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Opinion

Plea for an anatomical approach to abnormalities of the posterior fossa in prenatal diagnosis

As illustrated in this issue of the Journal[1,2], recent advances in prenatal imaging, both two- and three-dimensional ultrasound, have allowed a more accurate anatomical approach to fetal cerebral structures, especially the fetal posterior fossa. For instance, such anatomical landmarks as the position of the tentorium or the torcular and the presence of a normal brain stem can be visualized, and analysis of the vermis (including biometric parameters and anatomical analysis of the fissures) can be performed, using either magnetic resonance imaging (MRI)[3,4] or ultrasound, especially in the sagittal plane[5,6].

Such advances in prenatal imaging have resulted in an increasing number of prenatal diagnoses of abnormalities of the posterior fossa. Since the pre- and postnatal literature is extremely confusing[7–10], the main issue surrounding these diagnoses is prenatal counseling with respect to the postnatal prognosis. The confusion is due mainly to inadequate classification, with gross division of malformations of the posterior fossa into Dandy–Walker malformation, Dandy–Walker variant and megacisterna magna. Dandy–Walker malformation represents a well-defined anatomical entity, characterized by ascent of the cerebellar tentorium and the torcular, resulting in a large posterior fossa[11]. According to a review of the literature, Dandy–Walker variant remains a heterogeneous disorder, including vermian agenesis without enlargement of the posterior fossa, but also hypoplasia, two quite different lesions with respect to embryology, imaging, etiology and prognosis. Indeed, in this heterogeneous group are found entities such as syndromic malformations (e.g. Joubert, Walker–Warburg, OPHN-1 mutation), aneuploidies (e.g. trisomies 13 and 18), clastic lesions of infectious or vascular origin, polymalformative complex, and 'isolated' malformation (with a normal biological work-up and no associated malformations), all of which are genetic entities with a potential risk of recurrence[3,12,13]. Efforts to give a prognosis according to the literature in such a heterogeneous group is an impossible challenge. Therefore, based on anatomical analysis and terminology adequate for differentiating agenesis, hypoplasia and atrophy, a new classification of such abnormalities of the posterior fossa may be proposed.

'Agenesis' is defined, strictly speaking, as either complete or partial absence of an anatomical structure. In complete vermian agenesis, the vermis is absent, whereas in partial vermian agenesis, part of the vermis is absent and the remaining part is anatomically of normal volume. Due to the craniocaudal development of the vermis, partial agenesis involves its inferior (caudal) part. Such complete or partial agenesis can be suspected sonographically as early as 18 gestational weeks, especially in the presence of a proband[14].

Agenesis may be either isolated or part of a syndrome. It is observed regularly in Joubert and Walker–Warburg syndromes, and in cerebro-oculomuscular syndrome. In fact, vermian agenesis is found to be associated occasionally with many syndromes (e.g. CHARGE)[15,16]. If vermian agenesis is isolated, it is most frequently sporadic. However, in the presence of a proband, because genetic determinism cannot be excluded totally, any further pregnancy must involve a reference ultrasound examination at 20–22 weeks of gestation.

'Hypoplasia' is used to define a small but complete anatomical structure with a congenital volume diminution. The sonographic diagnosis of cerebellar hypoplasia is based on significant diminution of the transverse cerebellar diameter (TCD). One should note that this group of cerebellar and pontocerebellar hypoplasias is heterogeneous and does not correspond to a uniform pathophysiological mechanism[13,17]. Indeed, some autosomal recessive genetic hypoplasias are thought to be due to abnormal development of the definitive cerebellar cortex, arising during differentiation of the internal granular layer and leading to late onset hypoplasia, after the sixth month of pregnancy, which represents a time of intense neuroblast proliferation[13]. In the presence of a proband of primitive hypoplasia, it is impossible to rule out a recurrence on the basis of normal biometry at 20–22 gestational weeks, and such a situation should prompt measurement of the TCD during the third trimester of the pregnancy. On the other hand, in some forms of cerebellar hypoplasia, particularly those associated with cytomegalovirus fetopathy or a karyotypic abnormality, the diagnosis may be made as early as 20–22 gestational weeks[3].

'Atrophy' of the cerebellum is also defined as decreased cerebellar volume, although, as opposed to hypoplasia, in which the diminution of volume is congenital, atrophy is used to define a complete anatomical structure displaying a secondary volume diminution. However, a precocious atrophic process, beginning in the prenatal period, is indistinguishable from hypoplasia as far as imaging is concerned (e.g. in congenital disorders of glycosylation).

In routine practice, a normal posterior fossa is assessed sonographically on an axial plane by a normal cisterna magna which does not exceed 10 mm in depth, a normal TCD for gestational age, and identification of

normal cerebellar anatomy, including a distinct vermis surrounded by two well-defined hemispheres, with no communication between the fourth ventricle anteriorly and the cisterna magna posteriorly. Therefore, we propose in our algorithm (Figure 1) that the main abnormalities of the posterior fossa that can be depicted on routine ultrasound examination (axial plane) include: (1) increased cisterna magna: the so called 'cystic' malformations of the posterior fossa, for which the wider terminology of 'increased fluid-filled space of the posterior fossa' is preferred, (2) abnormal TCD (most often decreased) and (3) abnormal cerebellar anatomy. In such circumstances, a prenatal imaging work-up is mandatory for an accurate anatomical cerebral check-up based on further ultrasound planes, especially sagittal ones, and MRI.

(1) In the setting of an 'increased fluid-filled space of the posterior fossa', the main anatomical landmark is the position of the cerebellar tentorium and torcular. In the case of ascent of the torcular (Figure 2), the increased fluid-filled retro- or pericerebellar space is related to an expansion of the fourth

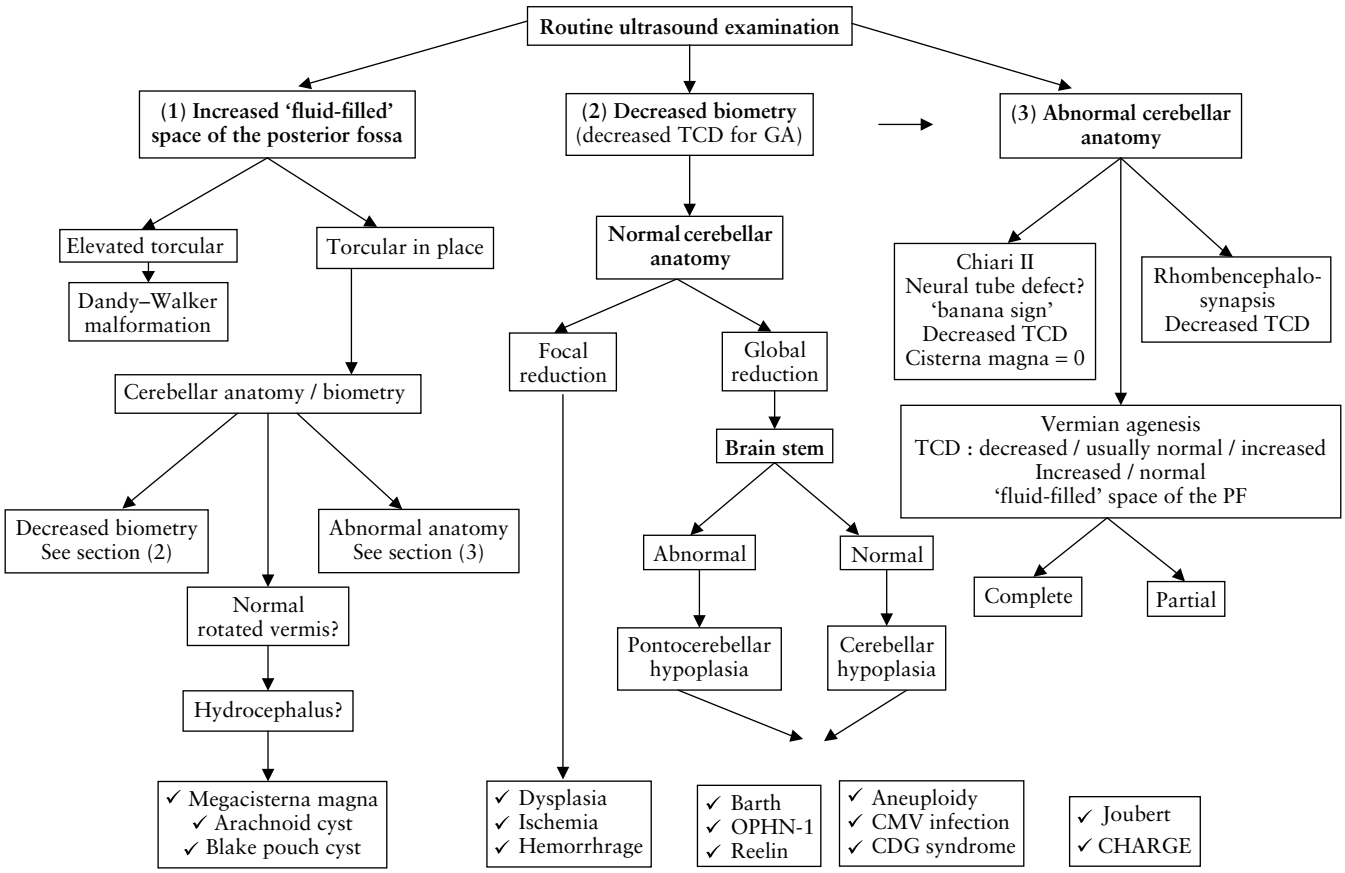

Figure 1 Algorithm showing an anatomical approach to classification of abnormalities of the posterior fossa according to main abnormal routine sonographic findings. CDG, congenital disorders of glycosylation; CMV, cytomegalovirus; GA, gestational age; PF, posterior fossa; TCD, transverse cerebellar diameter.

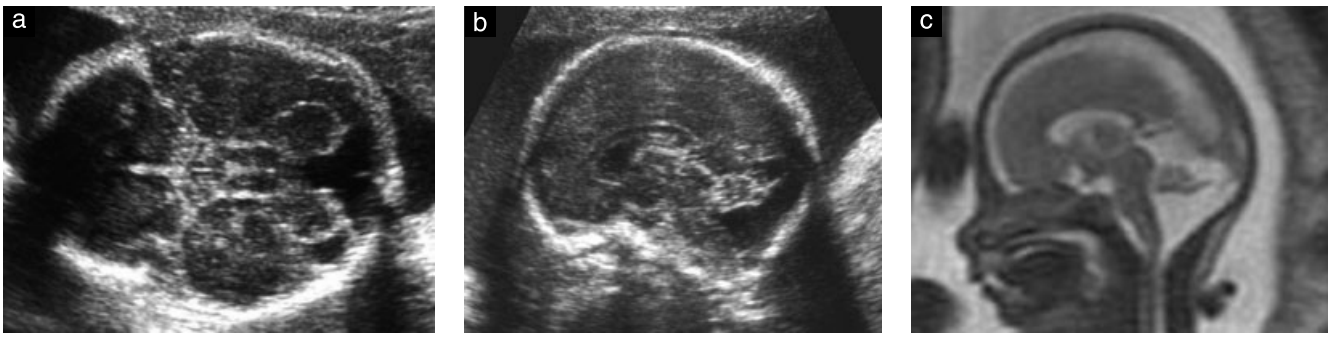

Figure 2 Dandy–Walker malformation in a patient referred for an 'increased fluid-filled space' in the posterior fossa. (a) Axial ultrasound image at 24 gestational weeks showing a communication between the fourth ventricle and the cisterna magna suggestive of vermian agenesis. (b) Median sagittal ultrasound image showing enlargement of the posterior fossa with ascent of the cerebellar tentorium associated with partial vermian agenesis and cystic dilatation of the fourth ventricle. (c) Fetal magnetic resonance imaging confirmed the sonographic data.

ventricle, and this is characteristic of Dandy–Walker malformation[11]. According to Klein *et al.*[18], the prognosis of this malformation is correlated with the anatomy of the vermis as well as the associated cerebral malformations. Therefore, such a malformation requires accurate anatomical imaging of the posterior fossa, especially in the identification of the vermian fissures[19].

In the case of normal positioning of the torcular, the main criterion on which to base diagnosis is the anatomy and biometry of the cerebellum. If the cerebellum is biometrically and anatomically normal (in some cases just deformed or compressed), the 'increased fluid-filled space' is related either to a rotation of a normal vermis (Figure 3), with or without a Blake pouch cyst, or to an arachnoid cyst or a megacisterna magna[4,7,20,21]. In such circumstances one should look for hydrocephalus, which can appear in the pre- or postnatal period and interfere with otherwise normal development. Therefore, follow-up of the occipitofrontal circumference is required during the first 2 years of life.

(2) Decreased cerebellar biometry can be associated with either normal or abnormal cerebellar anatomy. Decreased cerebellar biometry associated with normal cerebellar anatomy (i.e. cerebellum showing a distinct

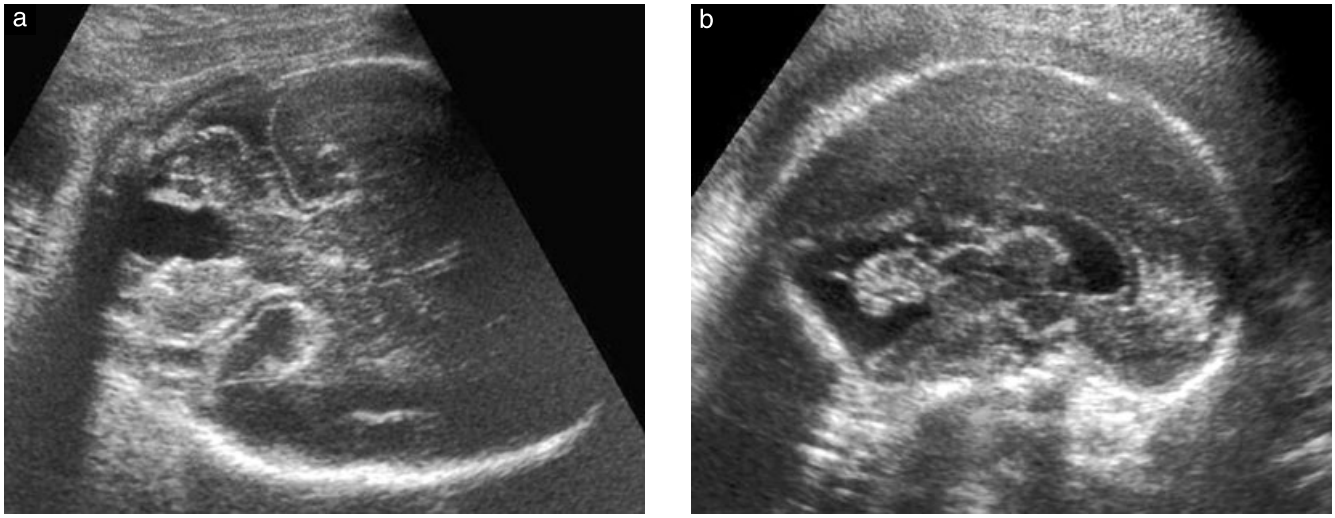

Figure 3 Rotation of a normal vermis in a patient referred for an 'increased fluid-filled space' in the posterior fossa and suspicion of 'abnormal cerebellar anatomy'. (a) Axial oblique ultrasound image at 26 gestational weeks, angled steeply towards the coronal plane, which led to an erroneous diagnosis of vermian agenesis. (b) Median sagittal ultrasound image showing simple rotation of a complete vermis leading to a posteroinferior opening of the fourth ventricle with no enlargement of the posterior fossa.

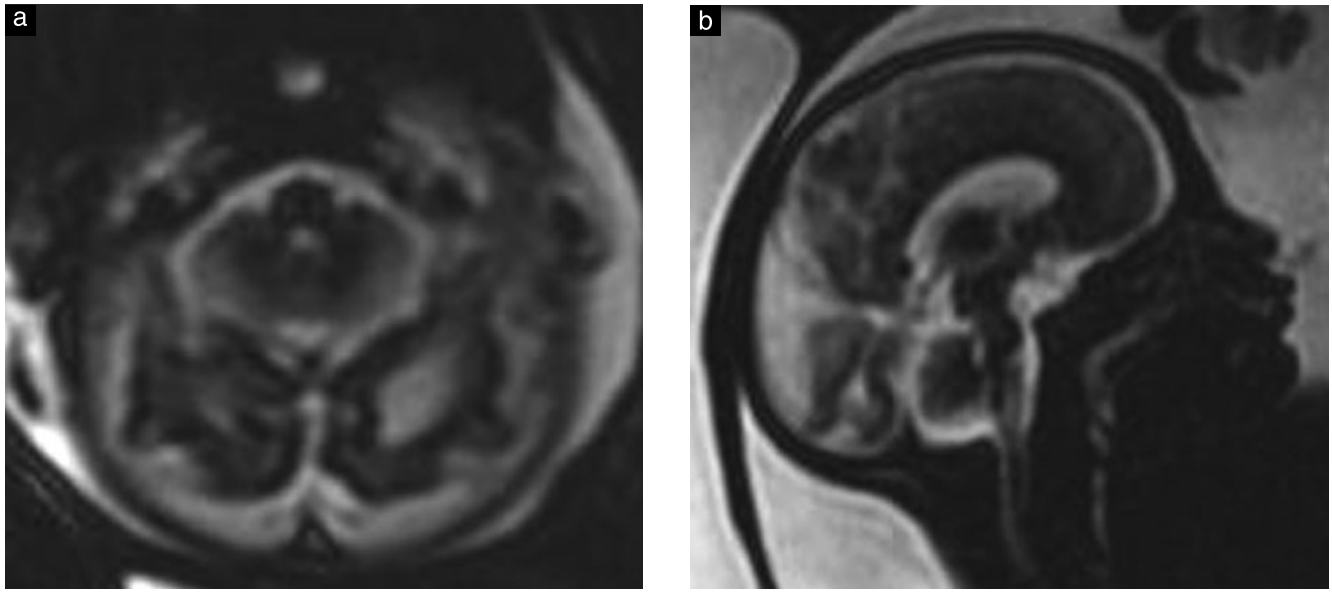

Figure 4 Pontocerebellar hypoplasia in a patient referred for a 'decreased transverse cerebellar diameter (TCD)'. Fetal magnetic resonance images (axial) obtained at 31 gestational weeks (a) confirming a decreased TCD (31 mm; median for gestational age = 37 mm) with normal cerebellar anatomy (which included a normal vermis on the median sagittal image), but (b) showing an abnormal brain stem with severe reduction of the anterior bulge of the pons. Karyotyping showed a 5p deletion.

vermis and two symmetrical ventricles) can be either focal or global. Global decreased cerebellar biometry requires a focus of attention on the brain-stem anatomy to differentiate cerebellar hypoplasia from pontocerebellar hypoplasia[3,4]. Such hypoplasia can be primitive or secondary to aneuploidy (Figure 4), infection or polymalformative syndrome[3,12,17,22,23]. Decreased cerebellar biometry can also be focal (i.e. located on one hemisphere), suggesting either focal dysplasia or ischemic and hemorrhagic events[24].

(3) Abnormal cerebellar anatomy is the third situation which can be encountered on a routine ultrasound examination. The diagnosis of Chiari II associated with myelomeningocele is easily made on the basis of the abnormal shape of the cerebellum ('banana sign') and the non-identified obliterated cisterna magna. The other entities revealed by an abnormal cerebellar anatomy require analysis of the vermis and cerebellar hemispheres, including identification of vermian fissures and hemispheric foliation, and identification of the fourth ventricle to differentiate rhombencephalosynapsis (Figure 5) from partial and complete agenesis of the vermis (Figure 6)[3]. In the case of partial vermian agenesis, identification of fissures may be of interest in order to assess a putative correlation between the degree of the vermian defect and psychomotor development, which remains unclear.

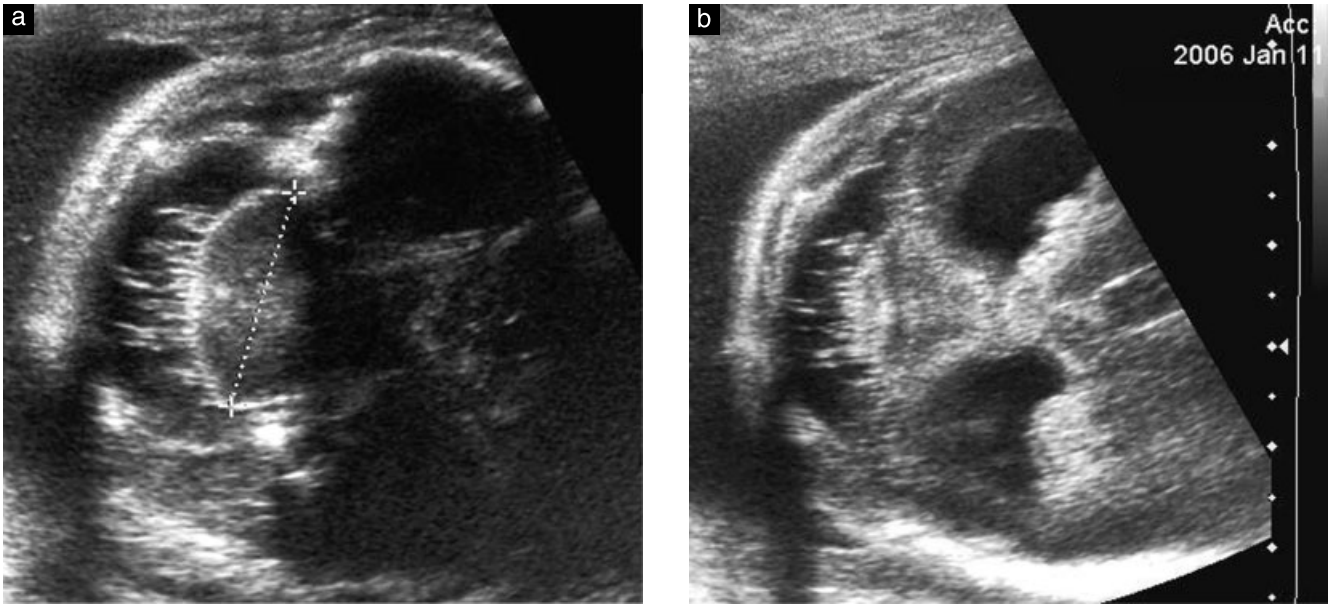

Figure 5 Rhombencephalosynapsis in a patient referred for a 'decreased transverse cerebellar diameter (TCD)' and 'abnormal cerebellar anatomy'. (a) Axial ultrasound image at 22 gestational weeks, confirming a decreased TCD (19 mm; median for gestational age = 22–23 mm) and showing an abnormal cerebellum formed of a single block with no individualization of vermian structure. (b) Coronal image showing the pathognomonic unique transverse foliation.

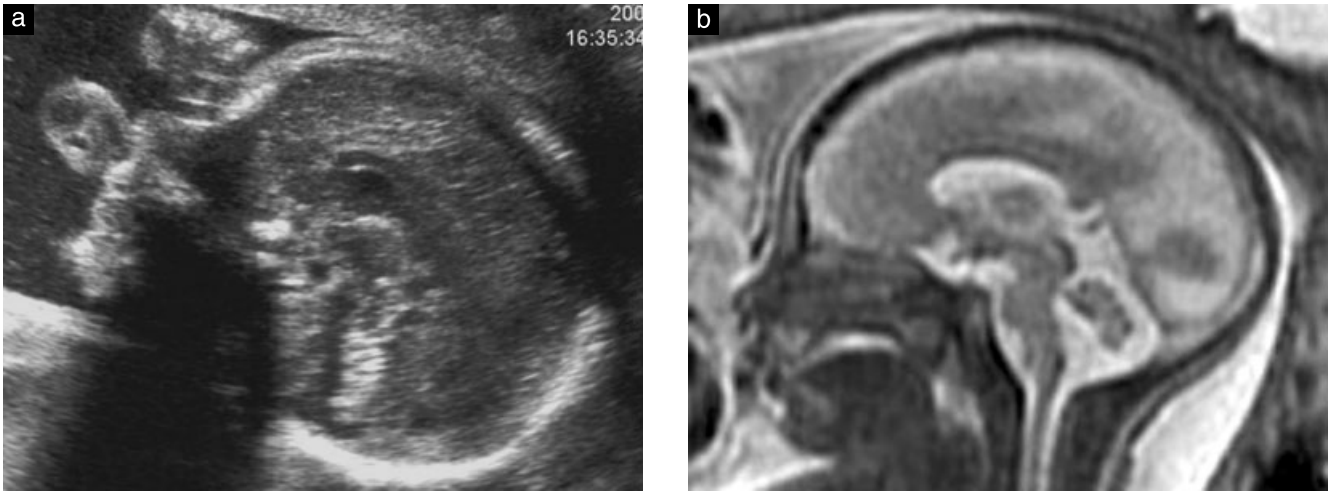

Figure 6 Partial vermian agenesis in a patient referred for an 'increased fluid-filled space' and 'abnormal cerebellar anatomy' associated with severe cardiopathy. Median sagittal ultrasound (a) and magnetic resonance (b) images at 25 gestational weeks, showing partial vermian agenesis with a wide communication between the fourth ventricle and the cisterna magna through the defective part of the vermis, with no enlargement of the posterior fossa. Note the normal bulge of the pons.

In the case of partial vermian agenesis, abnormal anatomy of the cerebellum is associated in most cases with an increased fluid-filled retrocerebellar space, due to a wide communication between the fourth ventricle and the cisterna magna through the defective part of the vermis. However, in a few cases, especially Joubert syndrome, this communication is not present, resulting in a cisterna magna of normal volume but with a deformation of the fourth ventricle associated with the typical 'molar tooth pattern' related to abnormal superior cerebellar peduncles[4,25,26].

Such anatomical classification is essential for identification of homogeneous groups of patients that may share the same prognosis. Indeed, the groups of abnormalities of the posterior fossa described above (hypoplasia, agenesis and atrophy) can be further divided into subgroups according to etiology (isolated, syndromic, infectious, vascular), for each of which a prognosis should be evaluated separately. Such efforts at classification in prenatal diagnosis are mandatory in order to carry out correlations with fetopathological data and prospective follow-up of patients, allowing refined prenatal counseling with respect to motor and cognitive outcome.

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