

Case Report

The 'Molar Tooth Sign' in Joubert Syndrome

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Abstract

The molar tooth sign is seen in very few conditions and is a very rare paediatric central nervous system congenital anomaly. Molar tooth sign is the result of cerebellar vermis hypoplasia, thick and maloriented superior cerebellar peduncles, and an abnormally deep interpeduncular fossa.¹ In Joubert syndrome this is seen in about 85% of patients.

We present a case of 13 months old baby boy with recurrent episodes of fits and hyperpnoea, regression of milestones and developmental delay. MRI examination showed the characteristic molar tooth sign with apposition of cerebellar hemispheres, batwing-shaped fourth ventricle communicating through a thin fissure with foramen of Magendie, cerebellar vermis agenesis and deep interpeduncular fossa consistent with diagnosis of Joubert syndrome.

Introduction

Molar tooth sign is a characteristic MR appearance of brainstem which results from cerebellar vermis hypoplasia, thick and maloriented superior cerebellar peduncles, and an abnormally deep interpeduncular fossa.¹ The presence of molar tooth sign in conjunction with appropriate clinical features is almost diagnostic of Joubert syndrome. This sign results from abnormal development in the brainstem and cerebellar vermis. These developmental anomalies can be picked prenatally by Ultrasound and MRI examinations if careful attention is paid to the posterior fossa structures especially on anomaly ultrasound scan. This may be helpful in counselling of the parents about the prognosis and outcome of their baby. However, this syndrome is mostly diagnosed after birth.² As expected clinical features almost reflect the structural defects. The main problems being disturbances of balance, respiration and vision.

Case Report

A 13 months old baby boy presented to the Paediatric Emergency Department in Aga Khan University Hospital, Karachi in May 2008 with developmental delay, regression of milestones and recurrent episodes of fits and hyperpnoea. After initial resuscitation and stabilization, the patient was shifted to paediatric ward where detailed examination was performed. On examination his weight and height were around 30th percentile for his age. Central nervous system

evaluation revealed central hypotonia and hypoesthesia. Ophthalmologic review revealed ptosis and left corneal ulcer with epithelial defect. The other systems were unremarkable.

Electroencephalogram (EEG) was performed which was normal. Subsequent MRI examination showed characteristic molar tooth sign (Figure-1) with prominent superior cerebellar peduncles, cerebellar vermian hypoplasia and deep interpeduncular fossa (Figure-2). Apposition of cerebellar hemispheres and bat wing-shaped fourth ventricle communicating through a thin fissure with foramen of Magendie were also noted. Ventricular system appeared slightly prominent with prominent cerebral peduncles. Normal grey- white differentiation was noted in the supra tentorial region. In post contrast images no abnormal meningeal enhancement or focal enhancing lesion was seen.

Family history revealed that he was the second offspring of a consanguineous marriage. The first offspring



Figure-1: Molar tooth sign. Axial image at the level of mesencephalon demonstrates prominent superior cerebellar peduncles giving the molar tooth appearance (arrow).



Figure-2: T2 weighted sagittal image at the midline showing cerebellar vermis agenesis and deep interpeduncular fossa (arrow).

had an intra-uterine death and was diagnosed on ante-natal ultrasound as having some central nervous system abnormality, the details of which are not known.

Based upon clinical features and characteristic MR features he was diagnosed as a case of Joubert syndrome.

Patient was managed conservatively for one week in paediatric ward for his respiratory symptoms and upon stabilization was discharged with instructions to follow up after one month. Patient, however, was lost to follow up.

Discussion

Joubert syndrome is a rare familial syndrome characterized by episodic panting in the newborn and jerky eye movements in the neonatal period with later development of mental retardation, cerebellar ataxia and episodic hyperpnoea with hyperventilation.^{1,2} Both sexes are affected almost equally with onset in early infancy. Most patients die in infancy or early childhood. The syndrome is believed to be transmitted as an autosomal recessive trait. However, definite etiological factor(s) remains unknown.

Marie Joubert described the syndrome in 1968-69. It is a rare developmental defect of the cerebellar vermis. The phenotype is highly variable and may include episodic

hyperpnoea, abnormal eye movements, hypotonia, ataxia, developmental delay, and mental retardation.³ Less common clinical features include seizures, hemifacial spasms, polydactyly, colobomas, ptosis, renal cysts, soft tissue tumours of tongue and occipital meningocele.

MRI is the imaging tool of choice. The main imaging findings consistently seen are partial or complete absence of the cerebellar vermis, thickened and abnormal orientation of the superior cerebellar peduncles, thinning of the isthmus portion of the brainstem with a deep interpeduncular cistern producing the pathognomonic molar tooth sign. The molar tooth appearance is also contributed by failure of normal decussation of the superior cerebellar peduncular fibres during embryonic development resulting in thickening of peduncles that follow a more horizontal course extending perpendicular to the brainstem between the midbrain and cerebellum. The absence of crossing fibres also leads to decreased anteroposterior diameter of the brainstem at the level of midbrain and deep interpeduncular cistern. Combination of these findings demonstrates the classical molar tooth configuration on axial and coronal MR images of the midbrain. Additional MR findings include absent or hypoplastic cerebellar vermis. Absence of vermis results in a midline cleft between the two cerebellar hemispheres resulting in batwing appearance of the fourth ventricle on axial images. At diffusion tensor imaging (DTI) and fiber tractography (FT) a thickened and elongated superior cerebellar peduncle with a horizontal configuration can be seen.⁴

Less commonly molar tooth sign is seen in other rare syndromes recently described as cerebello-oculo-renal syndromes. These are Varadi-Papp, COACH, Dekaban-Arima, and Senior-Loken syndromes. Varadi-Papp syndrome has been associated with cleft lip and palate, lingual nodule and a Y-shaped metacarpus. COACH (cerebellar vermis aplasia/hypoplasia, oligophrenia, ataxia, coloboma, hepatic fibrosis) syndrome is distinguished by absence of episodic hyperpnoea and oculomotor abnormalities. Renal and retinal pathologies are also seen in Dekaban-Arima and Senior-Löken syndromes, in addition to molar tooth sign, and distinguishes them from Joubert syndrome.^{2,3,5}

On histopathology, there is reduction of neurons of the basis pontis and reticular formation. Malformations of the medulla are also observed and include hypoplasia of the inferior olivary nuclei, solitary nuclei and tracts and the nucleus and spinal tracts of trigeminal nerve. In addition there is dysplasia of the caudal medulla at the cervicomedullary junction.²

The diagnosis of this syndrome is important for future procedures that require anaesthesia because these patients are extremely sensitive to the respiratory depressant effects of anaesthetic agents such as opioids and nitrous oxide. These

agents should be avoided and close perioperative respiratory monitoring is essential.⁵

To conclude; with appropriate clinical presentation, elaborate physical evaluation and the typical MR finding of the molar tooth sign, diagnosis of Joubert syndrome can be made without much difficulty.

References

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