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BRIEF COMMUNICATION

Joubert Syndrome: Classic Sonographic Signs at 19 Weeks of Gestation

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Abstract Joubert syndrome is a rare condition with an incidence of 1:100,000. It has primarily an autosomal recessive inheritance pattern. It is characterized by episodic hyperpnea, ataxia, hypotonia, abnormal eye movements, and varying degrees of intellectual disability. The causative genetic mutations are identifiable in only 50 % of the cases. Hence, neuroimaging in correlation with clinical features form the mainstay in the diagnosis of this entity. The classic imaging appearance is the 'molar-tooth' sign in the midbrain which was first described on MRI. The fourth ventricle has a bat-wing or umbrella-like configuration. Our case illustrates the classic imaging signs of Joubert syndrome at 19 weeks of gestation.

Keywords Joubert · Molar-tooth · Bat wing ventricle · Vermis · Fourth ventricle

Introduction

Joubert syndrome is a genetic condition with primarily an autosomal recessive inheritance pattern. It is characterized by episodic hyperpnea, ataxia, hypotonia, abnormal eye movements, and varying degrees of intellectual disability. Ancillary features include renal cysts, nephronophthisis, hepatic fibrosis, ocular coloboma, retinal dystrophy, occipital encephalocele, and polydactyly when a broader term of Joubert syndrome and related disorders (JSRD) is designated [1]. Till date, mutations in nineteen genes have been identified in patients with this disorder [2]. However, the mutations are identifiable in only 50 % of the cases. Hence, neuroimaging in correlation with clinical features form the mainstay in the diagnosis of this entity.

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Report of Case

A 28-year-old second gravida was referred for a detailed neurosonogram at 19 weeks of gestation due to suspicion of a posterior fossa fluid collection in the fetus. Her marriage was nonconsanguineous. She had a two-year-old son who had delayed motor milestones and had been diagnosed as Joubert syndrome. There was no other significant medical or family history. The transverse sonogram of the fetal head revealed an enlarged cisterna magna measuring 11 mm. The fourth ventricle was communicating with the cisterna magna posteriorly (Fig. 1a). It was altered in morphology with the anteroposterior dimension greater than the transverse dimension in the transverse plane at the upper level of the pons (Fig. 1b). The fourth ventricle had the 'bat-wing' or 'umbrella' appearance more caudally (Fig. 1c). In sagittal plane, the vermis was dysplastic and normal fastigium of the fourth ventricle was not perceptible (Fig. 1d). The midbrain showed the pathognomonic 'molar-tooth' sign (Fig. 1e).The sonographic findings of the fetus were identical with the magnetic resonance imaging (MRI) of the sibling (Fig. 2a, b). Based on these, a diagnosis of Joubert syndrome was made which was confirmed on fetal MRI. The couple opted for termination of the pregnancy. However, they refused fetal autopsy.

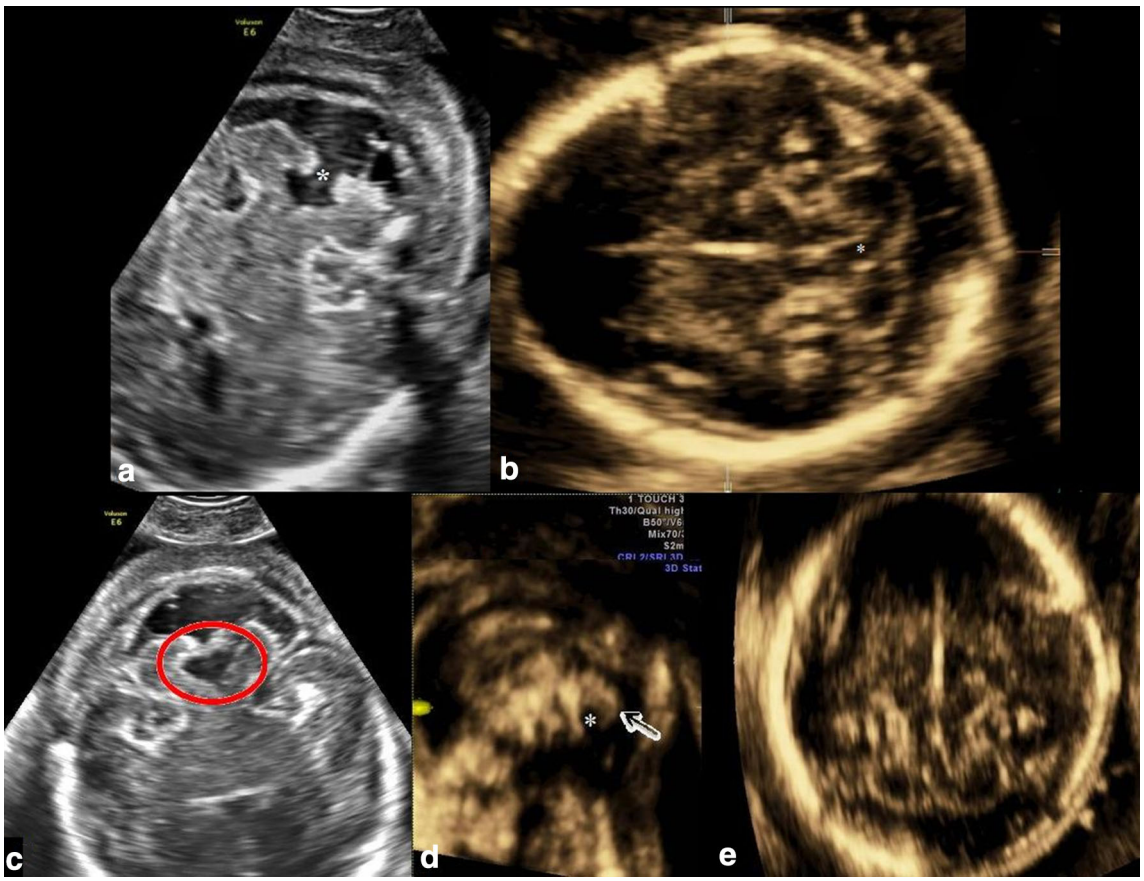

Fig. 1 Joubert syndrome at 19 weeks of gestation. **a** Transverse sonogram of the fetal head in the transcerebellar plane showing the communication (*asterisk*) between the cisterna magna and the fourth ventricle. **b** Anteroposterior dimension of the fourth ventricle (*asterisk*) greater than its transverse dimension. **c** Bat-wing or umbrella shape of the fourth ventricle (*circle*). **d** Sagittal volume contrast imaging (VCI) omniview image showing the small, dysplastic vermis (*arrow*) and enlarged, rounded fourth ventricle (*asterisk*) lacking the pointed fastigium. **e** Transverse image of the midbrain demonstrating the 'molar-tooth' sign

Discussion

Joubert syndrome was first described in 1969 [3]. It is relatively rare with an incidence of 1:100,000 [4]. It is characterized by defects in the midbrain and cerebellar vermis, which give rise to the clinical and imaging features. Joubert syndrome is classified under ciliopathies as it is believed to occur due to a malfunction of the primary cilia. Primary cilia are organelles, which detect and transmit vital sensory signals during embryogenesis. Hence, any defect in their function leads to malformations [5]. Despite having a genetic basis, a specific mutation may not be detected in all cases.

The classic imaging appearance is the 'molar-tooth' sign which was first described on MRI in 1997 by Maria et al. [6]. This sign occurs due to a combination of three anatomical aberrations: (1) deepened interpeduncular fossa in the midbrain; (2) thickened, elongated, horizontally oriented superior cerebellar peduncles; and (3) vermian hypoplasia. In addition, the fourth ventricle has a bat-wing or umbrella-like configuration. This is attributed to the rostral displacement of the fourth ventricle and midline cleft in the cerebellar vermis [7]. Quarello et al. have described the abnormal appearance of the fourth ventricle on axial and sagittal planes in feti with Joubert syndrome [8]. In axial plane, the normal fourth ventricle appears as a quadrangular anechoic space, with the anteroposterior diameter smaller than the maximum transverse diameter (Fig. 2c). In sagittal view, the fourth ventricle appears as a triangular anechoic space. The highest point of the roof of the fourth ventricle is the fastigium (Fig. 2d). As a result of dysgenesis of the isthmic portion of the brainstem, the shape of the fourth ventricle in cases of Joubert is abnormal. In axial view at the upper level of pons, the fourth ventricle appears enlarged and its floor is abnormal, pointing anteriorly due to the lack of normal decussation of the cerebellar peduncles in the tegmentum (Fig. 1e). In sagittal view, the fourth ventricle appears to be abnormally enlarged and rounded, lacking the characteristic posterior fastigial point and having a convex roof (Fig. 1d). An

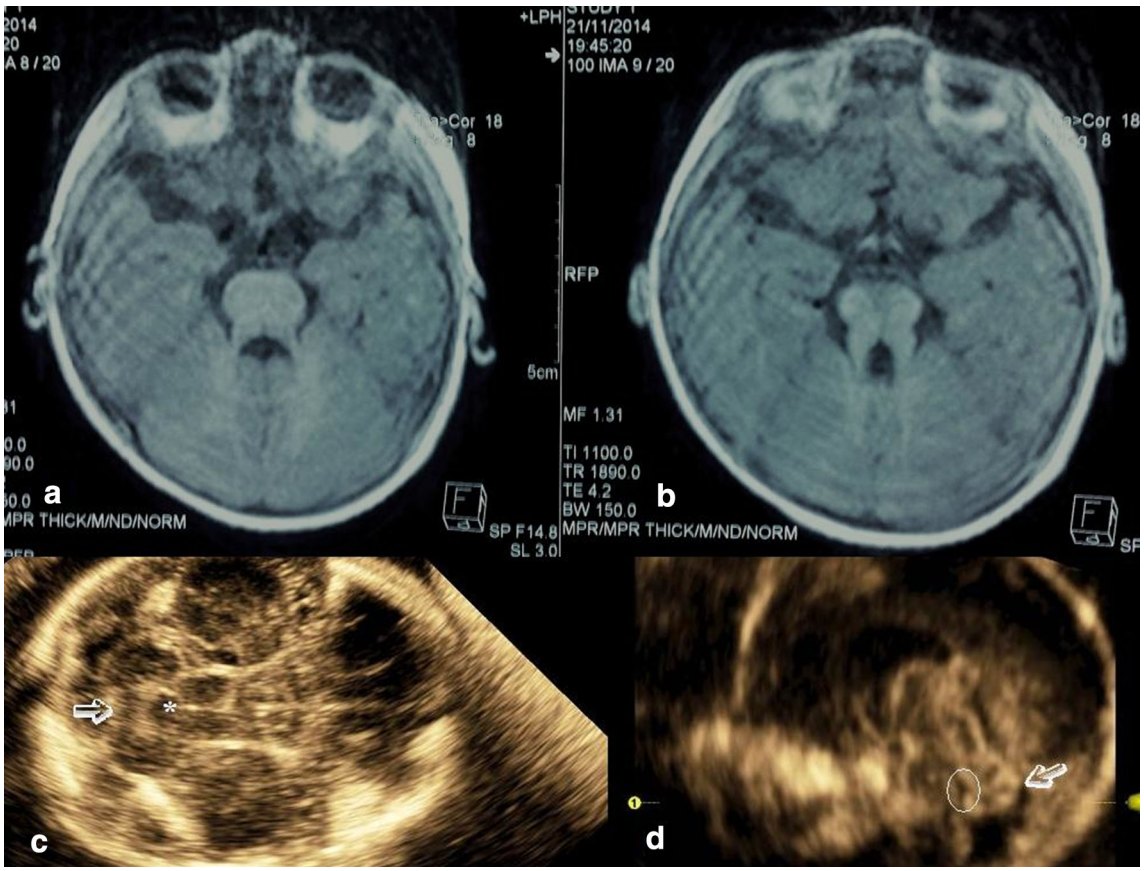

Fig. 2 **a** Axial MRI image of the brain of the sibling demonstrating the bat-wing appearance of the fourth ventricle. **b** MRI image showing the molar-tooth appearance of the midbrain. **c** Transverse sonogram of a normal 19-week fetus showing the normal shape of the fourth ventricle (*asterisk*) and the normal vermis (*arrow*) in between the cerebellar hemispheres **d** Sagittal reconstructed VCI omniview image illustrating the normal vermian morphology at 19 weeks (*arrow*) and the pointed fastigium (*circle*) of the fourth ventricle

analogy which may be drawn here is that, in the sagittal plane, the roof of normal fourth ventricle looks like a mountain with a sharp peak, whereas in Joubert, it resembles a plateau with a blunt apex.

The clinical presentation of Joubert syndrome can be diverse. Intellect can range from moderate to severe mental disability. There is impairment of gross motor functions. Ataxia sets in as age advances [9, 10]. The additional organ (ocular, hepatic, and renal) involvement can lead to significant morbidity and mortality. The affected couple need to be aware of a 25 % recurrence risk of the condition in subsequent pregnancy. Preimplantation genetic diagnosis or prenatal invasive testing is an option if a specific mutation is identified in the index case. The subsequent pregnancy of a couple at risk of Joubert syndrome can be assessed at 11–14 weeks (first trimester), 16, and 18–20 weeks to analyze the fetal posterior fossa in detail. Additional findings like occipital encephalocele, renal abnormalities, and polydactyly should also be sought for during these scans.

Compliance with Ethical Standards

Conflict of interest The author declares that they have no conflict of interest.

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