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Case Report

Joubert-Plus syndrome with an atretic cephalocele: a case report [☆]

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ARTICLE INFO

Article history:

Received 4 July 2022

Accepted 6 July 2022

Keywords:

Dandy-Walker

Joubert

Joubert-Plus

Atretic cephalocele

Case report

ABSTRACT

Joubert syndrome is a rare heterogeneous disease affecting the cerebellum. It usually presents with hypotonia, abnormal breathing pattern, with distinctive cerebellar and brain stem malformation called the molar tooth sign. It may present with different organ involvement or with other neurological alterations such as Dandy-Walker syndrome. Joubert syndrome with dandy walker syndrome is called Joubert-Plus syndrome, an exceedingly rare entity. Dandy-Walker syndrome is defined by hypoplasia and upward rotation of the cerebellar vermis and cystic dilation of the fourth ventricle. Atretic cephalocele is another rare diagnosis which is characterized by a herniation of intracranial contents through a skull defect. Herein, we present a case of a 6-month-old patient who presented with floppiness and a scalp nodule. After further evaluation, he was diagnosed with Joubert-Plus syndrome with an atretic cephalocele.

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Introduction

Joubert syndrome (JS) is a rare, genetically heterogeneous disorder of the cerebellum that is associated with cerebellar vermis hypoplasia. It is characterized by certain clinical features essential for diagnosis of classic JS including: hypotonia, developmental delay and either one of the following: abnormal breathing pattern in infancy or abnormal eye movements [1]. From a radiological point of view, a key feature of JS is “molar tooth sign” which happens due to widened interpeduncular fossa and enlarged superior cerebellar peduncles [2]. JS

usually presents with other features due to involvement of other organs including the kidneys, liver, eyes, and bones [3]. Also, it may present with other neurological alterations such as Dandy-Walker malformation. Such case is called Joubert-Plus syndrome [4].

Dandy-Walker malformation (DWM) is a congenital condition defined by hypoplasia of vermis cerebelli, fourth ventricle cystic enlargement and an overall enlarged posterior fossa [5]. Seventy-to-eighty per cent of DWM patients develop hydrocephalus which typically presents at around 3 months of age [6].

[☆] Competing Interests: All authors declare no conflict of interest.

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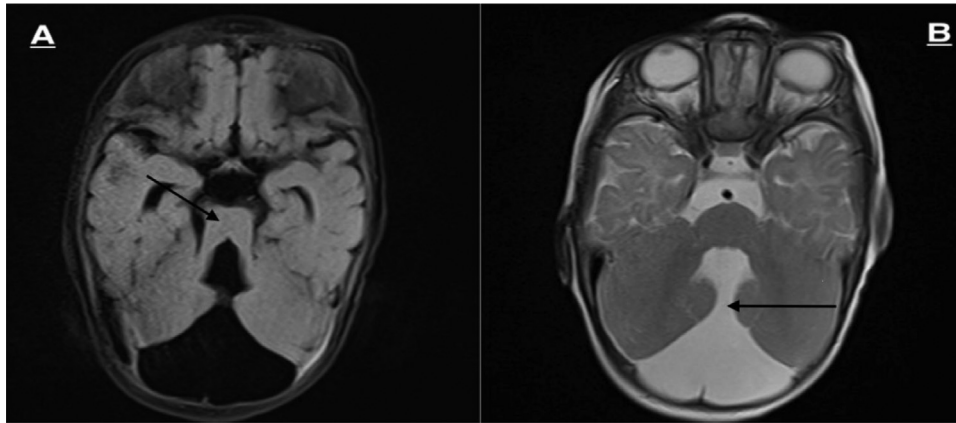


Fig. 1 – (A) An axial FLAIR image of the brain shows the ‘molar tooth sign’. **(B)** An axial T2 image shows the cystic dilatation of the posterior fossa with the connection with the 4th ventricle giving the keyhole appearance.

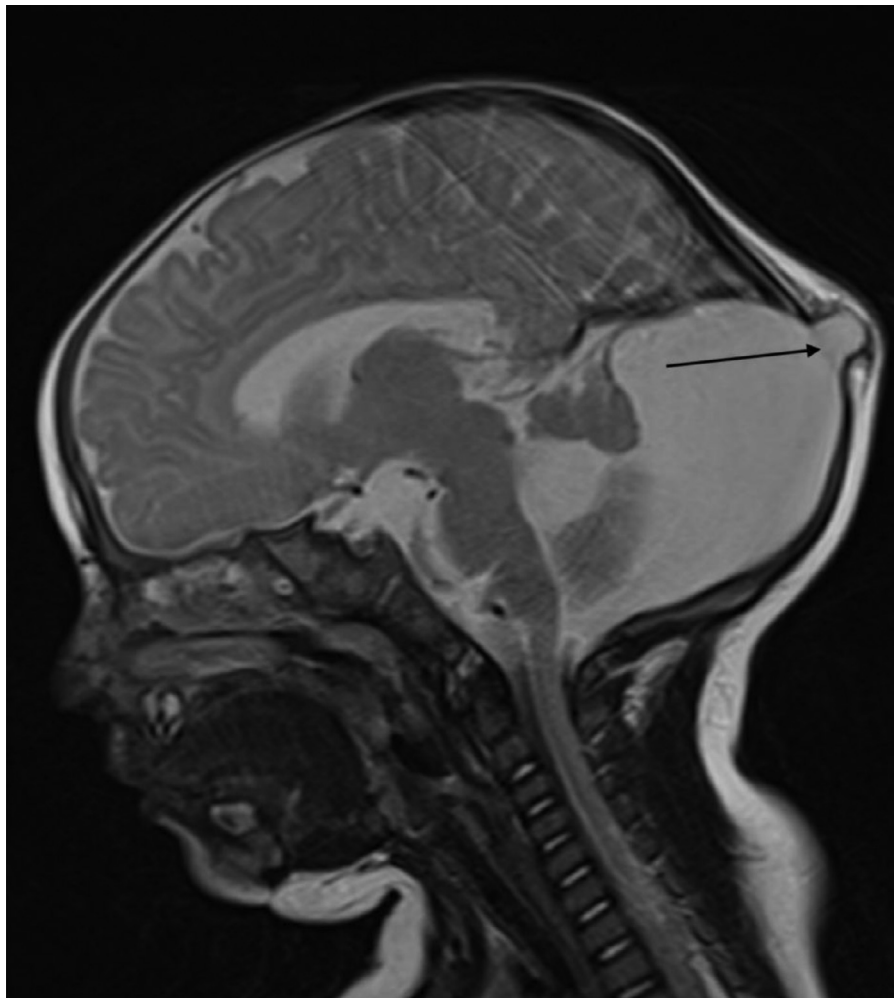


Fig. 2 – A sagittal T2 image shows an atretic cephalocele with cystic ballooning of the posterior fossa.

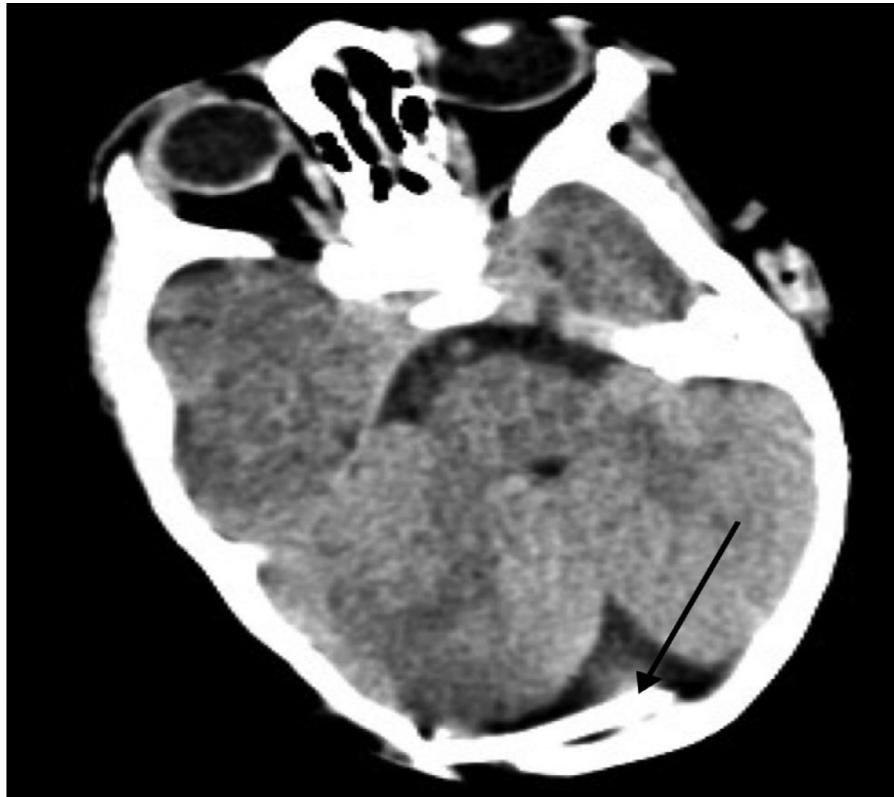


Fig. 3 – An axial CT image of the brain shows a VP shunt in the posterior fossa, which appears small in comparison with the previous images.

Atretic cephalocele is another rare diagnosis, a neural tube defect characterized by protrusions of intracranial contents (meninges, cerebrospinal fluid, or central nervous tissue) through a skull defect that occurs in the parietal and occipital scalp. Atretic cephalocele presents as a skin nodule with a hair tuft or an alopecic lesion and an MRI finding of cystic lesion with an underlying defect in the skull [7]. There have been no previous reports of the coexistence of Joubert-Plus syndrome and atretic cephalocele. Moreover, this is the second case reporting Joubert-Plus syndrome in the literature. Herein we present a case of a 6-month-old patient who presented with floppiness and a scalp nodule. After further evaluation, he was diagnosed with Joubert-Plus syndrome with an atretic cephalocele.

Case presentation

A 6-month-old patient presented to our clinic with his family complaining of floppiness, nystagmus, inability to follow objects, and a scalp nodule. The patient was a result of a consanguineous marriage, antenatal history was unremarkable, delivered vaginally with an uneventful neonatal period, and the patient vaccine history is up to date. There is no family history of the same presentation or any other diseases. On physical examination, the patient was vitally stable with a normal pattern of breathing, both legs were abducted and externally rotated resembling frog-legged posture, with flaccid extension

of the upper limbs. In addition to that, he was unable to keep his head still and failed to resist gravity on ventral and vertical suspension tests and a nodule was noted on the occiput. A central cause of hypotonia was suspected and for further evaluation of the nodule, an MRI was ordered. It showed a cystic dilatation of the posterior fossa with molar tooth appearance and a connection with the 4th ventricle giving the keyhole appearance. [Figures 1 and 2](#) also showed an atretic cephalocele. As a result of the aforementioned, the patient was diagnosed with Joubert-Plus syndrome with an atretic cephalocele. The patient was referred to the pediatric neurosurgery clinic for a ventriculoperitoneal shunt (VP) implantation to relieve the posterior fossa pressure. The patient was doing well after the surgery and was discharged.

Six months later, patient presented after a new-onset seizure. It was a generalized tonic-clonic seizure of a 3-minute duration. There was no history of trauma, sick contact, or change in the diet. On presentation, the patient was vitally stable, afebrile, and had a normal electrocardiogram. The patient was not in distress, had no skin rashes, and had no signs of trauma. Furthermore, there was no pain with neck flexion of positive brodzenski sign. Blood samples were drawn which all came back normal including (electrolytes, glucose, kidney function test, liver function test, blood culture, and others). A computer tomography scan (CT) was ordered to assess the functionality of the VP shunt which showed a smaller posterior fossa in comparison to the previous images indicating a well-functioning VP shunt ([Figure 3](#)). The patient was started on valproic acid which was increased gradually to 200 mg

per day to prevent recurrence presuming the cause was the anatomical malformations shown by the MRI, after excluding other causes.

Discussion

JS is a rare disorder with a grim prognosis. It is an autosomal recessive disorder with a prevalence fewer than 1 in 100,000. Classically, infants with JS present with hypotonia, abnormal eye movement, and respiratory control disorder. Radiologically, JS is recognizable by the presence of the “molar tooth sign” because of the characteristic brainstem and cerebellar defects. However, JS usually presents with other features due to involvement of other organs including the eye, kidneys, bones, and others [8]. As in our case, JS can also present with additional central nervous system alterations, particularly the mesencephalon or caudal fourth ventricle (i.e., Dandy-Walker malformation [9]), in such cases it is defined as Joubert plus syndrome [4].

DWM is a part of a rare neurodevelopmental diseases called Dandy-Walker Complex [10]. It is characterized by an enlargement of the posterior fossa, cystic dilatation of the fourth ventricle, agenesis (partial or complete) of the cerebellar vermis [11]. However, unlike JS, there is no “molar tooth sign” since the brainstem is unaffected [4]. In addition to that, patients with DWM lack intellectual disability [5].

Atretic cephalocele presents as an isolated finding, it has also been associated with several syndromes, including Walker Warburg and Dandy-Walker syndromes [12]. The prognosis of atretic cephalocele depends on many factors including its location, cephalocele sac content, associated malformations and the presence of hydrocephalus. The prognosis was unfavorable when the atretic cephalocele was accompanied by other intra and extracranial malformations, or when it was associated with hydrocephalus [13].

Our patient presented at 6 months of age with floppiness, nystagmus, and a scalp nodule for which MRI showed a constellation of Joubert-Plus syndrome with an atretic cephalocele. The initial management for DWM was placement of VP which is proven to considerably decrease morbidity and mortality compared to other options, i.e. open surgical procedures [14]. The patient's posterior fossa dilation had improved but he later developed a new onset seizure. There has been a rare association between seizures with DWM [15] and large occipital cephalocele [16]. Eventually, our patient started on the antiepileptic drug Valproic acid.

The primary takeaway lesson from this case study, is the need of raising awareness among pediatric neurologists and other healthcare professionals about the coexistence of JS, DWM and atretic cephalocele. In addition, the necessity to conduct early screening of family members of first degree relatives as a form of primary prevention.

Conclusion

Joubert syndrome is a rare disorder of the cerebellum, that presents classically with hypotonia, developmental delay, and

abnormal breathing pattern or abnormal eye movement. It can also present with other organs being involved. However, the involvement of the mesencephalon or caudal 4th ventricle it is defined as Joubert- plus syndrome. Atretic cephalocele is a herniation of intracranial content through a skull defect. If any of JS, DWM, or atretic cephalocele was suspected, an MRI should be requested bearing in mind a rare but possible coexistence of the 2 other associated conditions.

Ethical statement

An informed written consent was obtained from the patient's family.

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