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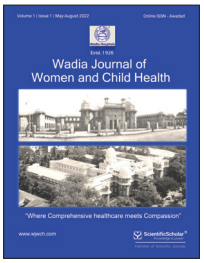

Case Report

Prenatal diagnosis of Joubert's syndrome overlapping with Dandy–Walker malformation on fetal MRI

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ABSTRACT

Magnetic resonance imaging (MRI) of the fetal brain plays an important role in the confirmation of congenital malformations diagnosed on ultrasound. It also helps in additionally detecting various associated central nervous system and other systemic abnormalities. We report a rare case of Joubert's syndrome overlapping with Dandy–Walker malformation (DWM), antenatally detected by fetal MRI whose findings were confirmed on post-natal MRI scan. Prenatal diagnosis of such an association is important in predicting the neurodevelopmental outcome of the child, and for genetic counseling of the parents, as Joubert's syndrome has a poorer prognosis, and a higher rate of recurrence than DWM.

Keywords: Molar tooth sign, Joubert syndrome, Dandy–Walker malformation, Fetal magnetic resonance imaging

INTRODUCTION

Joubert syndrome (JS) is an autosomal recessive disorder, characterized by vermian hypoplasia and the classical "molar tooth sign."[1] It's association with Dandy–Walker malformation (DWM), the most common posterior fossa malformation, is rare.[2] We report the role of fetal magnetic resonance imaging (MRI) in such rare association.

CASE SUMMARY

A 22-year-old primigravida with a non-consanguineous marriage was referred to us at 32 weeks of gestation for fetal brain MRI. As her trimester ultrasound scan showed cystic dilatation of the posterior fossa. Fetal MRI showed an enlarged posterior fossa with cystic dilatation of the 4th ventricle, elevated tentorium cerebelli, and torcular herophili along with torcular lambdoid inversion. There was complete agenesis of the vermis with hypoplastic cerebellar hemispheres. The superior cerebellar peduncles were thickened and horizontally oriented giving a molar tooth appearance. The midbrain was elongated, with a narrow pontomesencephalic junction [Figure 1]. These findings were suggestive of DWM with JS. Furthermore, asymmetric dilatation of the right lateral ventricle with displacement of the septum pellucidum to the left was noted.

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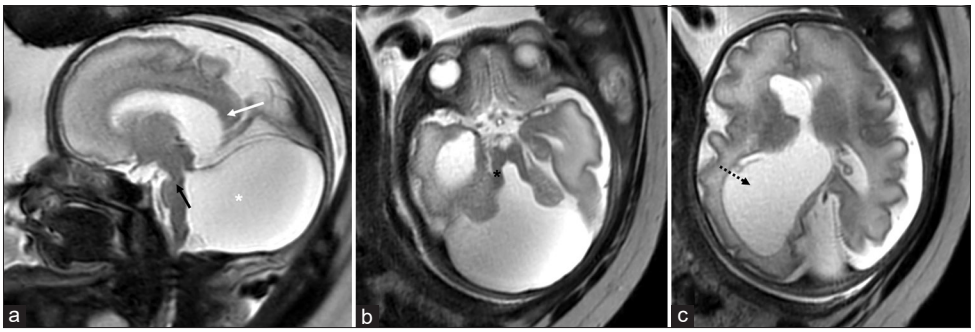

Figure 1: Magnetic resonance imaging of the fetal brain with single-shot fast spin-echo T2 sagittal (a) and axial (b and c) images show an enlarged posterior fossa and cystic dilatation of the fourth ventricle, vermian agenesis (white asterisk), narrow pontomesencephalic junction (black arrow), thickened superior cerebellar peduncles, that is, the molar tooth sign (black asterisk) and dilated right ventricle (dotted arrow) with displacement of septum pellucidum to right.

Post-axial polydactyly was seen in one of the upper limbs of the fetus [Figure 2]. The baby did not cry at birth and needed continuous positive airway pressure in view of repeated episodes of apnea with bradycardia and desaturations. On examination, she had an enlarged head circumference, frontal prominence, hypertelorism, wide spaced, downward displaced nipples, and post-axial polydactyly in both the upper and right lower limbs [Figure 3]. There was generalized hypotonia with normal reflexes. The spine was normal. The ophthalmological evaluation was normal. The liver and kidneys were normal on ultrasound of the abdomen. The prenatal findings were confirmed by an MRI of the brain [Figure 4] done on day 6 of life.

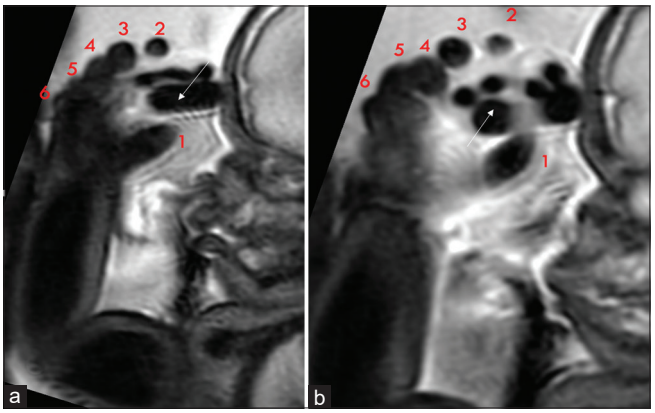

Figure 2: Fetal MRI with single-shot fast spin-echo T2 images (a and b) showing post axial polydactyly in one of the upper limbs (fingers number in red). Umbilical cord is seen in the image (white arrow).

DISCUSSION

JS is a mutational ciliopathy resulting in cerebellar and brainstem hypoplasia due to disordered neuronal proliferation and axonal migration.[3,4] The "molar tooth sign," which is the elongated appearance of the superior cerebellar peduncles in the axial sections, was initially considered specific for JS, but can also be seen in hepatic fibrosis, nephronophthisis, Cogan's syndrome, and pontine tegmental cap dysplasia.[5,6] JS and related disorders are an umbrella term used for JS presenting with ciliopathies involving other organs such as the kidneys, liver, eyes, and the limbs. Polydactyly has been reported in 8% cases of JS, and mesoaxial polydactyly is a known feature of JS with orofaciodigital defects.[3,7]

Joubert's syndrome has also been found to be associated with other central nervous system malformations such as hydrocephalus, corpus callosal dysgenesis, pituitary gland agenesis, and rarely, periventricular nodular heterotopia, polymicrogyria, and occipital encephaloceles.[3] DWM represents a posterior fossa malformation which occurs sporadically, and is characterized by vermian hypoplasia (or agenesis), cystic dilatation of the fourth ventricle, and torcular lambdoid inversion. It may also affect the normal cerebellar lobulation and development of the corpus callosum, which can lead to cognitive impairment.[2] The association of JS with posterior fossa malformations is reported to be <10%.[7] Its association with DWM has been reported only in few case reports of which Sartori *et al.* missed "molar tooth sign" in a child with DWM initially on imaging which was later seen when posterior fossa cystic decompression was done.[8-10] It is possible to suspect a posterior fossa abnormality in the first trimester ultrasound examination (as early as 11 weeks), on the basis of abnormal measurements of the intracranial translucency and brain stem-to-occipital bone diameter, absence of the normal echogenic line between the cisterna magna and the fourth ventricle, or by an excessively large fourth ventricle-cisterna magna complex on visual inspection.[11,12] However, as the vermis is not fully developed before 18 weeks, the diagnosis of DWM on antenatal ultrasonography should be made only in the second trimester after 18 weeks, to avoid a false-positive diagnosis.

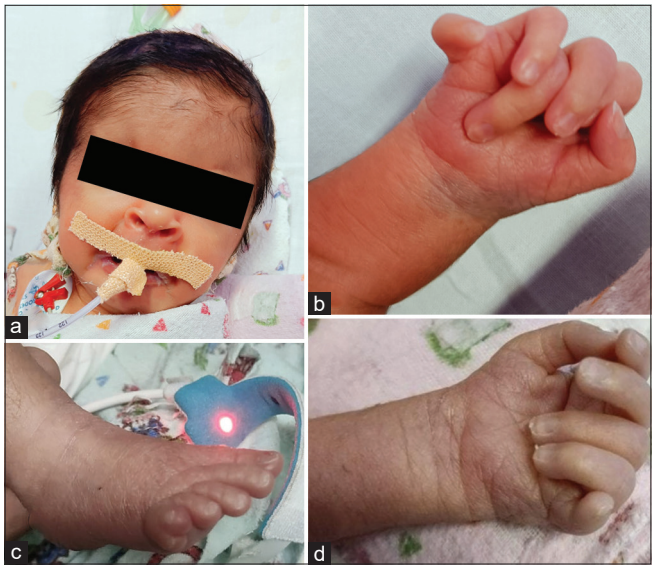

Figure 3: (a-d) Clinical images of the child show hypertelorism not seen as eyes are covered in image (a) and post-axial polydactyly in both upper limbs (b, d) and in the right lower limb (d).

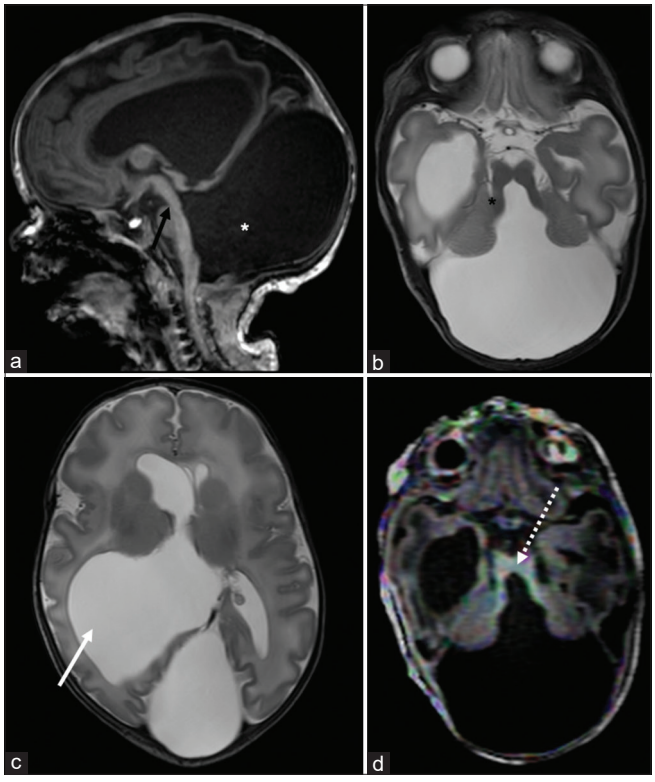

Figure 4: Post-natal magnetic resonance imaging brain T1-weighted sagittal (a), T2-weighted axial (b and c) and diffusion tensor (DTI) axial images (d) show enlarged posterior fossa and cystic dilatation of the fourth ventricle, vermian agenesis (white asterisk), narrow pontomesencephalic junction (black arrow), thickened superior cerebellar peduncles (black asterisk), and dilated right ventricle (white arrow). DTI images show non-decussation of superior cerebellar peduncles in the midbrain (d).

Some of the signs in the second trimester for suspicion of DWM include significant cisterna magna enlargement (>10 mm), absence of vermis in the mid sagittal plane, and a visible connection between the 4th ventricle and the cisterna magna resembling a cleft.

Prenatal sonographic abnormalities in JS are non-specific, and include elevated nuchal translucency, enlarged cisterna magna, and the molar tooth sign, and can be associated with occipital encephalocele. Non-neurologic findings such as hypoplastic phallus, renal cysts, and polydactyly may add a corroborative value.[13]

The diagnosis of such an association with prenatal ultrasonography may become even more difficult in the third trimester due to ossification of skull in the third trimester, fetal position, or less amniotic fluid. Although ultrasound examination is helpful to raise suspicion; fetal MRI can confirm it. It is important to diagnose JS along with other posterior fossa abnormalities, as it is an autosomal recessive disorder and has a recurrence rate of 25%, which is approximately five times higher than that of DWM.[14,15] The role of fetal MRI for prenatal diagnosis of isolated JS or DWM is known; however, their combination is yet to be reported.

CONCLUSION

Fetal MRI plays an important role in the diagnosis of Joubert's syndrome associated with posterior fossa malformations such as DWM. It is important for the radiologist to be aware of this association as it helps in predicting the outcome and neurodevelopmental prognosis of the child and also in the genetic counseling of parents.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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