

CASE REPORT

NYSTAGMUS AND BEYOND: A RARE OCULAR MOTILITY DISORDER

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Joubert syndrome is a rare autosomal recessive disorder predominantly involving the cerebellar vermis and brain stem. It is characterized clinically by global developmental delay, abnormal ocular movements, hypotonia, ataxia, intellectual disability and neonatal breathing abnormalities. Due to its uncommon and unconventional presentation, its diagnosis is usually delayed. Diagnosis of this atypical disease essentially relies upon the atypical finding of the “molar tooth” sign on Magnetic Resonance Imaging (MRI). We report a case of a 5-year-old boy who presented with abnormal eye movements, regression of milestones and developmental delay. MRI investigation revealed the distinctive molar tooth sign and bat wing shaped 4th ventricle. It requires high levels of clinical suspicion and holistic approach to such children who present with delayed milestones and abnormal eye movements, to reach at early detection and diagnosis of such rare pathologies.

Keywords: Autosomal recessive; Molar tooth sign; Joubert syndrome

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INTRODUCTION

Joubert syndrome is an autosomal recessive congenital malformation first reported in 1969 by Dr. Marie Joubert. She described this disease as a syndrome of abnormal ocular movements, episodic hyperpnoea, ataxia, and retardation.¹ The molar tooth sign, resulting due to the hypoplasia of the vermis of the cerebellum and thickening of superior cerebellar peduncles, on MRI is pathognomonic for Joubert Syndrome.² The prevalence of this rare disorder is estimated to be 1/100,000.³ Till today, only 200 cases have been reported worldwide.⁴ For the first time, we are reporting this disorder from Islamabad-Punjab Region of Pakistan.

CASE REPORT

A 5-year-old boy was brought to the eye clinic by his parents in November 2016 for poor vision, abnormal eye movements, and unsteady gait. History narrated by his mother revealed that he was born at term through a Caesarean section to non-consanguineous parents. The child did not cry immediately after birth and was admitted to the neonatal intensive care unit for the next few hours due to central cyanosis.

For the first month, he was lethargic and unable to suck properly and was fed through a nasogastric tube. He started holding his neck at the age of 1 year, sitting at 2 yrs, crawling at 3, walking and speaking single words at 4 years. The delayed acquisition of these milestones shows a global delay in his development. He is

the youngest of 6 children, 3 sisters aged 22, 18 and 15 and 2 brothers aged 16 and 13. All his sisters are healthy but both brothers are slow in learning and residing in the United States.

On inspection, he appeared awake and alert. General skeletal and facial examination was normal. CNS examination revealed mildly decreased muscle tone, gait ataxia, speech dysarthria and in general, developmental delay.

On Ocular examination, his VAR (Visual acuity right eye) was 3/60 and VAL (Visual acuity left eye) was 6/60. On motility examination, he had jerky and non-fixing eye movements. Pursuit movements were absent and only saccades were visible. Exotropia of the right eye in the primary position, oculomotor apraxia and see-saw nystagmus were observed. Both pupils were round and reactive to light. The retina was hypopigmented with no foveal landmark. The retinal vasculature and optic disc were normal in both eyes.

On the basis of these neurological signs and ocular findings and thinking it most appropriate, we ordered an MRI of the brain. Subsequent MRI investigation revealed hypoplasia of the vermis of the cerebellum with pronounced superior cerebellar peduncles that resulted in the typical molar tooth sign (Figure-1). The bat-wing shaped fourth ventricle was noted in the more caudal MR images (Figure-2). Based on these clinical and typical radiological findings we made a diagnosis of Joubert syndrome.

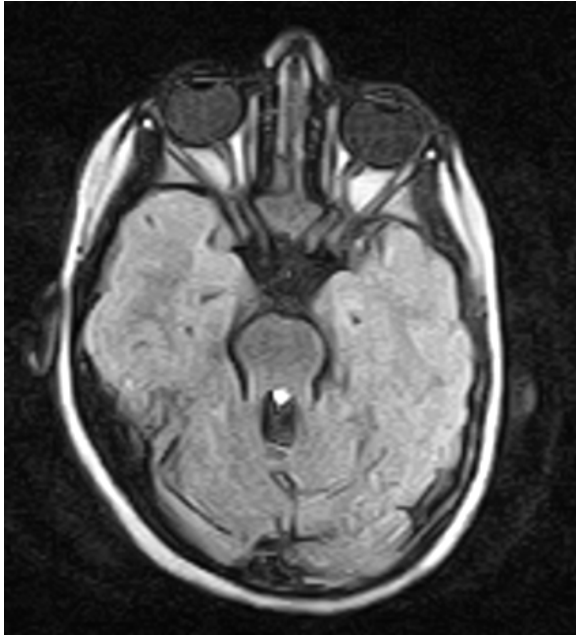


Figure-1: Molar tooth sign

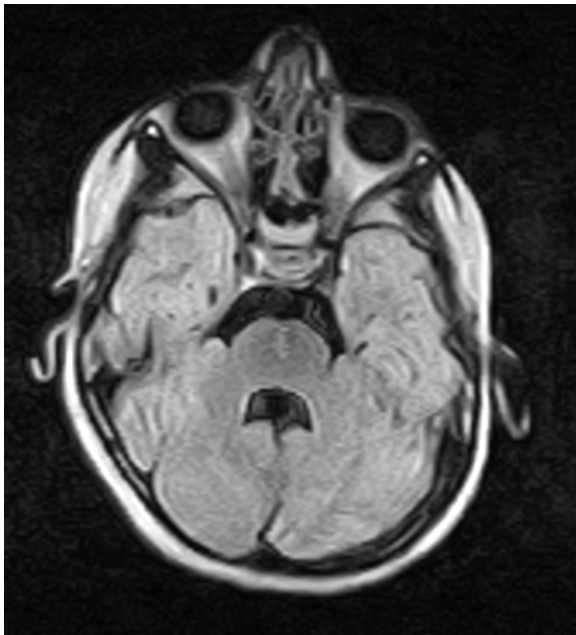


Figure-2: Bat-wing shaped fourth ventricle

DISCUSSION

Joubert syndrome is one of the rarest familial diseases and is almost unknown in our country. To our knowledge this has been hardly diagnosed in Islamabad. It is identified and diagnosed by specific clinical and radiological findings. There are three primary criteria for the diagnosis of Joubert syndrome, namely, a peculiar cerebellar and brainstem malformation described as the molar tooth sign, hypotonia, and global developmental delay.

These findings occur along with either atypical ocular or respiratory movements, or both.⁵

If there is multi-system organ involvement associated with the findings described above, it is titled as "Joubert syndrome and related disorders". This further has 8 phenotypic subtypes: Classic or pure Joubert syndrome; Joubert syndrome with retinal disease, with renal disease, with oculorenal disease, with hepatic disease, with oral-facial-digital features, with acro-callosal features and with Jeune asphyxiating thoracic dystrophy features.⁶

Mainstay of investigations in the diagnosis of Joubert syndrome are the findings on MRI. The important imaging findings are aplasia or agenesis of the vermis of the cerebellum, dysgenesis of the isthmus region of the brainstem with a buried interpeduncular cistern and thickened, elongated and abnormally oriented superior cerebellar peduncles. An amalgam of these three findings forms the "molar tooth sign", which is pathognomonic for Joubert syndrome.²

Associated with this are the umbrella or bat-wing appearance of the fourth ventricle and the vermian cleft, formed between the two normal cerebellar hemispheres due to the gap left by the aplastic vermis. Collectively, the bat-wing appearance, molar tooth sign and vermian cleft are regarded as the basic radiological findings of Joubert syndrome.⁷ Other signs include the "Buttock sign" which appears in the coronal images due to the absence of the posterior vermian lobe and the "Shepherd's Crook sign" which appears in the sagittal images where the abnormal superior cerebellar peduncles and surrounding cerebellar hemisphere form the arc of the crook and the brainstem and pons form the shaft of the crook.⁸

Management of such cases is difficult and needs yearly ophthalmic evaluation, correction of refractive error and monitoring of intraocular pressure. It requires urine analysis, blood urea nitrogen and creatinine levels, liver and kidney ultrasound and lifelong monitoring for obstructive and central sleep apnoea. Appropriate interventions are tailored to the needs of each individual. Parents need genetic counselling for further children and early detection of chromosomal abnormalities with the possibility of termination of pregnancy in mind.

Most of the time, patients present with unexplained features which do not fit into any clinical pattern rendering the diagnosis difficult. This multi system involvement and bizarre motility pattern warrant high levels of clinical suspicion, monitoring, holistic approach and timely relevant

investigation of such children for early detection and diagnosis of even rare pathologies such as Joubert syndrome.

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