally changes in respiratory pattern. Later, delay in the acquisition of developmental steps and intellectual disability of variable severity are seen in nearly all children, with expressive speech usually affected more than comprehension because of concurrent ocular motor apraxia. Nevertheless, patients with normal cognitive function have also been reported. Facial dysmorphisms are often present however, they do not aid the diagnosis, since in many patients they can be entirely normal. About 50% of children learn to walk independently and develop ataxia with a broad-based, unsteady gait, and have difficulties in running or climbing stairs [1].

The clinical picture of Joubert syndrome can be complicated by a large range of associated organ defects, which can manifest at different ages. Among these defects, the most common are retinal defects renal defects (nephronophthisis or cystic dysplastic kidneys), and congenital liver fibrosis. Rarer features include chorioretinal or optic nerve colobomas, congenital heart malformations, situs inversus, severe scoliosis, skeletal dysplasia, Hirschsprung disease, and midline oral and facial defects, such as cleft lip, cleft palate, or both, notched upper lip, lobulated tongue with multiple frenula, and lingual or oral soft tumours [1].

Diagnostic confirmation for JS is obtained by the MRI upon finding the MTS as the fundamental diagnostic imaging trademark. MTS is a cerebellar vermis hypoplasia that resulted from an abnormally deep interpeduncular fossa, and thickened, elongated cerebellar peduncles. In addition, the fourth ventricle appears as a "bat-wing". The partial or complete absence of cerebellar vermis results in the separation of bilateral cerebellar hemispheres at the midline, allowing fine-line cerebrospinal fluid. Both clinical and radiographic examination confirmed that the case had diagnostic criteria of JS [5].

Prenatally, the possibility of JS can be raised by cerebellar vermis hypoplasia detected on routine ultrasound. Fetal MRI may be helpful in further delineating anomalies identified by ultrasound; however, the typical MTS is often not detected prenatally [4]. In our case fetal US showed splenium callosal agenesis which gave rise to a differential diagnosis among 30 syndromes in which Aicardo syndrome. Agenesis of the corpus callosum has never been reported in children with Joubert syndrome except in less than hand full of case reports where the authors pushed for the attractive hypothesis of a developmental abnormality of midline structures extended to the supratentorial compartment [4].

It is good to remind that the differential diagnosis for JS includes other disorders with anomalies of the posterior fossa such as Dandy-Walker malformation, Poretti-Boltshauser syndrome and other conditions associated with ataxia and/or cerebellar vermis hypoplasia. Many children with JS are first given a diagnosis of ocular motor apraxia, or ataxic cerebral palsy before the MTS is identified [5].

The actuality in term of radiology in JS is the recent use of High-resolution diffusion tensor imaging and tractography that have added a new dimension in understanding of fiber tract abnormalities in Joubert syndrome. Absence and or thinning of the dorsal pontocerebellar tract and abnormal thickening of the ventral pontocerebellar tract are novel findings in Joubert syndrome and have not been previously described in the literature. In addition, abnormal decussation of superior cerebellar peduncles and absence of red dot sign is a further indication that they represent a spectrum of abnormal midline axonal migration, adding by that more pathognomonic diagnostic features to this rare disease [3].

Joubert syndrome is associated with poor prognosis. Treatment is generally supportive, depending on the presence of neurological deficits and cognitive impairment. These individuals are very sensitive to respiratory depressants, and therefore medication should be administered with caution, specifically if the JS in associated with other major brain structures such as the corpus callosum where the patient can be subject to frequent seizures and severe mental retardation [2].

Conclusion

The interacted correlation between Joubert syndrome and corpus callosum agenesis still need further research especially with the increase of similar case reports on the matter and yet to be codified subtypes of Joubert syndrome known as Joubert syndrome related disorders which is an overlap of a spectrum of genetic early life syndromes.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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