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Undiagnosed Joubert Syndrome Presenting with Ischemic Stroke Rare Case in Dhamar Yemen

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Abstract

Joubert syndrome (JS) is a rare congenital autosomal recessive inherited disorder. The usual presentation of patients with JS is hypotonia, developmental delay, abnormal eye movement, ataxia, hyperapnea, or ischemic stroke. However, there have been very few cases of JS presenting with ischemic stroke. We describe a case of undiagnosed JS in a 7-year-old boy who presented with new onset left side weakness and irritability. The patient had apparent signs of motor and developmental delay. On physical examination, he had noticeable dysmorphic features including a broad forehead, elongated face, strabismus, trapezoid shaped mouth with protruded tongue, and low set ears. Brain computed tomography (CT) imaging reveals diagnostic features of Joubert syndrome with hypotension of cerebellar vermis ''batwing" appearance of the fourth ventricle and "molar-tooth" appearance of midbrain on cross section. Literature shows only a few cases with Joubert syndrome and ischemic cerebrovascular disease concluding that patients with Joubert syndrome have a risk of developing ischemic cerebrovascular disease at any age.

Subject Areas

Internal Medicine

Keywords

JS, Joubert Syndrome, MTS, Molar Tooth Sign, CCA, Corpus Callosum Agenesis

1. Background

Joubert syndrome (JS) is a rare congenital autosomal recessive inherited disorder

[1]. It was first described by Marie Joubert in 1969 as it's described by a mixed group of congenital anomalies, and a molar tooth sign (MTS) as a main diagnostic hallmark in cross sectional diagnostic imaging (CT and MRI). This sign appears due to agenesis of cerebellar vermis and midbrain malformation [1]-[4].

Clinical presentation includes a wide range of clinical features, including hypotonia, ataxia, developmental delay, abnormal eye movement, and intellectual disability. Yet the presentation can vary among affected individuals. MTS is crucial to acknowledge its variable expressions and the presence of atypical presentation and rarely present with ischemic stroke. These symptoms often adorned with additional elements such as respiratory dysfunction, ocular, renal, hepatic, and orofacial-digital anomalies [5]-[8].

The classification of JS and its related disorders is still limited and requires further understanding of related genes. The outcome of this syndrome and its effect on a child is severe language and developmental delay with 94% showing severe impairments in development, behavior and comorbid autism [6] [7].

Prevalence of JS in most recent Population-based studies represented as 1.7 per 100,000 in the age range 0 to 19 years. The most frequently mutated genes in Joubert syndrome are AHI1, CC2D2A, CEP290, CPLANE1, KIAA0586, MKS1, RPGRIP1L, and TMEM67 [1] [7] [9] [10].

However, there have been very few cases of JS presenting with ischemic stroke. Here we describe a case of undiagnosed JS in a 7-year-old boy who presented with left hemiparesis consistent with the diagnosis of ischemic stroke, detailing his clinical presentation, and diagnostic workup.

2. Case Presentation

A 7-year-old boy from a closed rural area in Yemen was brought by his parents to our hospital's neurological clinic complaining of new onset left side weakness and irritability (excess crying) for 2 days. The patient had apparent signs of motor and developmental delay. He was unable to concentrate and had obvious autistic behavior, such as head banging and stabber. He was diagnosed with a case of cerebral palsy 5 years ago and has been receiving cognitive/behavioral therapy and physiotherapy for that.

On physical examination, he had tachypnea, could not sit, walk or talk and his weight was 15 kg. He also had noticeable dysmorphic features including broad forehead, elongated face, strabismus, trapezoid shaped mouth with protruded tongue, and low set ears. He had normal looking extremities and normal chest contour (**Figure 1**). On neurologic examination, he had nystagmus, generalized hypotonia and hyporeflexia, which were more obvious on his left side.

3. Investigations

Brain computed tomography (CT) imaging reveals diagnostic features of Joubert syndrome with hypogensis of cerebellar vermis "batwing" appearance of the fourth ventricle (**Figure 2**) and "molar-tooth" appearance of midbrain on cross section

Figure 1. Photograph of patient face revealing the dysmorphic features and strabismus.

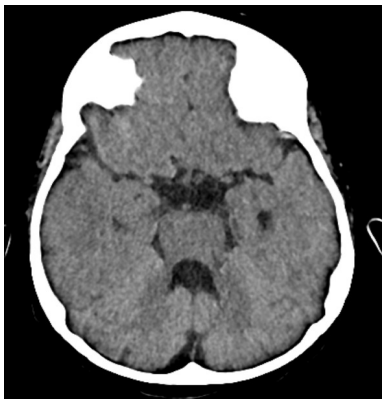

Figure 2. Axial section computed tomography image at level of posterior fossa showing hypogensis of cerebellar vermis and dilatation of fourth ventricle assuming "batwing" appearance.

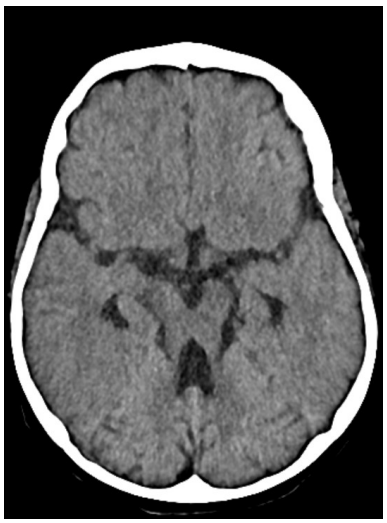

Figure 3. Axial section computed tomography image at level of midbrain showing elongated stretched superior cerebellar peduncles and deepened interpeduncular cistern resulting in "molar-tooth" appearance of midbrain.

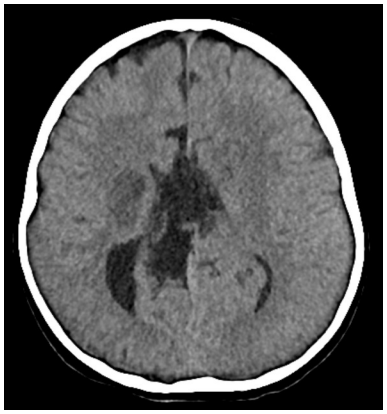

Figure 4. Axial section computed tomography image at level of lateral ventricles showing the ischemic infarction as a hypodense area in the right cerebral hemisphere white matter.

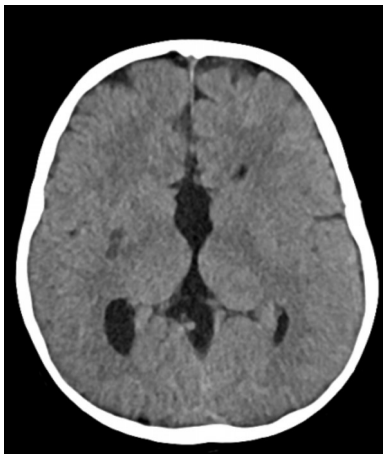

Figure 5. Axial section computed tomography image at level of lateral ventricles showing parallel and widely-spaced lateral ventricles giving "race-car" appearance and signifying an associated corpus callosum dysgenesis.

(**Figure 3**). The ischemic infarction is seen as rounded hypodense area in the right cerebral hemisphere white matter (**Figure 4**). Signs of corpus callosum agenesis (CCA) also seen on CT with widely spaced parallel lateral ventricles assuming a "race-car" appearance (**Figure 5**); CCA is a known association and frequently reported in patients with Joubert syndrome (3). EEG showed background slow wave, and Beta wave. With generalized epileptiform discharge. His lab studies were un-significant apart from elevated TSH (7.9 microgram/dl), T4 (1.48 microgram/dl), Abdominal-pelvic Ultrasound was un-significant and he had a normal echocardiography.

4. Discussion

A review of the literature reveals only a few cases showing a relation between

Joubert syndrome and ischemic cerebrovascular disease. The first case was published in 2011 reporting an acute ischemic stroke in a 21-year-old woman with Joubert syndrome who had no conventional risk factors for early onset cerebrovascular disease [2]. Another case was published in 2014 reporting a 69-year-old male with asymptomatic Joubert syndrome who was admitted to the emergency department with acute stroke [4]. Although, further studies are needed to establish the exact prevalence of early-onset ischemic cerebrovascular disease in patients with Joubert syndrome, our case report shows a relatively large ischemic infarction in a much younger patient (7-year-old); which strongly suggests an increased risk of developing early-onset ischemic cerebrovascular disease among patients with Joubert syndrome. Scientific research should be directed to clarify the genetic and molecular basis and pathogenic pathways leading to this increased risk, which would help in understanding the pathogenesis of ischemic cerebrovascular disease in general and may help to develop new potential methods for disease prevention and treatment.

5. Conclusion

In conclusion, we propose that patients with Joubert syndrome have an increased risk of developing ischemic cerebrovascular disease at a younger age. Understanding the genetic and molecular basis of cerebrovascular disease in patients with Joubert syndrome may help to better understand the pathogenesis of cerebrovascular disease in general and may open new potentials for its prevention and treatment.

Conflicts of Interest

The authors declare no conflicts of interest.

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