ORIGINAL ARTICLE

Dandy–Walker Malformation: is the 'tail sign' the key sign?

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ABSTRACT

Objective The study aims to demonstrate the value of the 'tail sign' in the assessment of Dandy–Walker malformation.

Methods A total of 31 fetal magnetic resonance imaging (MRI), performed before 24 weeks of gestation after second-line ultrasound examination between May 2013 and September 2014, were examined retrospectively. All MRI examinations were performed using a 1.5 Tesla magnet without maternal sedation.

Results Magnetic resonance imaging diagnosed 15/31 cases of Dandy–Walker malformation, 6/31 of vermian partial caudal agenesis, 2/31 of vermian hypoplasia, 4/31 of vermian malrotation, 2/31 of Walker–Warburg syndrome, 1/31 of Blake pouch cyst and 1/31 of rhombencephalosynapsis. All data were compared with fetopsy results, fetal MRI after the 30th week or postnatal MRI; the follow-up depended on the maternal decision to terminate or continue pregnancy. In our review study, we found the presence of the 'tail sign'; this sign was visible only in Dandy–Walker malformation and Walker–Warburg syndrome.

Conclusion The 'tail sign' could be helpful in the difficult differential diagnosis between Dandy–Walker, vermian malrotation, vermian hypoplasia and vermian partial agenesis.

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INTRODUCTION

Evaluation of posterior cranial fossa alterations and/or malformations is a routine but crucial step in a correct fetal ultrasound (US) examination.[1] US examination that includes a systematic survey of all the structures of the posterior fossa may allow the prenatal diagnosis of most cerebellar malformations.[2] US is a widely available, real-time imaging technique that provides an accurate evaluation of the brain; however, it is operator dependent. Prenatal US examination of this anatomic region is very demanding,[3] and the prenatal diagnosis of the malformations regarding the cerebellum is of great importance for an adequate follow-up of pregnancy as well as the relatives counseling; however, the differential diagnosis of cerebellar abnormalities is limited by 2D approaches, because of the complicated imaging of this region and overall the pons.[4]

Nowadays, the 3D approach in the evaluation of posterior fossa is a part of the complex study of cerebellar pathologies, and it is becoming a state of the art.[5] Three-dimensional US has been recently applied in the study of fetal central nervous system as a tool to overcome the difficulties of 2D US and its operator dependence. Although the new US technologies have revolutionized the approach in the study of the vermis, the differential diagnosis in vermian pathologies remains complex and often doubtful.

It has been widely demonstrated that magnetic resonance imaging (MRI) is highly accurate, even in the evaluation of fetal posterior fossa abnormalities and vermian pathologies, when US is inconclusive or doubtful. MRI is less useful than US before 19 weeks of gestation because of the small size of the cerebellar structures and the limited spatial resolution of MRI. As the vermis and the hemispheres increase in size, it becomes easier to evaluate the cerebellum using MRI. Fetal MRI using ultrafast sequences providing an optimal spatial resolution is a third-line examination widely established in the study of central nervous system diseases[6] and, today, particularly in the study of the posterior cerebral fossa.[7] Moreover, in cases of thick maternal wall, oligohydramnios, particularly when to use of the endovaginal approach is not possible because of fetal position, the cerebellum may be much better depicted with MRI than with US.

Unlike US, technical difficulties linked to oligohydramnios or maternal factors, such as obesity, do not affect the MRI procedure.[8–10]

Multiplanar MRI evaluation provides an optimal visualization of the cerebellum, permitting detection and characterization of different cerebellar pathologies.[11] The aim of our study was to find a sign that allows us, using fetal MRI, the differential diagnosis between Dandy–Walker malformation (DWM), vermian malrotation, vermian hypoplasia and vermian partial agenesis. A differential diagnosis between these pathologies is essential to provide an accurate counseling to parents.

METHODS

We evaluated retrospectively a total of 31 fetal MRI examinations, carried out from May 2013 and September 2014; the exams took place after a second-level US examination performed in the Department of Obstetrics and Gynecology at our university; the indication for fetal MRI was a prenatal US diagnosis of posterior fossa abnormalities. Mean maternal age was 29.7 years (range 21–38 years), and mean gestational age was 21 weeks + 2 days (range 19 weeks + 1 day to 23 weeks + 5 days) based on the date of the last menstrual period and confirmed by US examination performed before MRI examination. All fetal MRI were performed without maternal or fetal sedation. A written consent form was signed by the mother. Family history and clinical data were collected before MRI examinations.

Fetal MRI was performed within 2 days up to a maximum of 2 weeks after second-level US examination; the radiologist performing fetal MRI was informed about the US results. A complete follow-up was available for all the cases. Five out of 31 cases were based on fetal MRI after the 30th week, while in the remaining cases, follow-up data were obtained by fetopsy.

Imaging protocol

Fetal MRI was performed on a 1.5 Tesla (1.5 T) MRI scanner (Siemens Magnetom Avanto, Erlangen, Germany) using a multi-channel phased array coil to allow increased coverage of the fetal head and increased signal-to-noise ratio according to a standard protocol. The patient was in feet-first supine position throughout the examination (typical duration: 20–30 min), as comfortable as possible in order to minimize fetal movements. If the mother is uncomfortable in this position, MRI examination can be performed with the patient lying on the left side, although this position may affect the imaging quality. The same protocol has been used for all the fetal MRI.

Usually, an initial localizer has been obtained in three orthogonal planes; it is used to visualize the fetal position and sidedness, as well as to ascertain the coil centered on the region of interest. A T2 half-Fourier acquisition single-shot turbo spin echo (HASTE) in coronal plane has been used to investigate fetal position (longitudinal, axial or oblique) and fetal presentation (cephalic, breech or shoulder presentation). Our protocol provides T2-weighted HASTE images, (repetition time (TR) 1000 ms; echo time (TE) 149 ms; slice thickness 3 mm; field of view (FOV) 270 × 270 mm; matrix 256 × 179; flip angle 150°; total image acquisition time about 15–20 s) on coronal, sagittal and axial plane to evaluate cerebral anatomy and cerebellar biometry parameters.

T1 FLASH 2D w.i. (fast low-angle shot) on the axial plane with and without suppression of fat signal (TR 200 ms; TE 5 ms; slice thickness 4 mm; flip angle 70°; FOV 350 × 300 mm; matrix 256 × 205; acquisition time 30 s divided in two concatenations during maternal apnea).

Echo-planar diffusion-weighted imaging with gradient oriented on the three planes (b50, b200 and b700 s/mm^2; TR 8000 ms; TE 90 ms; TI 185 ms; slice thickness 4 mm; FOV 420 × 300 mm; matrix 192 × 192; acquisition time 45 s). These techniques were part of our protocol to investigate the fetal brain because T1 allows to evaluate the presence/absence of haemorrhagic foci and diffusion weighted imaging to evaluate ischaemic part of brain, complications that may occur in complex malformations of the fetal brain.

Structural evaluation and biometric parameters

In all cases, the morphobiometry of the cerebellum, of the brainstem and of the posterior fossa was evaluated, analyzing the following parameters:

- Cerebellar morphobiometry: Transverse cerebellar diameter (TCD) biometry of the hemispheres was considered normal if every antero-posterior diameter on the axial plane was 50% of TCD; moreover, hemispheric symmetries or asymmetries were always registered. The collected data were compared with standard biometric values related to the gestational age as described in the literature.[12–14]
- Vermis morphobiometry: presence or absence of primary fissure and fastigium; ratio of superior to inferior portion of the vermis (normal value 1:2). Antero-posterior diameter and longitudinal diameter of the vermis were calculated, defining it as normal or abnormal according to recently published MRI parameters of the vermis.
- Fourth ventricle: A triangular shape longitudinally covered by the cerebellar vermis on the sagittal plane was considered as normal development; a possible communication with the cisterna magna was also evaluated.
- Brainstem: Presence or absence of the anterior bulge of the pons and/or thinning of the brainstem was evaluated.
- Tegmento-vermian angle: considered abnormal if >10°. The landmark of insertion of the tentorium cerebelli is very well depicted by MRI, and the internal portion of the occipital bone is easily found on the sagittal plane as a linear hypointense structure separating the occipital lobe from the cerebellum.
- Cisterna magna: defined as the distance between the dorsal surface of the vermis and the internal side of the occipital bone on the axial plane. It was considered abnormal if >10 mm.
- Tentorium insertion: considered normal when situated on the occipital bone projection at the skull base.

Vermian abnormalities were described on the basis of the most recent classification reported in the literature[15]:

- DWM: partial or total vermian agenesis, widening of the posterior fossa, ascent of the tentorium cerebelli with a higher insertion on the occipital bone and cystic dilatation of the fourth ventricle. Prognosis is poor.
- Partial or total vermian agenesis: total absence of the vermis or of its inferior portion. Prognosis may vary and is strictly linked to associated encephalic or extra-encephalic pathologies.
- Vermian hypoplasia: vermian biometry <10° percentile without morphological alterations. Prognosis may vary.
- Vermian malrotation: communication between cisterna magna and the fourth ventricle in the presence of normal morphology and biometry of the vermis, preserved ratio of superior to inferior portion of the vermis (1:2), presence of the principal fissures and normal morphology of the pons. This finding is regarded as an anatomical variant; prognosis is variable.

Table 1 **Morpho-structural and biometric parameters: differential diagnosis criteria**

Pathology	Cerebellar biometry	Vermis	Fourth ventricle	Brainstem	Cerebellopontine angle	Cisterna magna	Tentorium insertion	Tail sign
Dandy–Walker malformation	Reduced	Altered ratio, no visualization of primary fissure and fastigium	Altered morphology, communication with cisterna magna	Normal	Enlarged	Enlarged	High	Yes
Partial vermis agenesis	Reduced	Altered ratio, primary fissure and fastigium preserved	Altered morphology, communication with cisterna magna	Normal	Enlarged	Enlarged	Regular	Inconstant
Vermis hypoplasia	Reduced	Normal ratio, primary fissure and fastigium preserved	Normal	Normal	Normal	Enlarged	Regular	No
Malrotation	Normal	Normal ratio, primary fissure and fastigium preserved	Altered morphology, communication with cisterna magna	Normal	Enlarged	Normal	Regular	No
Walker–Warburg syndrome	Reduced	Altered ratio, no visualization of primary fissure and fastigium	Altered morphology, communication with cisterna magna	hypoplastic	Enlarged	Enlarged	Regular	No
Blake pouch cyst	Normal	Normal ratio, primary fissure and fastigium preserved	Altered morphology, presence of a cyst not in communication with cisterna magna	Normal	Enlarged	Enlarged	Regular	No
Rhombencephalosynapsis	Reduced	Absent	Normal	hypoplastic	Normal	Enlarged	Regular	No

- Walker–Warburg syndrome: lissencephaly, hydrocephalus and cerebellar abnormalities: hypoplasia of the cerebellar hemispheres and hypoplasia or partial aplasia of the cerebellar vermis.
- Rhombencephalosynapsis: absence of the vermis, reduced TCD with fusion of the cerebellar hemispheres and dentate nuclei. Prognosis is unfavorable.

It is crucial to attempt to differentiate between the different entities that may be associated with an abnormal vermis: DWM, vermian hypoplasia, vermian agenesis and vermian agenesis with associated brainstem malformations.

RESULTS

All MRI exams were completed, and in all cases, fetal MRI provided a satisfactory image quality.

Out of these 31 pathological cases, fetal MRI identified DWM in 15 cases, partial caudal agenesis in six cases, vermian hypoplasia in two cases, vermian malrotation in four cases, Walker–Warburg syndrome in two cases, Blake pouch cyst in one case and rhombencephalosynapsis in one case (Table 1).

Discordant US and fetal MRI findings were observed in 19/31 cases: For DWM, US diagnosis was performed in 9/15 cases, for partial caudal agenesis in 1/6 cases, for vermian hypoplasia in 1/2 cases, for vermian malrotation in 1/4 cases, for Walker–Warburg syndrome in 0/2 cases, for Blake pouch cyst in 0/1 case and rhombencephalosynapsis in 0/1 case.

In the 15 cases of MRI related to DWM, we investigated all the anatomical features of DWM: dorsal rotation of the vermis with enlarged fourth ventricle, widening of the tegmento-vermian angle, flat fastigium and dysmorphic appearance of the posterior lobe of the vermis, which presents a thick and elongated nodulus with the appearance of a 'tail'. So, we identified the presence of a linear hypointensity in T2-weighted images at the inferior portion of the vermis showing a radiological appearance of a 'tail'. This feature is a sign of increased thickness of the fourth ventricle roof associated with dysmorphic aspect of the vermian inferior portion (Figures 1 and 2).

In the six cases of partial caudal agenesis, MRI showed the absence of the inferior portion of the vermis; in 3/6 cases, supratentorial alterations were noted (hydrocephalus, corpus callosum agenesis (CCA) and absence of septum pellucidum). MRI-based diagnoses were confirmed by fetopsy. The 'tail sign' is very inconstant in those cases; we found it in 2/6 cases. In the two cases of vermian hypoplasia at MRI and partial vermian agenesis, no evidence of 'tail sign' was seen. MRI findings were confirmed by fetopsy.

In all the four cases of malrotation, the tail sign was not found because in this pathology, the vermis is completely normal but there is a late on closure. As found from the early MRI at 23 weeks, the tail sign is absent, and there, the MRI at 30 weeks shows a completely rotated vermis (Figure 3).

In the two fetuses with Walker–Warburg Syndrome (Figure 4), MRI showed the hypoplasia of the cerebellar hemispheres and the hypoplasia of the cerebellar vermis with the simultaneous presence of central nervous system anomalies (partial/complete corpus callosum agenesis) associated to severe ventriculomegaly and lissencephaly. In these cases, the tail sign was not visualized, and both results were confirmed at fetopsy.

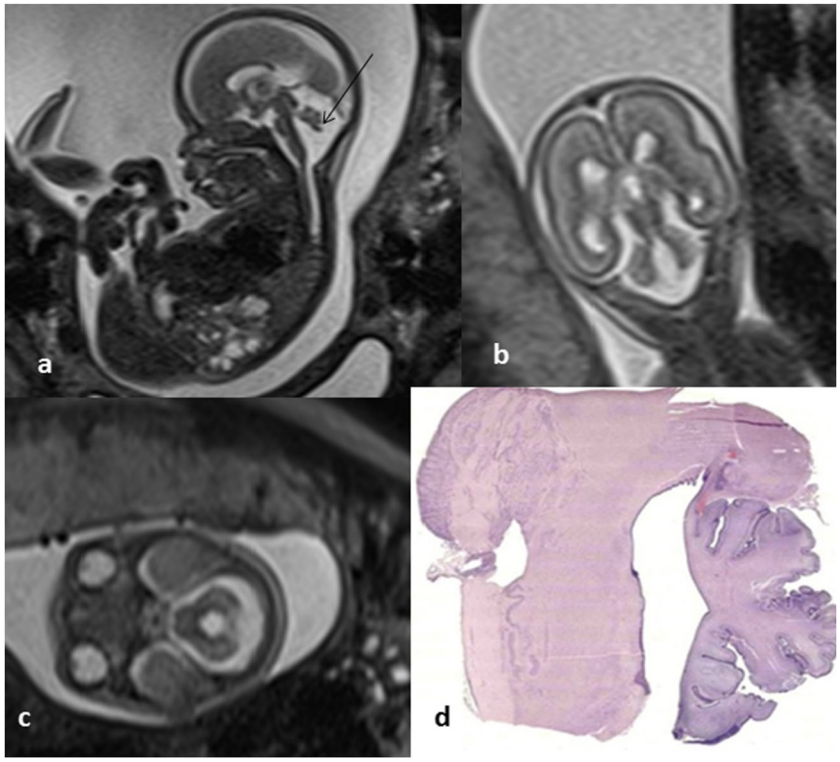

Figure 1 Fetus at 21 weeks + 4 days of gestation. Magnetic resonance imaging shows altered cerebellar biometry (5–10° percentile for the gestational age) in T2 sequences on the sagittal (a), coronal (b) and axial (c) planes with an enlarged tegmento vermian angle (65°). A sagittal section shows the presence of the 'tail sign' (a, black arrow). At the histology, the superior vermis has a relatively normal architecture, while inferior lobules are disproportionately short and simplified. Brainstem has a normal appearance (d)

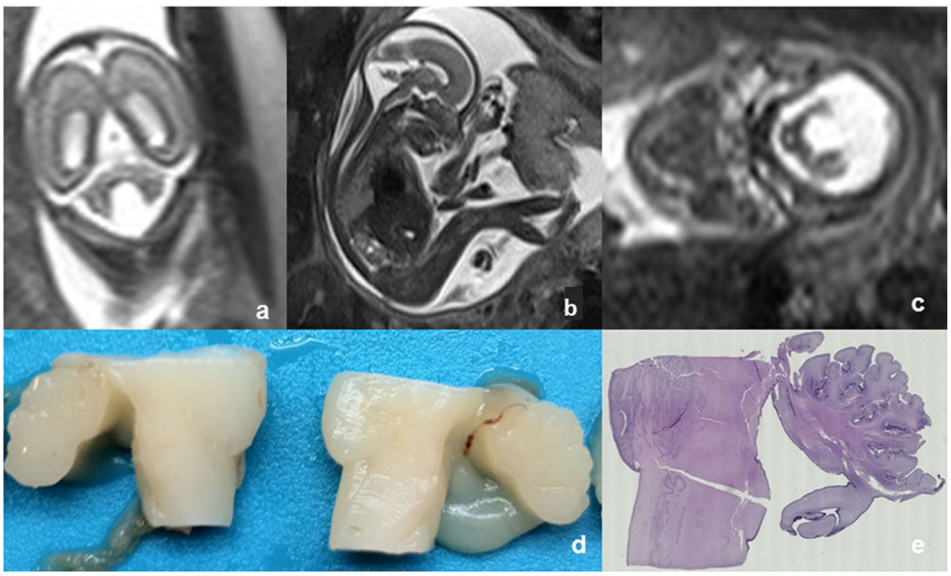

Figure 2 Fetus at 22 weeks of gestation + 3 days. Magnetic resonance imaging shows the diastasis of cerebellar emispheres associated to the agenesis of the inferior part of the vermis (a–c) with an enlarged cisterna magna (b); fastigium and primary fissure are not visualized. Sagittal section of the vermis shows dorsal rotation, widening of the tegmento-vermian angle, flat fastigium and enlarged fourth ventricle (d). Dysmorphic appearance of posterior lobe, with simplified uvula, thick and elongated nodulus describing the appearance of a 'tail' (e). These findings are in accordance with 'Dandy–Walker malformation'

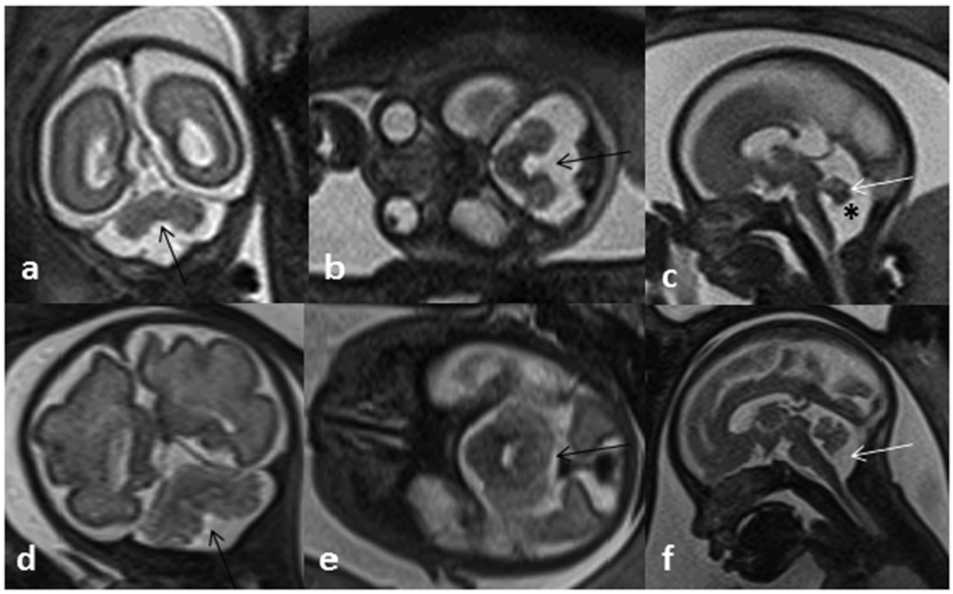

Figure 3 Fetus at 22 weeks + 4 days of gestation. Magnetic resonance imaging (MRI) shows enlargement of cisterna magna. The axial and coronal planes (a, b) show apparent absence of the inferior portion of the vermis, but the sagittal plane demonstrates a normal appearance of the morphology and regular biometry (c, white arrow). The features and the absence of 'tail sign' (c, *) suggest the hypothesis of a vermian malrotation for a retarded closure. MRI at 30 weeks + 5 days shows a normal vermis (d, e) with a complete closure (f). The finding confirms the first MRI diagnosis

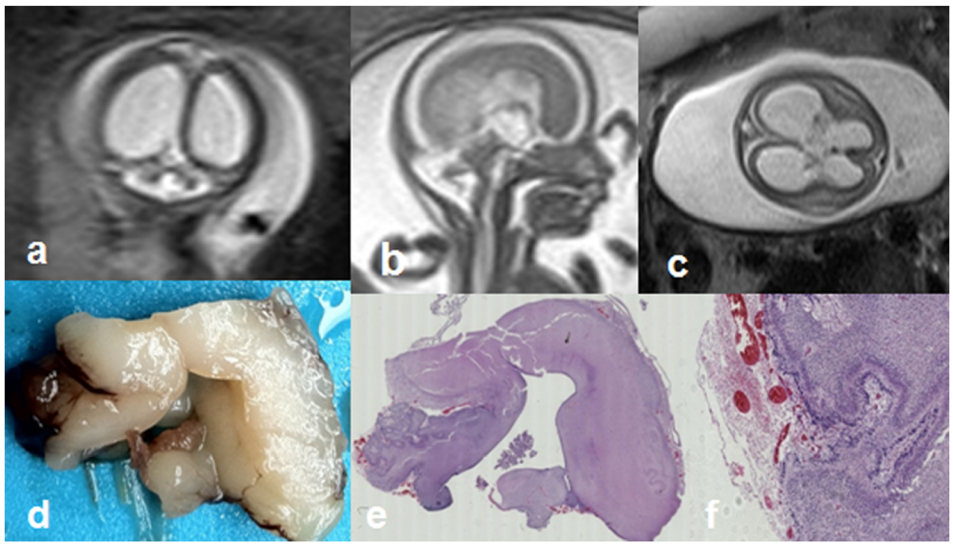

Figure 4 Magnetic resonance imaging showed the absence of the inferior portion of the vermis and the ascent of the tentorium cerebelli and the enlargement of the cisterna magna with the thickness of the fourth ventricle (a–b) and the malformation of the pons. The fetus had severe ventriculomegaly. The cerebellar vermis was dorsally rotated, with widened tegmento vermian angle, enlarged IV ventricle and flattened fastigium (d–e). The pontine protuberance was absent at macroscopics (d). Histology showed arachnoid thickness with neuroglial ectopia (f); the external granular layer was discontinuous and irregular with very simplified vermian folia and flattened fastigium. Magnetic resonance diagnosis of Walker–Warburg syndrome was then confirmed

In the only case of Blake pouch cyst, MRI showed the presence of the cyst with a rotated upwards but complete normal vermis in morphology and biometry. In this case, the tail sign was not visualized.

In the only case of rhombencephalosynapsis, MRI showed the absence of the vermis and the reduction of TCD with fusion of cerebellar hemispheres; in this last case, the tail sign was not visible. The findings were confirmed at fetopsy.

DISCUSSION

The cerebellum and the vermis are better visible after 24 to 26 weeks of gestation, but because of the time constraints for voluntary interruption of pregnancy in many states, we are

forced to evaluate the posterior fossa and its structure in a very early gestational age (<24 weeks).

Fetuses with anomalies in the morphology and biometry of the cerebellum and/or mega cisterna magna identified by US should always be submitted to fetal MRI examination.[16,17]

Basic US imaging of the fetal brain visualizes the posterior fossa on an axial plane[18]; however, this approach is not sufficiently accurate in the differentiation of cerebellar anomalies, such as vermian malrotation and abnormal tentorium insertion,[18,19] and additional sagittal and coronal planes are necessary but not always easy to obtain.

Because of this limitation, Paladini and Volpe introduced the 3D approach to study vermian and cerebellar pathologies[20] identifying morphometric parameters and abnormalities of the posterior fossa.

Numerous classifications of cerebellar pathologies can be found in the literature,[21,22] but they are not all considered adequate for evaluating fetal imaging, especially in DWM.

In 2009, Malinger *et al.*[16] reviewed the study published by Limperopoulos *et al.*[23,24] and highlighted that in 19 fetuses with prenatal diagnosis of vermian hypoplasia, only three developed psychomotor retardation and language-deficit disorders. Malinger *et al.* therefore affirmed that fetuses with a good prognosis at the follow-up should be considered to have vermian malrotation and not vermian hypoplasia. Their proposed classification of vermian pathologies was the starting point of our study.

Although adequate visualization of the cerebellar vermis is possible, under ideal condition of imaging, before 24 weeks of gestation, some caution is necessary before taking clinical decision on US imaging of the vermis. Malinger *et al.* support this theory, caution suggesting that US diagnosis of vermian pathologies is not adequate before 24 weeks of gestation, as the vermis is not completely developed.[16]

Thanks to ultrafast sequences, which are little influenced by fetal movements, multiplanarity and optimal spatial resolution, fetal MRI allows a good evaluation of the posterior fossa, cerebellum and brainstem.[24]

We highlighted the presence of a linear hypointensity on T2 images in correspondence with the inferior part of the vermis, and we called it the 'tail sign'. This feature corresponds histologically to a thickness of the fourth ventricle roof that appears raised and dysplastic.

Our results suggest that DWM, with the upward displacement of a dysplastic/hypoplastic vermis, is associated with enlargement of the cistern magna and 'tail sign' in all cases.

This is the first time a specific sign of DWM has been described in the literature, as the MRI 'tail sign' reached a diagnostic accuracy of 100% in our study.

In vermian hypoplasia (previously referred to as Dandy–Walker variant), the cisterna magna is of normal size, and the vermis is normally developed but biometrically small (although not always), but there is no evidence of 'tail sign'.

In vermian malrotation, there is a communication between cisterna magna and fourth ventricle with normal morphology and biometry of the vermis, preserved ratio of superior to inferior portion of the vermis (1:2), presence of the principal fissures and normal morphology of the pons; the 'tail sign' is not visible in most of the cases.

Distinguishing these three entities is important, because of their different prognoses because DWM and vermian hypoplasia are true malformations frequently associated with abnormal neurodevelopment.[25]

In partial vermis agenesis, MRI showed an abnormal ratio between the superior portion and the inferior portion of the vermis (2:1 instead of 1:2), whereas the flattening of the fastigium and the 'tail sign' are inconstant findings. Indeed, we found it in only 2/6 cases. On the basis of our knowledge, we can speculate that the anterior portion of the vermis, involved in most of the cases of partial agenesis, does not cause 'tail sign' as it occurs in the abnormalities of the posterior pars.

In the Blake pouch cyst, MRI showed the retrocerebellar localization of the cyst with a well-developed, nonrotated cerebellar vermis (as opposed to a DWM) and a cystic dilation of the fourth ventricle without cisternal communication. In this case, the 'tail sign' was not visible, and the inferior portion of the vermis was in continuum with the thin wall of the cyst.

Enlargement of the tegmento-vermian angle is not always an indirect sign of cerebellar pathology, although this sign is often present in partial vermian agenesis, making this diagnosis very challenging; on this side, we underline that the evidence of the 'tail sign' is, in our experience, always indicative of a vermian pathology.

Fetal MRI defined US diagnosis with more accuracy, and in 19 fetuses, MRI identified the associated pathologies not detected by US: ventriculomegaly associated with vermian hypoplasia; partial CCA associated with partial vermian agenesis; hydrocephalus, partial CCA and septum pellucidum agenesis in DWM; rhombencephalosynapsis in a case of reduced cerebellar biometry; and cerebellar trunk hypoplasia associated with features consistent with Walker–Warburg syndrome in two cases of hydrocephalus and reduced cerebellar biometry.

In this study, we demonstrate how cerebellar abnormalities suspected by US examination may be identified by MRI and how it is possible to perform an accurate differential diagnosis of cerebellar vermis anomalies. We also evidenced a new marker the tail sign that is present in almost all the cases of Dandy–Walker that promise a differential diagnosis between the different vermian pathologies.

Although the cerebellum and vermis are better visible after 24 weeks, we hereby demonstrated how it is possible to perform accurate diagnosis in an earlier gestational age.

The most important limitation of our study is that fetal MRI is less accurate in the early stages of pregnancy because vermis should 'close' over the fourth ventricle by 18 weeks but can be as late as 24 weeks. Further, the relative low number of fetuses included in this study does not allow to reach definite clinical conclusions. Future studies in larger group of fetuses with vermian anomalies are needed to better establish the clinical significance and prognosis of the 'tail sign'.

CONCLUSIONS

Fetal MRI is a third-line examination in the evaluation of posterior fossa malformations. Multiplanariety allows an optimal visualization of the brain structures, making it possible to assess the cerebellar biometry and the presence of associated malformations. We encourage the use of the tail sign as it is a significant indicator of disease, especially in DWM.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- US examination may allow the prenatal diagnosis of most cerebellar malformations however the differential diagnosis of cerebellar abnormalities is limited by 2D–3D approaches, due to the complicated imaging of this region and overall the pons.

WHAT DOES THIS STUDY ADD?

- Fetal MR can represent an useful imaging technique in order to confirm and characterize the different cerebellar malformation thanks to the multiplanes orientation which allows to study biometry and morphology of all the structures involved and the "tail sign" may allow a differential diagnosis between vermian malrotation and DW malformation particularly in early stage (19–24 weeks of gestation).

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