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Case Report

Jouberts Syndrome: A Case Report

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Abstract: Jouberts syndrome is an uncommon autosomal recessive neurodevelopmental disorder involving cerebellar vermis and brain stem. We report a case of 5 year old male boy presented with global developmetal delay, abnormal eye moments and abnormal respiratory moments. On examination decreased muscle tone, nystagmus, and gait ataxia is present. Magnetic resonance imaging (MRI) revealed characteristic Molar tooth sign and bat wing appearence of fourth ventricle.
Keywords: Jouberts Syndrome, Cerellum, Developmental Delay, Nystagmus, Autosomal Recessive

INTRODUCTION

In 1969, Dr. Marie Joubert and colleagues first described four siblings with cognitive impairment, ataxia, episodic tachypnea, eye movement abnormalities, and cerebellar vermis agenesis in a large French-Canadian family with consanguinity traced 11 generations to a common ancestor [1]. The incidence of Jouberts syndrome has been estimated as between 1/80,000 and 1/100,000 live births[2]. Joberts syndrome is an autosomal recessive neurodevelopmental disorder [3]. Many children with Joubert syndrome exhibit dysmorphic facial features that include broad forehead, arched eyebrows, eyelid ptosis, wide-spaced eyes, open mouth configuration, and facial hypotonia[4]. Joubert syndrome also have other clinical manifestations involving the CNS (occipital encephalocele, corpus callosal agenesis), eyes (coloboma, retinal dystrophy, nystagmus, oculomotor apraxia), kidneys (nephronophthisis, cystic dysplasia), liver (hepatic fibrosis), and limbs (polydactyly)[2].

CASE REPORT:

A 5 year old male child was brought to our hospital by her father with the chief complaints of delayed milestones, abnormal eye moments and abnormal respirations. Boy attained sitting, walking, and speech milestones at 1, 2, and 4 years respectively and they are delayed. He has abnormal eye moments being noticed by parents since age of 9 months in form of upward rolling of his eyes with head tilt and poor fixation. His father stated that he had hyperventilation episodes when he was nervous. There is no history of consanguineous marriage. The birth history consisted of delivery at full term gestation by vaginal route at tertiary care hospital. Child did not cry immediately after birth, cried after rescuitation. Child was admitted in NICU for irregular respiration. Physical examination child had no dimorphic facial features. Central nervous system examination revealed nystagmus, decreased muscle tone, and gait ataxia. There was global delay in developmental mile stones. There is moderate developmental delay with developmental quotient 40. Routine hematological, urine examination, 2d ECHO, and thyroid profile were unremarkable. MRI scan done revealed brainstem is small, volume loss involving the left half of brain stem and cerebellar vermis is hypoplastic. The Molar tooth sign appearence of pontocephalic junction (figure 1) and Bat wing appearance of the fourth ventricle (figure 2). The Genetic analysis was done revealed homozygous TCTN2 gene mutation. With all these features diagnosis of jouberts syndrome was made.

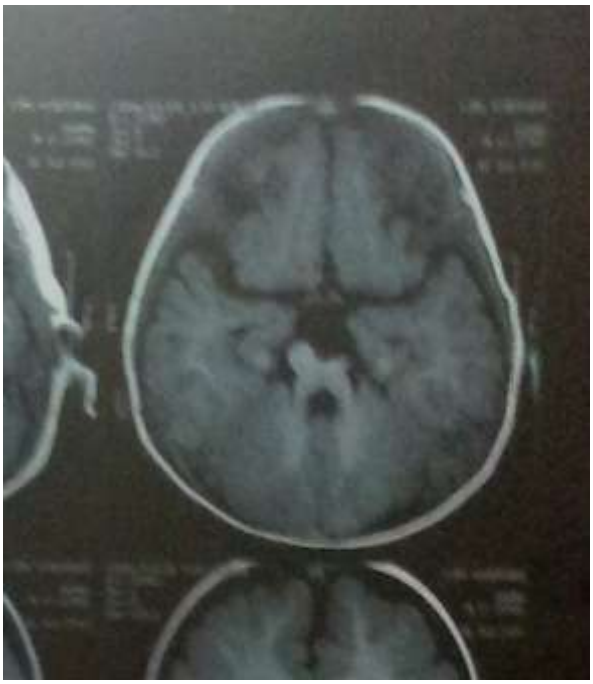

Figure-1: Molar Tooth Sign.

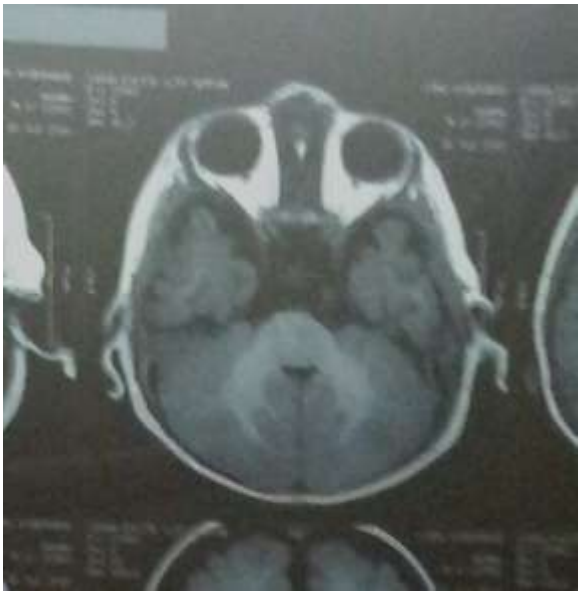

Figure-2: Bat Wing Appearance of Fourth Ventricle.

DISCUSSION:

The features necessary for a diagnosis of classic JBTS include the following (a) The molar tooth sign on axial views from cranial MRI studies comprised of these 3 findings: cerebellar vermis hypoplasia (CVH), deepened interpeduncular fossa, and thick, elongated superior cerebellar peduncles (b) intellectual impairment/developmental delay, of variable degree; (c) hypotonia in infancy; (d)one or both of the following (not required but supportive of the diagnosis): irregular breathing pattern in infancy (episodic apnea and/or tachypnea, sometimes alternating) and abnormal eye movements (nystagmus and/or oculomotor apraxia (OMA))[4]. The dentate nuclei, the major source of cerebellar output to the cerebral cortex, are fragmented into islands. Malformation of various pontine and medullary structures, including the basis pontis, reticular formation, inferior olivary, dorsal column and solitary tract nuclei, have been reported, which may explain the respiratory defects in JS.(5) Developmental abilities, in particular language and motor skills, are delayed in all JSRD patients, with variable degrees of severity. (CNS) malformations include hydrocephalus, cystic enlargement of the posterior fossa, abnormalities of the corpus callosum, white matter cysts, and absence of the pituitary gland . Abnormal migration defects, mainly periventricular nodular heterotopia, and polymicrogyria [5].

The term "Joubert syndrome and related disorders" (JSRD) refers to those individuals with JS who have additional clinical findings [6]. JSRD are categorized into six phenotypic subgroups: Pure JS, JS with ocular defect, JS with renal defect, JS with oculorenal defects, JS with hepatic defect, and JS with orofaciodigital defects [7]. The 19 genes in which biallelic mutations are known to cause Joubert syndrome and related disorders are: NPHP1, AHI1, CEP290 (NPHP6), TMEM67 (MKS3), RPGRIP1L, CC2D2A, ARL13B, INPP5E, OFD1, TMEM216, KIF7, TCTN1, TCTN2, TMEM237, CEP41, TMEM138, C5orf42, TMEM231, and TCTN3 [6]. Mutations of AHI1 have recently been shown to cause a form of JS. TCTN2 (tectonic family member 2) comprises 18 exons and encodes several transcripts. Nonsense, frameshift, and splice site mutations in this gene have been implicated in JSRD [6].

The hallmark imaging features of JS are: dysgenesis of the isthmus (part of the brainstem between the pons and inferior colliculus), which is seen as elongation and thinning of the pontomesencephalic junction, and deep interpeduncular fossa; thickening of the superior cerebellar peduncles; hypoplasia of the vermis characterized by incomplete lobulation and enlarged fourth ventricles; and incomplete fusion of the halves of the vermis, creating a sagittal vermis cleft seen on axial or coronal MRI planes. Combination of the first three features produce the characteristic MTS on axial MRI. Hypogenesis of the vermis results in a triangular- shaped midfourth ventricle and a bat-wing-shaped superior fourth ventricle [8]. Initiation of periodic, comprehensive developmental assessments and a program of interventions including special education, physical, occupational, and speech therapy, with adaptive equipment as needed, have shown significant benefits in attainment of developmental milestones for many children with JSRD [4].

CONCLUSION:

Jouberts syndrome is a rare autosomal recessive disorder involving cerebellum. Most of the cases present with abnormal eye moments, irregular respiration and developmental delays. Examination will reveal hypotonia and gait disorders. This syndrome has characteristic molar tooth appearance on MRI imaging.

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