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Case Report on Joubert Syndrome

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Abstract

The uncommon hereditary autosomal recessive heterogeneous neurodevelopmental illness known as Joubert syndrome is characterized by cerebral vermis malformation and mostly manifests as molar tooth sign, hypotonia, and developmental delay. In addition to the CNS, JS can impact other systems that are referred to Joubert . All illnesses that show the Molar tooth indication on brain imaging are classified as JSRDs (Joubert syndrome related disorders). The primary cause of JS is abnormalities in the cilium called cilium aberrations, an organelle involved in organogenesis that serves as a hub for signals. We describe a boy infant born one month and fifteen days ago who had MRI imaging evidence of MTS. Pediatricians and neurologists must work together to detect and treat disorders in their early stages in order to prevent any serious abnormalities.

Keywords: Molar tooth sign, Joubert syndrome related disorders, Cilium aberrations.

Introduction

Joubert syndrome identified in 1969 in small, isolated groups with enhanced consanguinity[1], Joubert syndrome (also called Joubert Bolthauser syndrome)[2] is a rare disease with an autosomal recessive pattern linked to mutations in multiple genes, including NPHP1, CEP290, and AH11[3]. Mutations of more than 35 genes are involved to cause Joubert syndrome[1]. These mutations affect multiple signaling pathways, causing irregular proliferations and migrations of neuronal cells, which results in neurological and respiratory abnormalities[3] that affect 1 in 80000 to 1 in 100000 newborns named after Marie Joubert. Biallelic pathogenic variants of overlapping genes are present in 50–92% of individuals with joubert syndrome. Therefore, next-generation sequencing with matched gene panels is the most effective way to diagnose Joubert syndrome[4,1].

Clinical manifestations

- Hypotonia
- Ataxia
- Strabismus
- Nystagmus
- Ptosis
- Abnormal breathing patterns
- Hyperpnoea
- Occulomotor apraxia
- Choriorectal coloboma [3,4]

Case presentation

A 1 month 15 days old male child presented through out patient department with complaints of tachypnea, noisy breathing, refusal of feeds and not gaining weight. The child was born out of a second degree consanguineous married couple with history of NICU admission i/v/o Meconium aspiration syndrome, respiratory distress for 37 days was on cpap for 10 days. On general examination child was irritable and archy was present. The child was examined in supine position. Other systemic examination, cranial nerve examination were normal. By seeing above complaints child was provisionally diagnosed as failure to thrive with sepsis with meningitis and started treatment with antibiotic Inj.ceftriaxone(150mg), Inj.gardinal(8mg), Inj. levipill(60mg) through intravenously and managed .

USG abdomen was done showed normal study. Laboratory examination revealed elevated levels of CRP. MRI brain was done showed JOUBERT anomaly features. On 1st day Hb was 7.0 g/dl one time blood transfusion was done and post transfusion Hb was 10.2. child was continuously monitored for RR, HR, and GRBS, Lumbar puncture was done to assess meningitis but it was normal. Inflammatory markers raised so antibiotics upgraded to Inj. Vancomycin (60 mg) and Inj. Pipzo (300 mg), on due course of treatment condition of the child got better and discharged with Syrup Gardinal (2 ml), Syrup levipill (0.6 ml) multivitamin drops, Syrup ossapan D 1 ml and Ultra D3 drops and advised for exclusive breastfeeding till 6 months, immunization as per NIS, hygiene advice and physiotherapy

Figure 1

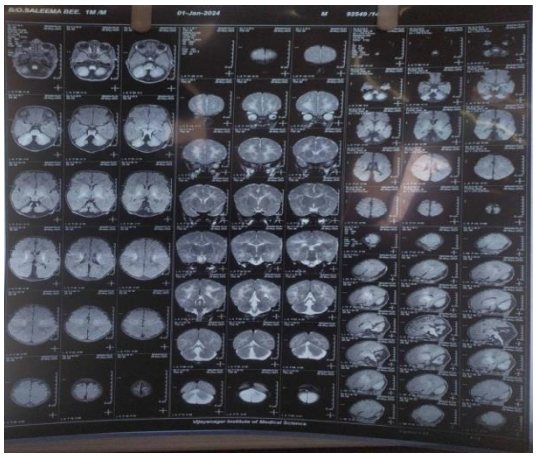

Figure 1 – MRI imaging showing joubert anomaly features

Discussion

Joubert syndrome is an autosomal recessive, rarely X-linked recessive[1], characterized by “Molar tooth sign” an obligatory hallmark, is formed by malformations of the midbrain and hindbrain, including anomalies in the cerebellum and life-threatening condition that affects multiple organs, primarily retinal dystrophy, nephropthasis, hepatic fibrosis, and polydactyl. It has both intra- and inter-familial variability and manifests various features, including neurological (hypotonia, intellectual disability, altered respiratory pattern), renal (progressive interstitial fibrosis, Dekaban-Arina syndrome), hepatic (congenital hepatic fibrosis, portal hypertension, liver cirrhosis), skeletal (postaxial polydactyl, scoliosis), and ocular (retinal blindness, colobomas)[2]. Researchers have recently reported the shepherd’s crook sign and in 10 % of cases observed features of Dandy-Walker malformation[5]. Ciliopathies are group of genetic disorders that presents characteristic features of Joubert syndrome and

related disorders including cerebello occuo-renal syndrome, dekaban-arima syndrome, varadipapp syndrome, malta syndrome and senior loken syndrome.

To date, mutations in over 10 genes have been identified as causative for joubert syndrome : JBTS1, JBTS2, JBTS4, JBTS5, JBTS6, JBTS7, JBTS8, JBTS9, JBTS10 that encodes for proteins of the primary cilium[2]. CBYI contributes to the development and operation of cilia by localizing to the distal end of the mother centriole. No further mutative biallelic pathogenic variation was found in the comprehensive reanalysis of Whole exome sequencing(WES) data collected from a large cohort of people with a clinical diagnosis of ciliopathy from all over the world. This suggests that CBYI is most likely an extremely uncommon source of illness. Since there is currently no proven cure, patients are treated conservatively using a combination of behavioral and cognitive techniques to address their symptoms[5,6].

Diagnosis of JS can be made only based on MRI imaging, but in absence of appropriate MRI, diagnosis can be ruled out by classic brain features of hypotonia, developmental delay, ataxia, occulomotor apraxia and hypoplasia by ultrasound or CT imaging.

Genetic counseling is an important part of management as it mainly involves the mechanism of inheritance, risk recurrence, genetic testing and explaining about the risk of having second affected child. Family support is often very rewarding[7]. Our patient presented with tachypnea, noisy breathing, refusal of feeds with history of meconium aspiration syndrome and respiratory distress. After thorough examination of all organs and system of body we found MTS on MRI, that was labelled as case of pure JS. These types of cases are extremely rare throughout the world, difficult to diagnose and usually lead to a wide range of disabilities due to possibilities of late diagnosis. Adding to this, most of patients lack ease of access to subspeciality who must be consulted in order to promptly diagnose and treat the disease.

Conclusion

Given JS is an uncommon inherited condition caused by mutations of various genes. Since from last decade, various studies have given evidence for the genetic cause of JS including phenotype spectrum, assosciation with specific genes. But also still a lot of work is essential to understand the prognosis of disorder and metabolic pathways involved with the long term goal to optimize treatment. As it is rare condition affecting children under 5 years of age, proper genetic counseling is necessary to avoid the risk of recurrence. Awareness of characteristic clinical and radiological finding in JS will help in early diagnosis and appropriate counseling and proper rehabilitation.

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