CASE REPORT

Joubert syndrome with autism in two siblings: A rare presentation

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ABSTRACT

Joubert syndrome is a rare autosomal recessive disorder with partial or complete agenesis of cerebellar vermis. This syndrome is identified mainly by the presence of molar tooth sign in magnetic resonance imaging of the brain since it has a varied phenotypic presentation. Of the 200 cases reported so far in the literature, only three reports show the presence of autistic symptoms in siblings suggesting a link between the cerebellar vermis and autistic spectrum disorders. In this case report of two siblings, the female child satisfied the criterion for autistic spectrum disorder in accordance with Diagnostic and Statistical Manual of Mental Disorders Fifth Edition. The boy showed developmental delay with autistic features (not amounting to diagnostic threshold). This report is important in that it adds evidence to the literature that abnormalities of cerebellum are involved in the cognitive development and autistic symptoms.

Key words: Autism spectrum disorder, cerebellum, Joubert syndrome

INTRODUCTION

Joubert syndrome is a rare autosomal recessive disorder which presents with the episodic abnormal respiratory pattern, oculomotor findings, hypotonia, ataxia, and developmental delay.[1] The patients with Joubert syndrome show the evidence of neuropathological abnormalities in the cerebellum in the form of partial or complete agenesis of cerebellar vermis. The prevalence of this syndrome is <1 in 100,000 with only about 200 cases been reported worldwide, but it may be underestimated.[2]

Recent research findings suggest that there is a link between the abnormalities of cerebellum and autism.[3] However, case reports where patients presenting with cerebellar abnormalities along with autism are very rare in the literature. Hence, we present this rare case report of two siblings having Joubert syndrome with autistic features.

CASE REPORTS

Case 1
SW, a 5-year-old female child, presented the complaints of developmental delay in the form of not walking without support and not vocalizing any word. History revealed that she is the second child and was born out of the second degree consanguineous marriage between uncle-niece. Prenatal and perinatal period was uneventful with full-term normal vaginal delivery and birth weight of 2.5 kg. She had gross developmental delay affecting the motor, language, social, and cognitive systems.

Examination revealed facial dysmorphism in the form of bilateral epicanthic fold and mongoloid slant of eyes. The
head circumference was 47 cm (falls under <3rd percentile) which falls under microcephaly range. Her ocular and hearing examination were normal. She had difficulty in walking. On neurological examination, power was reduced in both upper and lower limbs and exaggerated reflex found in both lower limbs. Her planter was flexor.

She did not respond when called by her name. She did not interact with her mother and had no social smile. She also lacked the nonverbal communication (absence of gaze contact and facial gestures) for the social interaction with others. She sat by herself and was playing with a particular toy she was interested in.

She was administered Vineland Social Maturity Scale (VSMS) and Childhood Autism Rating Scale (CARS). On VSMS, her social age was 6 months, and her social quotient was 8. She scored 36.5 in CARS which is indicative that she was having autism spectrum disorder.

The axial T1-weighted and T2-weighted magnetic resonance imaging (MRI) showed dysplasia of the superior cerebellar vermis and thickened superior cerebellar peduncles giving a molar tooth appearance of the midbrain [Figure 1].

Based on the history, examination, and imaging studies, she was diagnosed to be having Joubert syndrome, severe intellectual disability, and autism spectrum disorder.

Case 2
KS, 2 years 11 months old, the younger brother of the girl described in the case history 1, was born at term by normal delivery after an uneventful pregnancy. He was the third born in the family preceded by two elder sisters, the first elder sister is normal, and the second elder sister was diagnosed to be having Joubert syndrome, severe intellectual disability, and autism spectrum disorder. The child cried immediately after birth and had no difficulty in breathing after delivery. His birth weight was 2.3 kg. He was bought along with the sister for the complaints of developmental delay in walking and talking. There was no history of seizures. In the developmental history, he had attained social smile by the age of 7 months and head control by 1 year. He was able to sit with support by 2 years of age but not attained sitting without support or standing with support. He started cooing recently.

On examination, his head circumference was 47.5 cm which falls between 15th and 50th percentile. Facial dysmorphism, epicanthi fold, and mongoloid slant of eyes were present. Deep tendon reflexes were present in all the limbs and planter was flexor. Power of the limbs was reduced in all four limbs. He was able to respond when called by his name and had a social smile when interacted or played with him. He had repetitive behavior such as flapping of hands, and he was interested in playing with one particular toy. He was also interested in hearing one particular advertisement in the television. Nonverbal communication was reduced but not absent. On testing, his social quotient was 22. When administered CARS, he scored 30.

The axial T1-weighted and T2-weighted MRI showed vermian hypoplasia with superior cerebellar hypoplasia producing bat wing appearance of fourth ventricle and molar tooth appearance of brain stem [Figure 2].

Based on the history, examination and imaging studies, he was diagnosed to be having Joubert syndrome and severe intellectual disability with autistic features.

DISCUSSION
These two case reports of Joubert syndrome with autistic features highlight the link between the abnormalities of
the cerebellum and the autism. Similar case reports in the past also have a similar association between the cerebellar abnormalities and autism spectrum disorders.[4]

The cerebellum is the most consistent part of the brain where its abnormality is associated with autism.[3] Certain developmental disorders of cerebellum, like Joubert syndrome, have overlaps with the autism spectrum disorder in clinical, anatomical, and genetic dimensions. This relationship between the cerebellum and autism can be used to understand both the disorders well.

The cerebellum is important for the integration of sensory information, and it plays an important role in motor control and coordination. The traditional view of the functions of cerebellum explains that it has an exclusive motor function. However, according to the recent studies of cerebellum, it has wide connections with various parts of the brain, and it is involved in various functions other than pure motor functions such as language, cognitive, and affective functions.[5] Neuroimaging findings also inform us that cerebellum has varied functions in the areas of cognition, social functions, and emotion.[6] These findings help us to strengthen the link between cerebellum and autism spectrum disorder.

Postmortem studies in autism spectrum disorder have consistently shown a reduction in the number of Purkinje neurons in the cerebellum. Some studies have reported that the reduction in the number of Purkinje neurons is widespread all over the cerebellum, but other studies have shown that the reduction is specific areas of cerebellum, namely, the posterolateral neocerebellar cortex and anterior hemispheres.[7]

Neuroimaging studies in autism have also thrown evidence of cerebellar pathology. In young individuals with autism, there is a significant increase in the total cerebellar volume. Gray matter volume in the whole of the cerebellum is normal, whereas the white matter volumes are significantly increased.[8] Hence, the overall increase in volume can be attributed to the increase in white matter. Some studies using voxel-based morphometry (which is used to examine the group differences in the brain volumes) have found out bilateral reductions in the white matter concentration in the cerebella of individuals with high functioning autism.[9] In some of the MRI studies examining the region-specific abnormalities in cerebellum, reduced size of one or more regions in the cerebellar vermis (which is predominantly gray matter) is reported frequently.[10] While reduced size of posterior vermis lobule VI-VII is frequently noted, a similar reduction in anterior vermis lobule I-V is less commonly reported. Other than this, reduction in the cerebellar hemispheres is also reported.[8]

CONCLUSION

There have been very few case reports of siblings presenting with Joubert syndrome along with features of autism spectrum disorder. The involvement of cerebellum in both these disorders has been highlighted in the two case reports.

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Conflicts of interest
There are no conflicts of interest.

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