Case Report

Joubert Syndrome – a case report

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ABSTRACT

Joubert's syndrome is a rare genetic disorder associated with delayed development, ataxia, hypotonia, cerebellar dysgenesis and other multisystemic manifestations. A three and a half year old boy presented with delayed development, speech impairment, ataxia and hypotonia to the child guidance clinic. His cognitive development was average but mild impairment in social functioning with speech delay and impaired clarity of speech was noted. Neuroimaging revealed findings suggestive of Joubert syndrome. The child was suggested speech and occupational therapy and the parents were psychoeducated about the genetic condition. Clinicians must keep in mind neurodevelopmental genetic disorders like Joubert syndrome when they have a triad of ataxia, hypotonia and muscle weakness combined with cognitive delays and speech impairment.

Keywords: Joubert's syndrome, cerebellar dysgenesis, hypotonia, ataxia, delayed development, speech impairment.

INTRODUCTION

Joubert Syndrome is a rare autosomal recessive inherited disorder which was named after the French neurologist Marie Joubert who introduced it first in 1969, with manifestations that included hyperpnoea, eye movement disorder, ataxia, mental retardation and vermis agenesis [1]. The incidence of Joubert Syndrome and Related Disorder (JSRD) range between 1/80,000 and 1/100,000 live births, although these figures may represent an underestimate [2]. It is characterized by midbrain-hindbrain malformations which are severe hypo-dysplasia of the cerebellar vermis with midline clefting, fragmentation of the cerebellar nuclei and heterotopia of Purkinje-like neurons, along with dysplasia of pontine and medullary structures such as the basis pontis, reticular formation, inferior olivary, dorsal column and solitary tract nuclei [3]. This may be accompanied by a lack of decussation both of the superior cerebellar peduncles and of the corticospinal tracts at the medullary pyramids [4]. Genetic studies till date have identified 16 causative genes, all encoding for proteins expressed in the primary cilium or its apparatus and Joubert syndrome presents the clinical and genetic overlap in a growing field of disorders due to mutations in ciliary proteins and centomeres that are collectively known as "ciliopathies" [5]. It is multisystemic in nature and affects multiple organs like the central nervous system, ocular system, musculoskeletal, hepatobiliary and renal systems [6]. The syndrome manifests as muscle hypotonia due to cerebellar dysgenesis which results in delayed motor milestones, ocular movement disorders, respiratory muscle problems causing apneas and delayed speech development due to tongue muscle hypotonia. It is also characterized by impairment in language, learning, visuospatial memory and attention due to

cerebellum involvement in higher cognitive function [7]. Here we present a case of the syndrome that presented to our child guidance clinic along with its neuroimaging correlates.

CASE REPORT

A three and a half year old boy, born of a non-consangiunous marriage presented to our child guidance clinic with a chief complaint of delayed cognitive development. The child was born of a full term normal delivery and immediately post delivery developed respiratory distress and was admitted in neonatal intensive care unit for a week. After that the baby was discharged. At home, the mother observed that the child had difficulty in breast feeding and was advised to give him expressed breast milk. According to the mother, he has always had weak muscles. He was able to sit without support after one year of age and was able to walk without support after two and half years. Speech did not develop clearly and cognitive development was delayed too. He spoke monosyllables after one and a half year of age and bisyllables at two and a half years. Social milestones had however developed normally. At the time of presentation, his parents were able to understand words said by child like '*papa'* and '*mumma*'. He was able to identify and name animals, body parts and recognize people by name correctly. However there was a problem in clarity of speech. He was able to create a tower till three cubes while the pincer grasp had not developed but was able to draw a straight line by palmar grasp. These were suggestive of average cognitive abilities at 3 years of age though speech impairment persisted.

He had no ptosis on examination or abnormal movements such as twitching. No history suggestive of seizures was present. His limbs appeared normal with no evidence of polydactyly or deformities. His family history was unremarkable for a similar condition. He was investigated for mental retardation and hypotonia and supportive therapy was recommended. All routine laboratory and special metabolic tests including blood and urine amino acid levels, serum lactate, and serum ammonia levels were within normal limits.

On neurological examination, the muscle tone was reduced in all limbs. On fundoscopy and slit lamp examination, no abnormalities were found. Magnetic resonance imaging study of brain revealed cerebellar vermis atrophy along with superior peduncle hypertrophy which was suggestive of Joubert Syndrome [Figures 1&2]. On psychological assessment his social quotient (SQ) was mildly impaired on the Vineland Social Maturity Scale (VSMS). No formal genetic testing was done as the patient could not afford the same. A pediatric neurology opinion was sought; that confirmed the diagnosis. The patient was referred for regular occupational therapy sessions.

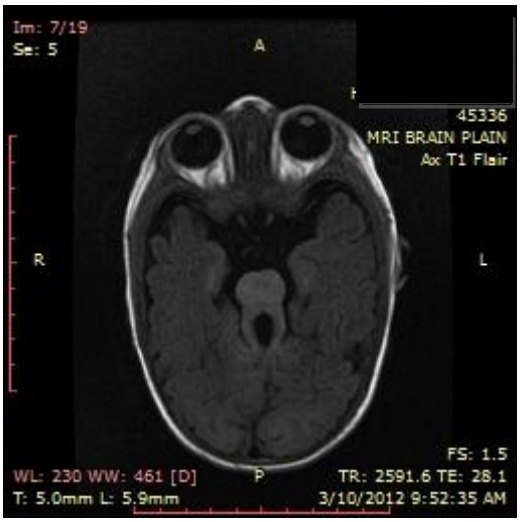

Figure 1 – MRI with suggestive findings

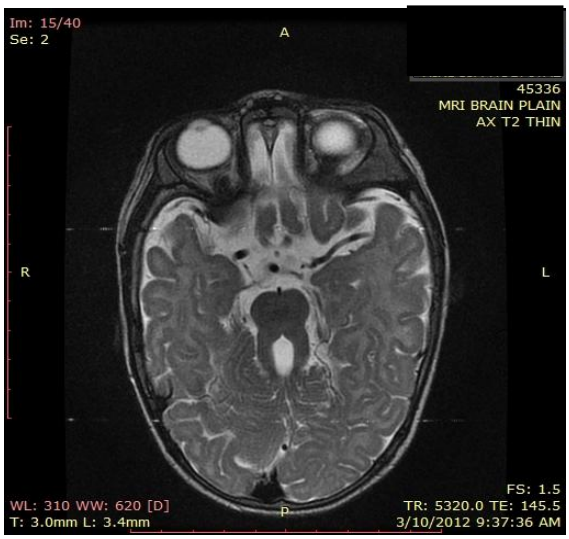

Figure 2 – MRI of the patient with Joubert's syndrome

DISCUSSION

Joubert Syndrome is a rare disorder and children with this condition present with breathing difficulties at birth and needing intensive neonatal care as in our case [8]. Due to cerebellar dysgenesis, there is muscle hypotonia and ataxia in the affected child which delays motor and speech development and can also manifest along with Hirschsprung's disease [9]. Usually children with the syndrome may have impaired cognitive functions difficulty in attention, speech and learning and this may lead to cause intellectual impairment [10]. These patients should be screened properly for multisystem involvement once the diagnosis is confirmed but usually clinicians feel that screening is better done when symptoms reveal mild impairment. It is important that the triad of hypotonia, ataxia and muscle weakness when combined with cognitive delays must evoke suspicion of the disorder in clinical practice.

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