ELSEVIER

European Journal of Radiology 57 (2006) 226–232

EJR
EUROPEAN JOURNAL OF RADIOLOGY

www.elsevier.com/locate/ejrad

Normal and abnormal fetal brain development during the third trimester as demonstrated by neurosonography

G. Malinger*, D. Lev, T. Lerman-Sagie

Fetal Neurology Clinic, Department of Obstetrics and Gynecology, Genetics Institute and Pediatric Neurology Unit, Wolfson Medical Center, Holon, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Holon 58100, Israel

Received 11 November 2005; received in revised form 14 November 2005; accepted 16 November 2005

Abstract

The multiplanar neurosonographic examination of the fetus enables superb visualization of brain anatomy during pregnancy. The examination may be performed using a transvaginal or a transfundal approach and it is indicated in patients at high risk for CNS anomalies or in those with a suspicious finding during a routine examination. The purpose of this paper is to present a description of the normal brain and of abnormal findings usually diagnosed late in pregnancy, including malformations of cortical development, infratentorial anomalies, and prenatal insults.

Keywords: Ultrasound; Prenatal diagnosis; Third trimester; Brain anomalies; Cortical malformations; Prenatal insults

1. Introduction

The classic approach to the evaluation of the fetal brain by ultrasound is based on the transabdominal visualization of three different axial planes: the transventricular; the transthalamic; and the transcerebellar. Retrospective studies on the diagnosis of fetal CNS anomalies have shown that the use of these three planes help in the diagnosis of most, but not all, pathologies [1,2].

The major disadvantages of the use of these axial planes are poor visualization of the hemisphere proximal to the transducer and difficult depiction of midline brain structures, mainly the corpus callosum, the third ventricle, and the cerebellar vermis.

The use of a more comprehensive, multiplanar approach, in which coronal and sagittal planes are added to the classical axial planes, can overcome these limitations [3]. A transvaginal approach to fetuses in a vertex presentation or a transfundal approach to fetuses in a breech presentation are required in order to perform this detailed neurosonographic examination.

This article will describe our experience with normal and abnormal brain development during the third trimester of pregnancy, as depicted by multiplanar neurosonography.

2. Axial planes

Axial planes are routinely used for biometry assessment and screening for CNS anomalies (Fig. 1). The transventricular plane enables visualization of the posterior horn and atrium of the lateral ventricle and is used for the measurement of the lateral ventricular width. The cavum septi pellucidi is also depicted in this plane.

The transthalamic plane is used for the measurement of biparietal diameter and head circumference. The transcerebellar plane shows the cerebellum, vermis, and posterior fossa.

3. Coronal planes

In contrast with neonatal brain ultrasound, which is usually performed through the anterior fontanel, fetal brain ultrasound is performed through both the anterior and posterior

* Corresponding author.
E-mail address: malinger@nashim.net (G. Malinger).

0720-048X/$ – see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ejrad.2005.11.022

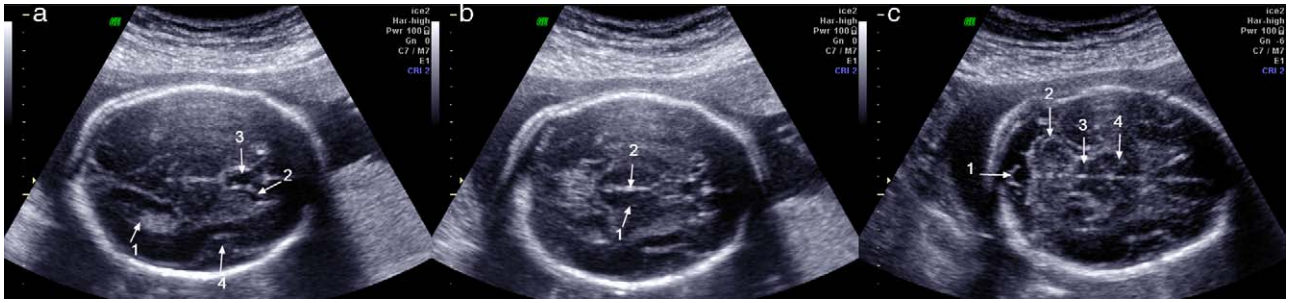

Fig. 1. Transabdominal axial planes at 25 weeks. (a) Transventricular plane shows the atrium and occipital horn of the distal lateral ventricle (1), the frontal horn (2), the cavum septi pellucidi (3), and the insula (4); (b) transthalamic plane shows the thalamus (1) and very thin third ventricle (2); (c) transcerebellar plane shows the cisterna magna (1), the cerebellum, and the vermis (2), middle cerebellar peduncles (3), and thalamus (4). Note the poor visualization of the proximal hemisphere.

fontanels and the sagittal suture. This results in the depiction of parallel coronal planes, rather than radial ones. During real time examination, a continuum of the brain is visualized. Four different coronal planes are described: transfrontal; transcaudate; transthalamic; and transcerebellar (Fig. 2).

The transfrontal coronal plane enables visualization of the frontal horns of the lateral ventricles, the interhemispheric, uninterrupted fissure, and the frontal cortex with the sulci and gyri at different stages of development according to the gestational age. The transcaudate coronal plane depicts the anterior portion of the corpus callosum. The cavum septi pellucidi is found inferior to the corpus callosum, with the lateral ventricles at each side. The caudate nuclei are well delineated from the cortex.

The transthalamic coronal plane shows the third ventricle, the foramina of Monro, and the insulae.

The last coronal plane is the transcerebellar, showing both occipital horns of the lateral ventricles (note that they may be slightly asymmetric), and the normal sulcation of the occipital lobes.

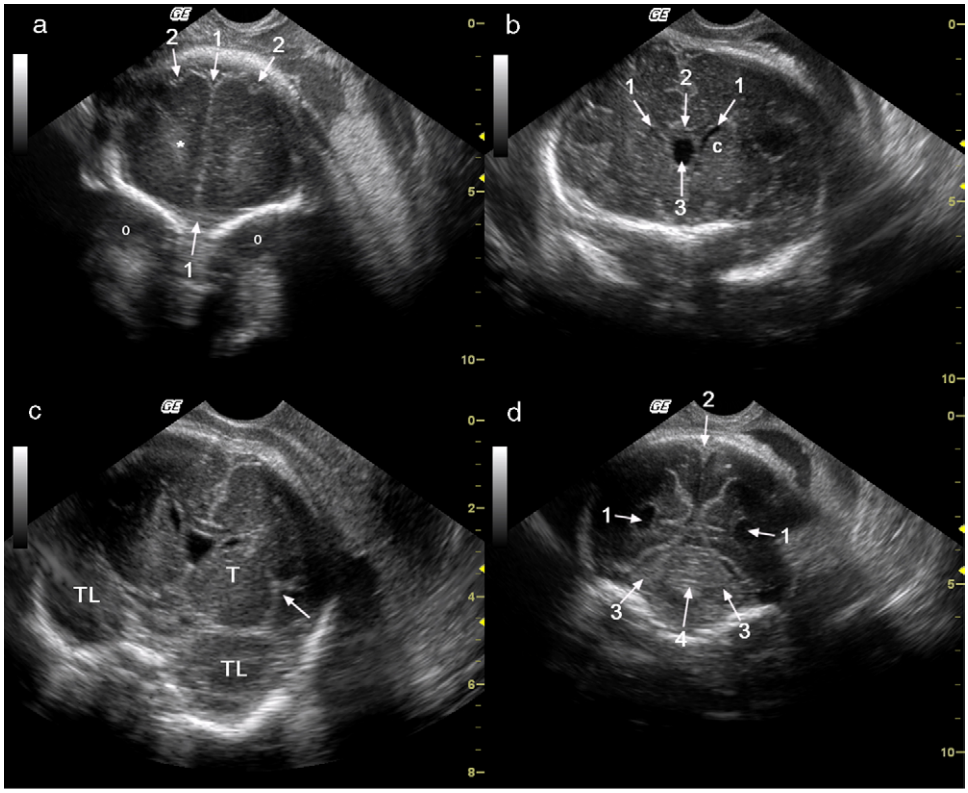

Fig. 2. Transvaginal coronal planes at 29 weeks. (a) Transfrontal plane slightly anterior to the frontal horns shows the hyperechogenic periventricular tissue (asterisk), the uninterrupted intrahemispheric fissure (1), the superior frontal sulci (2), and orbits (O); (b) transcaudate plane shows both frontal horns of the lateral ventricles (1), the corpus callosum (2), the cavum septi pellucidi (3), and the caudate (C; note the normal sulcation pattern); (c) transthalamic plane shows the insula (white arrow), the thalamus (T) and the temporal lobes (TL); (d) transcerebellar plane shows the occipital horns (1), the superior sagittal sinus (2), the cerebellar hemispheres (3), and the vermis (4).

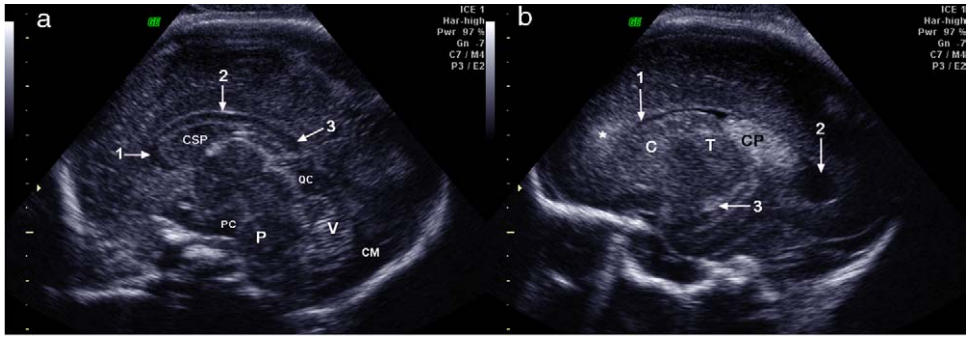

Fig. 3. Transvaginal sagittal planes at 25 weeks. (a) Midsagittal plane shows the corpus callosum (white arrows), including the genu (1), the body (2), the splenium (3), the cavum septi pellucidi (CSP), the pons (P), the vermis (C), and the subarachnoid cisterns, including the prepontine cistern (PC), the quadrigeminal cistern (QC), and the cisterna magna (CM). (b) Parasagittal plane shows the lateral ventricle (white arrows) frontal horn (1), occipital horn (2), temporal horn (3), and the choroid plexus (CP). The caudate (C) and thalamus (T) are also depicted. Note the normal hyperechogenicity anterior to the lateral ventricle (asterisk).

The coronal planes are also useful for the evaluation of the subarachnoid space, the superior sagittal sinus, and the sagittal suture.

4. Sagittal planes

Three sagittal planes are usually studied: the midsagittal and the parasagittal of each side of the brain (Fig. 3).

The midsagittal plane shows the corpus callosum with all its components; the cavum septi pellucidi; the cavum vergae and cavum interpositum; the brain stem; the pons; the vermis; and the posterior fossa. Using color Doppler, the anterior cerebral artery, the pericallosal artery and its branches, and the vein of Galen, can be depicted.

The parasagittal plane depicts the entire lateral ventricle, the choroid plexus, the periventricular tissue, and the cortex.

5. Diagnosis of brain pathologies during the third trimester

Late diagnosis of different brain pathologies is not rare. In a previous study, we found that as many as 11.5% of cases were diagnosed during the third trimester, following a normal second trimester examination [4]. This is sometimes attributable to misdiagnosis of the anomaly in an earlier scan; but, in the majority of cases, the cause is the late development of a specific, congenital or acquired pathology.

Some of these pathologies will be presented in the next sections.

6. Malformations of cortical development

Malformations of cortical development (MCD) include anomalies of neuronal proliferation, migration, and organization [5]. Although the migration process terminates around the end of the first half of pregnancy, there are only isolated case reports or small case series describing the prenatal ultrasonographic diagnosis of abnormal cortical development. This may be explained in some cases by the focal expression of the disorder; by the late appearance of significant morphological changes beyond the time of the recommended anatomic scan; by ultrasound evaluation of the brain that is often limited to visualization of the lateral ventricles and cerebellum; and by an incomplete knowledge of these entities and their ultrasonographic manifestations. Disorders of abnormal proliferation are usually expressed by an abnormal head circumference that may not be obvious until the last weeks of pregnancy or the first months postnatally and, therefore, may be missed by a second trimester ultrasound. Associated neurosonographic findings are scarce.

Recently, Fong et al. [6] published a retrospective study showing that, in fetuses suffering from Miller-Dicker and Walker-Warburg lissencephaly, abnormal sulcation landmarks could be observed as early as the 22nd week of gestation.

Isolated case reports and small series describing the prenatal diagnosis of MCD have been published [7–14].

According to our experience [15], associated CNS and non-CNS malformations are common in most prenatally diagnosed cases. The most frequently associated CNS anomalies are: callosal hypoplasia; vermian dysgenesis; periventricular changes; ventriculomegaly; large subarachnoid spaces; and cerebellar hypoplasia.

In patients with abnormal migration disorders, the ultrasound usually demonstrates one of the following patterns: delayed appearance of sulcation; a thin and irregular cortical mantle; abnormal overdeveloped sulci and gyri; or wide opening of isolated sulci (Fig. 4). A detailed ultrasound examination may provide some clues regarding the specific migration anomaly, but a definitive diagnosis may be possible only after the pathological examination. In some cases, the genetic diagnosis can be made by FISH or DNA analysis. Ultrasound cannot definitively differentiate, at present, between polymicrogyria and pachygyria, but can identify the abnormal migration.

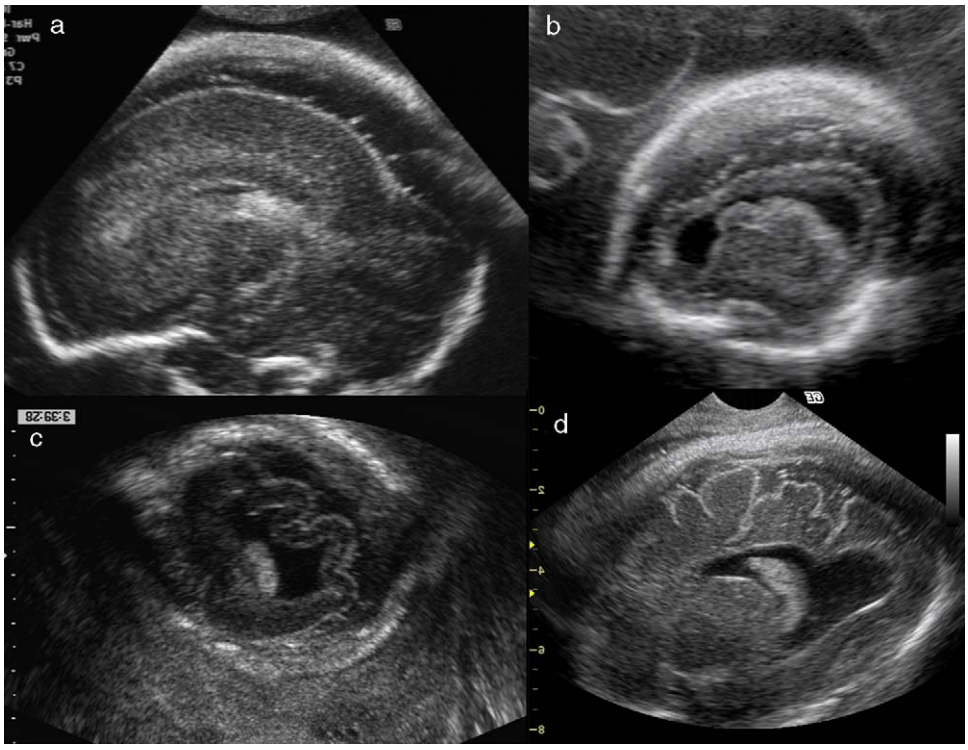

Fig. 4. Ultrasonographic patterns associated with migration disorders. (a) Lack of normal sulcation at 28 weeks; (b) thin and irregular cortex at 26 weeks; (c) abnormal overdeveloped sulci at 22 weeks; (d) wide and deep sulci at 31 weeks.

7. Infratentorial anomalies

Infratentorial anomalies associated with an enlarged cisterna magna, with or without an abnormal fourth ventricle, can easily be diagnosed during fetal life. The most frequently made diagnoses are: Arnold-Chiari malformation type 2; macro cisterna magna; arachnoid cyst; and Dandy-Walker malformation/variant [16,17].

However, the prenatal diagnosis of cerebellar and/or vermian dysgenesis is difficult, and may be impossible to perform during a routine second trimester US examination. The complexity of the normal and abnormal development of these structures, particularly the cerebellar vermis and brainstem, is probably the cause of the relatively high percentage of false-positive and negative diagnoses reported in the literature [18].

The correct approach to the evaluation of infratentorial structures is based on the depiction of these structures in the axial, coronal, and sagittal planes. The suspicion for the presence of an anomaly rises, in most cases, following the visualization of a small cerebellum or a "communication" between the fourth ventricle and the cisterna magna using the transcerebellar axial plane. Confirmation of the diagnosis necessitates the visualization of the cerebellum in the coronal planes, and a true midline sagittal picture of the vermis, brain stem, and fourth ventricle. Particular care should be taken in order to differentiate between the vermis and the cerebellar hemisphere in cases of suspected vermian agenesis or hypoplasia. Frequently, the cerebellar hemisphere may be seen as a continuation of the abnormally small vermis in the mid-sagittal plane. We have found that visualization of the normal, triangular shape of the fourth ventricle, and of the primary vermian fissure, are useful signs that facilitate exclusion of vermian pathologies (Fig. 5). The depiction of the hyperechogenic vermis with its lobes, in a coronal plane, is also important.

Diagnosis of isolated vermian hypoplasia is extremely important for counseling reasons since the prognosis may be more bleak in cases of vermian hypoplasia without enlargement of the fourth ventricle and cisterna magna [19].

Vermian hypoplasia may also be part of the molar tooth-associated syndromes. This anomaly, which consists of deep posterior interpeduncular fossa, thick and elongated superior cerebellar peduncles, and hypoplastic or aplastic superior cerebellar vermis, is difficult to identify in utero [20]. Searching for associated anomalies, such as polydactyly, hepatic fibrosis, or renal cysts, may improve the diagnostic yield.

The association of cerebellar and pontine hypoplasia can be seen in the group of syndromes designated the pontocerebellar hypoplasias [21]. In order to identify this group of syndromes in fetal life, it is important to measure the pons circumference in addition to the cerebellar dimensions [22].

8. Prenatal insults

A prenatal insult may occur at any time in pregnancy, thus precluding its diagnosis if the ultrasound examination

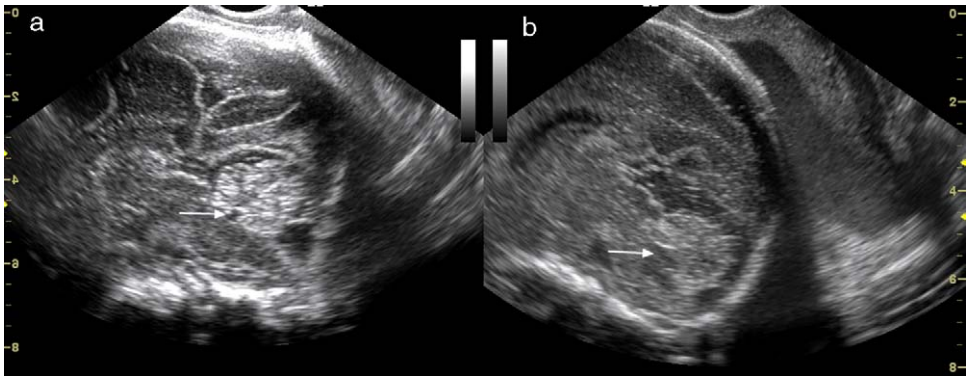

Fig. 5. Transvaginal midsagittal planes. (a) Normal vermis and fourth ventricle; (b) abnormal shape of the fourth ventricle in a fetus with dysgenetic vermis. The arrows show the fourth ventricle.

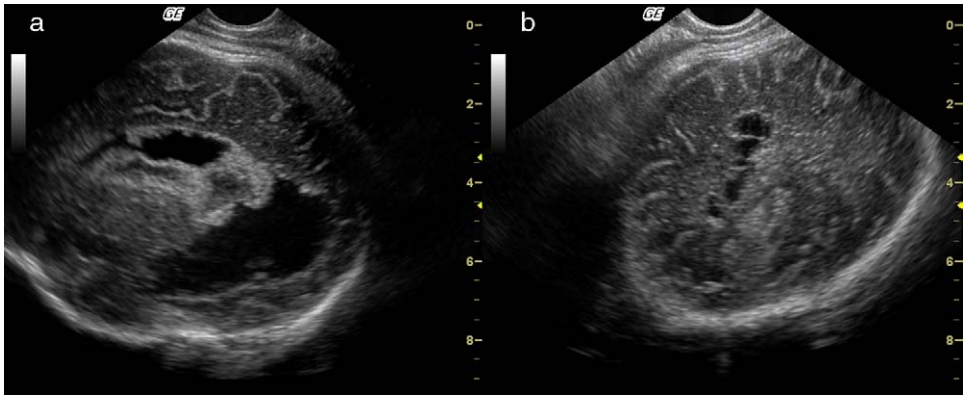

Fig. 6. Intraventricular hemorrhage, grade IV, with periventricular infarction and cystic formation at 35 weeks. (a) Transvaginal parasagittal plane shows the dilated lateral ventricle with clots around the choroid plexus and ventricle walls; (b) a more lateral parasagittal view shows the presence of multilocular cyst.

is performed before or close to the time of its occurrence. Prenatal insults may be classified according to their etiology as ischemic, hemorrhagic, infective, or teratogenic events. Fetal brain tumors are also included in this group of disorders.

The in utero identification of prenatal insults is increasingly being made and relatively large series or reviews of these events have been recently published [23,24].

Ischemic and hemorrhagic insults are usually diagnosed following visualization of ventriculomegaly or by chance during a routine third trimester US examination. Hemorrhage may be limited to the periventricular germinal matrix, or may extend into the lateral ventricles; in severe cases, intraparenchymal bleeding may produce periventricular infarction followed by the development of cystic lesions or porencephaly (Fig. 6). The prognosis is based on the severity of the intraventricular hemorrhage. Perinatal mortality and morbidity may be as high as 100% in newborns with prenatal intraventricular hemorrhage Grade III–IV [25].

Periventricular cysts that are not associated with hemorrhage may be identified by ultrasound; the prognosis depends not only on the position and the size of the lesions but also on the patient's history (Fig. 7). Periventricular pseudocysts may be diagnosed based on their typical appearance and position: below the roof of the lateral ventricle and in proximity to the caudo-thalamic groove. The prognosis in these cases is usually good [26].

The prenatal imaging findings in fetuses with intrauterine infections can include a wide range of affected sites and be

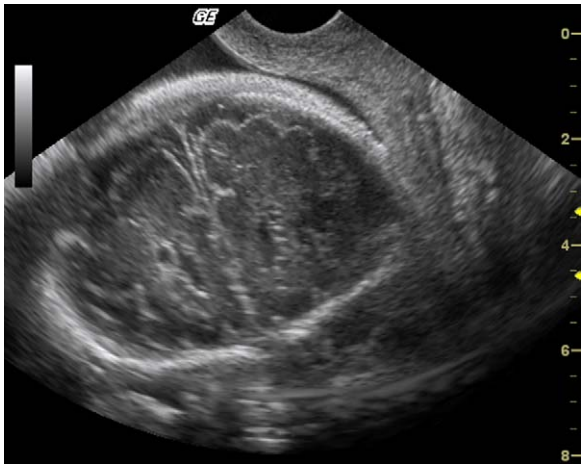

Fig. 7. Bilateral multiple small periventricular cysts in a consanguineous couple with a history of two children who died of an undiagnosed neurological disease. Following delivery, this child developed neonatal convulsions and died at the age of 2 months.

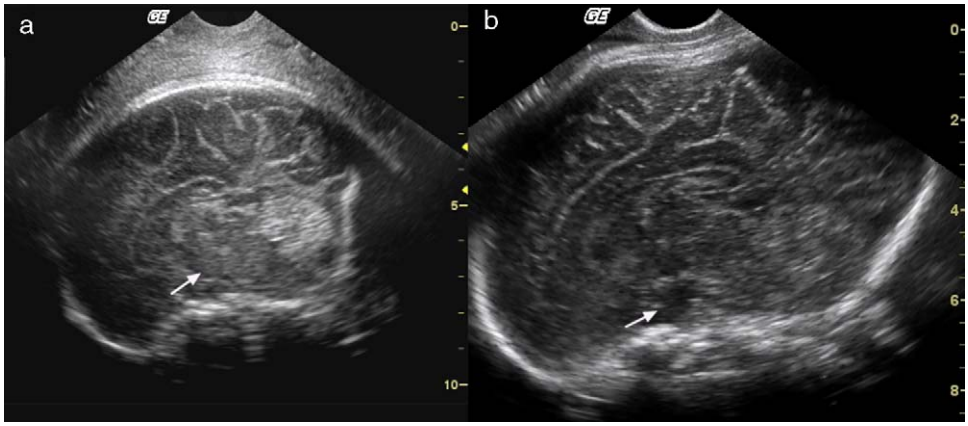

Fig. 8. Transvaginal sagittal plane. (a) Hypothalamic hamartoblastoma at 34 weeks in a fetus with Pallister-Hall syndrome (white arrows); (b) normal cistern with fluid at the same gestational age (white arrows).

of different grades of severity. The presence of associated microcephaly is almost always a poor prognostic sign.

Intrauterine cytomegalovirus infection is the most frequently diagnosed infective fetopathy. The common CNS abnormalities found in this category include: abnormal periventricular echogenicity; periventricular cysts; intraventricular adhesions; calcifications; striatal vasculopathy; abnormal sulcation; dysgenesis of the corpus callosum; dysgenesis of the cerebellum; and intracranial hemorrhages [23].

In patients with known CMV seroconversion and a normal US examination, amniocentesis is performed at around 22 weeks for CMV PCR analysis; when the test is positive for CMV, follow-up neurosonographic and MRI studies are indicated.

Solid fetal brain tumors are extremely rare and difficult to diagnose (Fig. 8). Intracranial cysts, particularly arachnoid cysts, are much more common and, when isolated, have a good prognosis (Fig. 9).

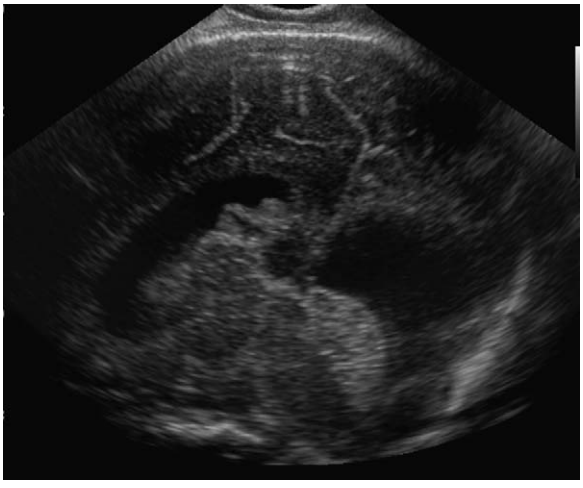

Fig. 9. Retrocerebellar arachnoid cyst at 34 weeks that produced compression of the cerebellum and progressive ventriculomegaly. Normal postnatal development following neurosurgery.

9. Conclusions

The comprehensive multiplanar ultrasonographic approach enables accurate depiction of intrauterine brain development. A knowledge of normal brain development enables identification of abnormal development. Malformations of cortical development, infratentorial anomalies, and prenatal insults can be accurately identified during a third trimester scan, thus enabling appropriate counseling.

References

[1] Filly RA, Cardoza JD, Goldstein RB, Barkovich AJ. Detection of fetal central nervous system anomalies: a practical level of effort for a routine sonogram. Radiology 1989;172:403–8.
[2] Reece EB, Goldstein I. Three-level view of fetal brain imaging in the prenatal diagnosis of congenital anomalies. J Matern Fetal Med 1999;8:249–52.
[3] Malinger G, Katz A, Zakut H. Transvaginal fetal neurosonography. Supratentorial structures. Isr J Obstet Gynecol 1993;4:1–5.
[4] Malinger G, Lerman-Sagie T, Watemberg N, Rotmensch S, Lev D, Glezerman M. A normal second-trimester ultrasound does not exclude intracranial structural pathology. Ultrasound Obstet Gynecol 2002;20:51–6.
[5] Volpe JJ. Neuronal proliferation, migration, organization and myelination. In: Volpe JJ, editor. Neurology of the newborn. Philadelphia: Saunders WB; 1995. p. 43–90.
[6] Fong KW, Ghai S, Toi A, Blaser S, Winsor EJT, Chitiyat D. Prenatal ultrasound diagnosis of Lissencephaly associated with Miller-Dieker syndrome: correlation with pre- and postnatal magnetic resonance imaging. Ultrasound Obstet Gynecol 2004;24:716–23.
[7] Holzgreve W, Feil R, Louwen F, Miny P. Prenatal diagnosis and management of fetal hydrocephaly and lissencephaly. Childs Nerv Syst 1993;9:408–12.
[8] McGahan JP, Grix A, Gerscovich EO. Prenatal diagnosis of lissencephaly: Miller-Dieker syndrome. J Clin Ultrasound 1994; 22:560–3.
[9] Bornemann A, Pfeiffer R, Beinder E, et al. Three siblings with Walker-Warburg syndrome. Gen Diagn Pathol 1996;141:371–5.
[10] Greco P, Resta M, Vimercati A, et al. Antenatal diagnosis of isolated lissencephaly by ultrasound and magnetic resonance imaging. Ultrasound Obstet Gynecol 1998;12:276–9.

[11] Onyeije CI, Sherer DM, Jarosz CJ, Divon MY. Prenatal sonographic findings associated with sporadic subcortical nodular heterotopia. Obstet Gynecol 1998;91:799–801.
[12] Mitchell LA, Simon EM, Filly RA, Barkovich AJ. Antenatal diagnosis of subependymal heterotopia. AJNR Am J Neuroradiol 2000;21:296–300.
[13] Saltzman DH, Krauss CM, Goldman JM, Benacerraf BR. Prenatal diagnosis of lissencephaly. Prenat Diagn 1991;11:139–43.
[14] Okamura K, Murotsuki J, Sakai T, Matsumoto K, Shirane R, Yajima A. Prenatal diagnosis of lissencephaly by magnetic resonance image. Fetal Diagn Ther 1993;8:56–9.
[15] Malinger G, Kidron D, Lev D, Lerman-Sagie T. Imaging and histopathological features of fetal cortical malformations. Ultrasound Obstet Gynecol 2004;24:261.
[16] Van den Hof MC, Nicolaides KH, Campbell J, Campbell S. Evaluation of the lemon and banana signs in one hundred thirty fetuses with open spina bifida. Am J Obstet Gynecol 1990;162:322–7.
[17] Klein O, Pierre-Kahn A, Boddaert N, Parisot D, Brunelle F. Dandy-Walker malformation: prenatal diagnosis and prognosis. Childs Nerv Syst 2003;19:484–9.
[18] Carroll SG, Porter H, Abdel-Fattah S, Kyle PM, Soothill PW. Correlation of prenatal ultrasound diagnosis and pathologic findings in fetal brain abnormalities. Ultrasound Obstet Gynecol 2000; 16:149–53.
[19] Adamsbaum C, Moutard ML, Andre C, et al. MRI of the fetal posterior fossa. Pediatr Radiol 2005;35:124–40.
[20] Gleeson JG, Keeler LC, Parisi MA, et al. Molar tooth sign of the midbrain–hindbrain junction: occurrence in multiple distinct syndromes. Am J Med Genet 2004;125:125–34.
[21] Boltshauser E. Cerebellum-small brain but large confusion: a review of selected cerebellar malformations and disruptions. Am J Med Genet 2004;126:376–85.
[22] Achiron R, Kivilevitch Z, Lipitz S, Gamzu R, Almog B, Zalel Y. Development of the human fetal pons: in utero ultrasonographic study. Ultrasound Obstet Gynecol 2004;24:506–10.
[23] Malinger G, Lev D, Zahalka N, et al. Fetal cytomegalovirus infection of the brain: the spectrum of sonographic findings. AJNR Am J Neuroradiol 2003;24:28–32.
[24] Ghi T, Simonazzi G, Perolo A, et al. Outcome of antenatally diagnosed intracranial hemorrhage: case series and review of the literature. Ultrasound Obstet Gynecol 2003;22:121–30.
[25] Elchalal U, Yagel S, Gomori JM, et al. Fetal intracranial hemorrhage (fetal stroke): does grade matter? Ultrasound Obstet Gynecol 2005;26:233–43.
[26] Malinger G, Lev D, Ben Sira L, Kidron D, Tamarkin M, Lerman-Sagie T. Congenital periventricular pseudocysts: prenatal sonographic appearance and clinical implications. Ultrasound Obstet Gynecol 2002;20:447–51.