WAPM Recommendations

Valentina De Robertis*, Cihat Sen, Ilan Timor-Tritsch, Rabih Chaoui, Paolo Volpe, Alberto Galindo, Reuven Achiron, Ritsuko Pooh, Asma Khalil, Nicola Volpe, Francesco D'Antonio and Roee Birnbaum

WAPM-World Association of Perinatal Medicine Practice Guidelines: Fetal central nervous system examination

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Abstract: These practice guidelines follow the mission of the World Association of Perinatal Medicine in collaboration with the Perinatal Medicine Foundation, bringing together groups and individuals throughout the world, with the goal of improving the ultrasound assessment of the fetal Central Nervous System (CNS) anatomy. In fact, this document provides further guidance for healthcare practitioners for the evaluation of the fetal CNS during the mid-trimester ultrasound scan with the aim to increase the ability in evaluating normal fetal anatomy. Therefore, it is not intended to establish a legal standard of care. This document is based on consensus among perinatal experts throughout the world, and serves as a guideline for use in clinical practice.

Keywords: anatomy scan; central nervous system; fetal brain; fetal spine; guidelines; second trimester; WAPM.

***Corresponding author: Valentina De Robertis**, Fetal Medicine Unit, Di Venere and Sarcone Hospitals, ASL BA, Via Ospedale Di Venere, Bari, Italy, Phone: +390805015007, E-mail: derobertis_v@libero.it
Cihat Sen, Perinatal Medicine Foundation, Istanbul, Turkey
Ilan Timor-Tritsch, Division of Obstetrical and Gynecological Ultrasound, NYU School of Medicine, New York, NY, USA
Rabih Chaoui, Center for Prenatal Diagnosis and Human Genetics, Berlin, Germany
Paolo Volpe, Fetal Medicine Unit, Di Venere and Sarcone Hospitals, ASL BA, Bari, Italy
Alberto Galindo, Department of Obstetrics and Gynaecology, Fetal Medicine Unit, Maternal and Child Health and Development Network, University Hospital 12 de Octubre, Complutense University of Madrid, Madrid, Spain
Reuven Achiron, Department of Obstetrics and Gynecology, Fetal Medicine Unit, The Chaim Sheba Medical Center Tel-Hashomer, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
Ritsuko Pooh, Fetal Diagnostic Center, CRIFM Clinical Research Institute of Fetal Medicine, Osaka, Japan
Asma Khalil, Fetal Medicine Unit, St George University Hospital NHS Foundation Trust, London, UK
Nicola Volpe, Department of Medicine and Surgery, Unit of Surgical Sciences, Obstetrics and Gynecology, University of Parma, Parma, Italy
Francesco D'Antonio, Department of Obstetrics and Gynecology, Center for Fetal Care and High-Risk Pregnancy, University of Chieti, Chieti, Italy
Roee Birnbaum, OB-GYN Ultrasound Unit, Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Introduction

Rationale of this recommendation

Fetal central nervous system (CNS) abnormalities are fairly common, with an incidence of about 0.1–0.2% in live births and an even higher occurrence of about 3–6% in stillbirths. Such anomalies have clinical importance as they are associated with high rates of morbidity and mortality, influencing the neurocognitive and motor development of the survivors, who may have lifelong sequelae. Therefore, it is extremely important to evaluate the fetal CNS anatomy throughout the pregnancy in order to assess its normal and abnormal development.

Prenatal ultrasound (US) has been shown to be an effective primary imaging modality for depiction of normal development of CNS anatomic structures and it offers a relatively accurate, safe, and cost-effective screening in pregnancy [1, 2].

Although some abnormalities may be suspected and diagnosed in the first trimester of pregnancy [3–5], most efforts to detect CNS malformations occur during the second trimester, in the examination of fetal morphology conducted at 22 (18–24) weeks of gestation. The majority of national and international guidelines recommend at this gestational age an US examination to delineate fetal anatomy as a part of standard obstetric care.

As a matter of fact, at this gestational age, the major intracranial structures have formed from their embryologic origins and can be well visualized by US.

The aim of the mid-trimester scan in low-risk pregnancies is fundamentally to establish the normal anatomy of the fetal brain and spine. For anatomical evaluation of CNS in routine practice, axial planes have been proposed as the standard planes. However, the major disadvantages of the use of these axial planes are the poor visualization of the hemisphere proximal to the transducer and the difficult depiction of midline brain structures, mainly the corpus callosum and the cerebellar vermis due to its anatomical location and orientation. Therefore, additional planes such as median/midsagittal view should be taken into consideration [6].

If the ultrasonographic finding of CNS structures differs from normal anatomy, a further evaluation by a competent/expert operator is required in order to make a conclusive diagnosis or reassure the patient when structural anomalies are ruled out. Therefore, all the suspected abnormal cases at the anatomy scan should be referred for a "fetal neurosonography", a dedicated examination of the fetal brain and spine that requires specific expertise and sophisticated ultrasound equipment.

The prenatal detection of CNS anomalies allows, not only a specific prenatal management and counseling, but also facilitate appropriate prognostic definition with the support of supplementary diagnostic tests as MRI [7–9] and genetic tests [10]. However, it is important to emphasize that a normal CNS assessment in the second-trimester morphology scan does not rule out the emergence of fetal anomalies later in pregnancy. In fact, some of the CNS anomalies can be diagnosed only during late second and third trimesters of pregnancy. Consequently, in patients who have a third trimester scan for any reason, assessment of the fetal CNS should be considered [11, 12].

The scope of this document is to reach a consensus about an optimized approach to the evaluation of the CNS anatomy in routine obstetric care in low-risk pregnancies at 22 (18–24) weeks of gestation in order to improve the prenatal detection of these severe anomalies.

Technical issues

Ultrasound transducers

High-frequency ultrasound transducers increase spatial resolution but decrease the penetration of the sound beam. The selection of the optimal transducer and frequency depends on gestational age, maternal habitus, position of the fetus, and the scanning approach used. Transabdominal transducers with 3–5 MHz, are mostly used, however while they "penetrate" deeper, their resolution is lower than high frequency probe such as 4–8 MHz and those of the transvaginal probe, which operate at higher frequencies increasing resolution [6].

The examination is usually performed with grayscale 2D ultrasound. It may be important to mention that harmonic and speckle-reduction filters, may enhance image quality mainly in patients with increased body mass index or abdominal scars.

The use of transvaginal probes should be always entertained if the fetus is in cephalic presentation. At times, if relevant, a gentle external version of a breech to vertex presentation can be helpful [12].

Methods

With the scope of reaching a consensus among experts, a survey was conducted among members of the group.

All possible anatomical structures of the fetal brain and spine were listed and group members were asked to answer the following questions:

- Should the following anatomical structures be evaluated always, possibly or never at the time of second trimester anatomy scan?
- Do you suggest one or more planes?
- Which would be the need for transvaginal approach to visualize the listed anatomical structures on each plane?

Agreement among members was evaluated for each anatomical structure and scanning plane.

The evaluation of anatomical structures and scanning planes that should always be evaluated with an agreement among members exceeding 75%, are referred in this document as "recommended" as part of the mid-trimester anatomy scan. The evaluation of anatomical structures and scanning planes that should be possibly evaluated with an agreement among members exceeding 75%, are referred in this document as "suggested" as part of the mid-trimester anatomy scan. The evaluation of anatomical structures and scanning planes that should never be evaluated with an agreement among members exceeding 75%, are considered in this document as not being part of the mid-trimester anatomy scan.

The same method was applied for the quantitative assessment.

All possible anatomical structures of the fetal brain reported in the literature as measurable were listed and group members were asked to answer the following questions:

- Should the following anatomical structures be measured always, possibly or never?
- Do you suggest one or more planes?

The measurements of anatomical structures and scanning planes that should always be evaluated with an agreement among members exceeding 75%, are referred in this document as "recommended" as part of the mid-trimester anatomy scan. The measurement of anatomical structures and scanning planes that should be possibly evaluated with an agreement among members exceeding 75%, are referred in this document as "suggested" as part of the mid-trimester anatomy scan. The measurement of anatomical structures and scanning planes that should never be evaluated with an agreement among members exceeding 75%, are considered in this document as not being part of the mid-trimester anatomy scan.

CNS examination in routine practice

1) Skull ossification

Under normal condition the skull has a regular oval shape with no bony defects (distortion or disruption) (Figure 1A). An hypoechoic rim is identifiable only at the level of the sutures, in particular the coronal one between the frontal and the parietal bones.

Recommendations

- The normal shape of the fetal head/skull and the cranial bone ossification should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).
- It is suggested to look specifically for bone ossification also in sagittal plane. The frontal area should be examined and to rule out frontal bossing and the occipital area for posterior encephalocele.

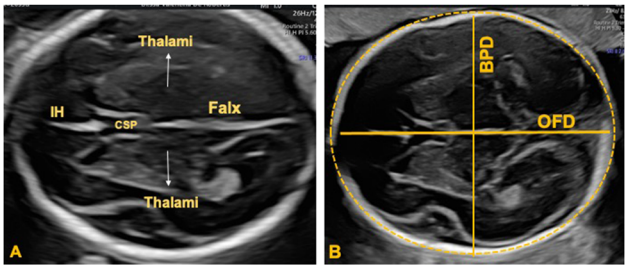

Figure 1: Trans-thalamic plane.
(A) The cavum septi pellucidi (CSP), the interhemispheric fissure (IH), the falx, the thalami and the symmetry of the cerebral hemispheres can be assessed. (B) Biometric measurements of the fetal head: biparietal diameter (BPD), occipito-frontal diameter (OFD) and head circumference (dotted line).

- The measurement of biparietal diameter (BPD) and circumference of the head (HC) should be performed at the anatomy scan by axial scan (trans-thalamic plane).

Technical issues

- BPD should be measured with the caliper either on the external edges of the parietal bones (out-out), or with just one caliper on the outer and the other on the inner edge of these bones, according to the methodology described for the chosen growth charts. The HC could either be measured adjusting the ellipse tool of the ultrasound machine on the calvarium, or it can be calculated by the ellipsoid formula after combining the BPD and the occipito-frontal diameter (OFD) (Figure 1B).

2) Symmetry of hemispheres

Under normal condition the hemispheres appear symmetrical (Figure 1A) (Supplementary Material Video 1).

Recommendation

- Symmetry of hemispheres should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

3) Falx (interhemispheric fissure)

Under normal condition the hemispheres appear separated by a clearly visible interhemispheric fissure and falx (Figures 1A and 2A) (Supplementary Material Video 1).

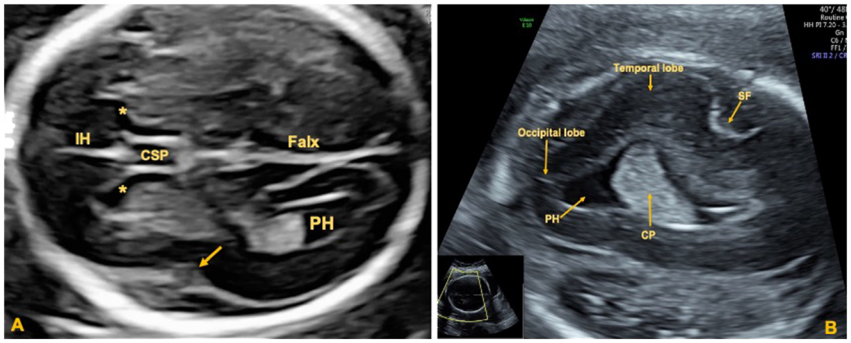

Figure 2: Qualitative evaluation of the occipital horns of the lateral ventricle.
(A) Trans-ventricular plane: The transventricular plane provides an adequate visualization of the hemisphere distal to the transducer. In this plane the interhemispheric fissure (IH), cavum septi pellucidi (CSP), two frontal horns (*), falx and insula (arrow) can also be assessed. (B) Angling the transducer from the axial transthalamic view cranially by up to 45°, the ultrasound access to the proximal hemisphere is feasible (PH, posterior horn; CP, choroid plexus; SF, sylvian fissure).

Recommendation

- The presence of a central interhemispheric fissure and a falx dividing equally the hemispheres should be assessed at the anatomy scan by axial scans (transthalamic or trans-ventricular planes).

4) Lateral ventricles: occipital horns (atrium)

Under normal condition the occipital horns of lateral ventricles appear as sonolucent structures with the echoic choroid plexuses filling the ventricular bodies and atria. Atria are characterized by the presence of the glomus of the choroid plexus, which is highly echogenic and fills the cavity of the ventricle at the level of the atrium, while the occipital horn is filled with cerebrospinal fluid (Figure 2A) (Supplementary Material Video 1).

Recommendations

- The occipital horn of the lateral ventricle distal to the transducer should be assessed at the anatomy scan by axial scans (trans-ventricular plane).
- Efforts should be made to evaluate both occipital horns of the lateral ventricles.
- The atrial width of the lateral ventricle distal to the transducer should be measured at the anatomy scan by axial scan (trans-ventricular plane).

Technical issues

- The transventricular plane provides an adequate visualization of the hemisphere distal to the transducer. However, one of the major disadvantages of the use of this axial plane is the poor visualization of the hemisphere proximal to the transducer. In order to reduce near-field reverberation to the bony calvarium, the suggestion is to angle the transducer from the axial transthalamic view cranially by up to 45° (Figure 2B). This technique showed to allow the ultrasound access to the proximal hemisphere [12, 13].
- For evaluating the atrial width of the lateral ventricle distal to the transducer the line should be traced perpendicular to the axis of the posterior horn, at the level of the glomus. Some authors suggest to use the parieto-occipital fissure as landmark, in order to improve the reproducibility of this measurement (Figure 3A) [14]. Calipers should be placed “in to in” as shown in Figure 3B. The axial width of the atrium has a normal range <10 mm, independently from gestational age.
- There is no a standardized technique for the measurement of the atrial width of the lateral ventricle proximal to the transducer. To detect unilateral ventriculomegaly affected the proximal ventricle, a qualitative assessment should be performed to obtain a valuable information on the global symmetry of the ventricles. In the case of ventricular asymmetry with the proximal ventricle significantly larger than the distal ventricle, the suggestion is to wait until fetal position changes and the suspected abnormal ventricle becomes distal to the transducer or the patient should be referred for expert evaluation [14].

5) Lateral ventricles: frontal horns

Under normal condition the anterior portion of the lateral ventricles (frontal or anterior horns) appears as two comma-shaped, fluid-filled structures medially separated by the cavum septi pellucidi (CSP) (Figures 2A and 4A) (Supplementary Material Video 1).

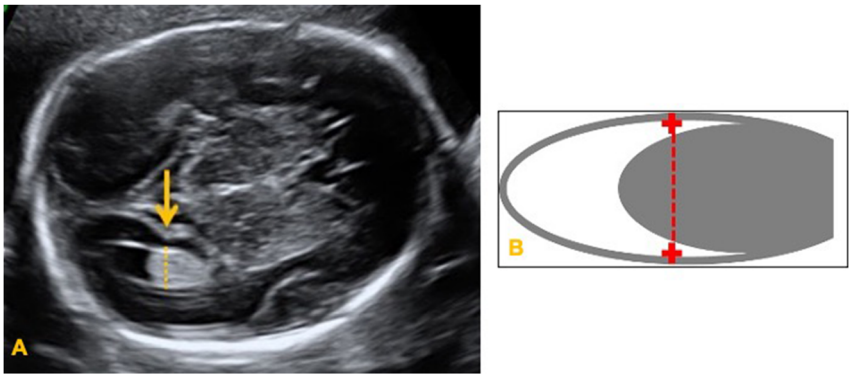

Figure 3: Quantitative assessment of the atrial width.
(A) Trans-ventricular plane for evaluating the atrial width of the lateral ventricle distal to the transducer: the line should be traced perpendicular to the axis of the posterior horn, at the level of the glomus using the parieto-occipital fissure (arrow) as landmark. (B) Calipers should be placed “in to in”.

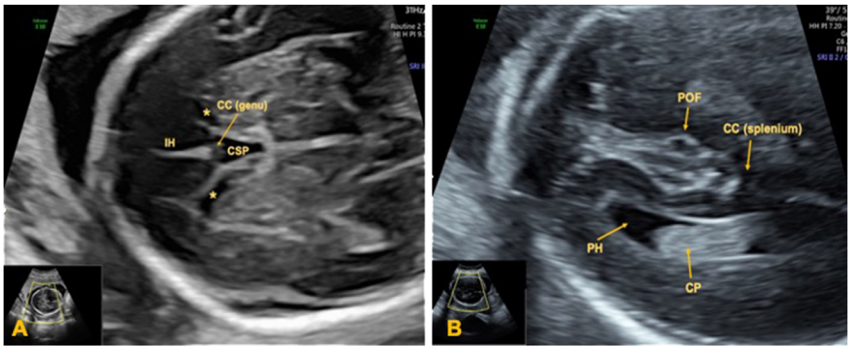

Figure 4: Anterior and posterior complex. (A) The anterior complex visible in the routine transventricular plane, shows the interhemispheric fissure (IH), two frontal horns (*) medially separated by the cavum septi pellucidi (CSP) and a cross section through the genu of the CC. (B) The posterior complex shows a cross section through the splenium of the CC (PH, posterior horn; CP, choroid plexus; POF, parieto-occipital fissure).

Recommendation

- The presence and orientation of two frontal horns of the lateral ventricles medially separated by CSP should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

6) Cavum septi pellucidi

Under normal condition the CSP is detected as a fluid-filled cavity between two thin membranes located between the frontal horns of the lateral ventricles (Supplementary Material Video 1). The CSP becomes visible at about 16–18 weeks. It remains visible until about 37 weeks, when the fluid disappears and the cavity is closed by the fusion of the two layers of the septum pellucidum. It is best visible on anterior coronal views transecting the genu and the anterior portion of the body of the corpus callosum (CC) as well as the transventricular view of the brain [15] (Figures 2A and 4A). Failure to visualize the CSP or its abnormal appearance [16] is predictive of commissural anomalies. However, the normal appearance of CSP does not exclude all CC abnormalities.

Recommendation

- The presence of the CSP should be assessed at the anatomy scan by axial scans (trans-thalamic or trans-ventricular planes).

7) Corpus callosum

The CC represents the major commissure between the two cerebral hemispheres; it extends from the frontal lobe anteriorly to above the quadrigeminal plate and into the quadrigeminal cistern posteriorly. Under normal condition the corpus callosum is present with all its components, going front to back: rostrum, genu, body and splenium. The leaves of the septum pellucidum enclose the space of the cavum septi pellucidi, which is located under the CC.

The CC appears as hypoechoic midline structure at US. Recently the possibility to visualize some portions of CC in axial planes has been described [15]. The anterior complex, a group of anatomical structures visible on the routine transventricular imaging plane, allows to visualize a cross section through the genu of the CC (Figure 4A). Although technically more difficult, slicing cranially from the transventricular plane, the posterior complex may be depicted showing a cross section through the splenium of the CC (Figure 4B).

However, the ultimate proof of the presence of the CC has been proven only by median/mid-sagittal plane of the fetal brain. Although some indirect signs of the absence of the CC could be identifiable in axial scans, the direct evaluation of CC in all its components requires a median/midsagittal plane (Figure 5) (Supplementary Material Videos 2 and 3) [17]. In addition, it is worth mentioning that the depiction of an apparently normal corpus callosum is not necessarily a guarantee that it will remain normal, since this does not exclude the possibility of subtle callosal developmental congenital anomalies or callosal pathologies that may develop later in pregnancy or even after delivery due to brain insults such as ischemia or infection [18].

Recommendation

- The median/midsagittal view should be performed to directly demonstrate the CC in terms of presence/absence (complete-partial).

Technical issues

- The median/midsagittal plane is obtained aligning the transducer with the large midline acoustic window,

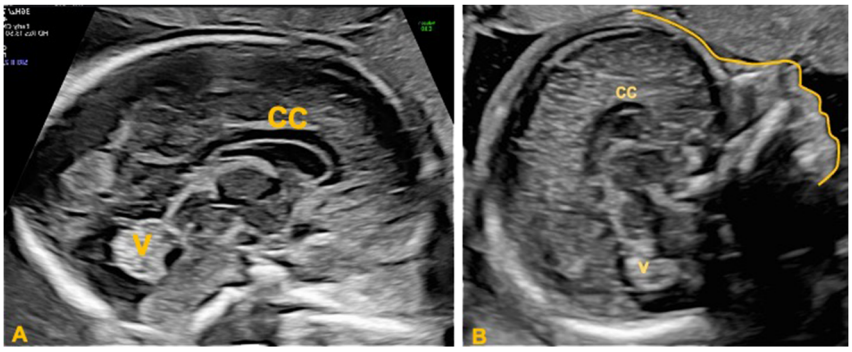

Figure 5: Median/midsagittal plane. (A) The plane obtained through the anterior fontanelle showing simultaneously the corpus callosum (CC) and the cerebellar vermis (v). (B) Transfrontal view: The median/midsagittal plane obtained through the frontal or metopic suture showing simultaneously the facial profile, the corpus callosum (CC) and the cerebellar vermis (v).

formed from anterior to posterior by the frontal or metopic suture, the bregmatic fontanel, the sagittal suture and posterior fontanel. During mid pregnancy, the large anterior fontanelle provides the optimal acoustic window for the midsagittal visualization of the entire CC, enabling a shadow free and perpendicular insonation approach (Figure 5A) (Supplementary Material Video 2). When technically limited, a more frontal midsagittal view obtained through the metopic suture, showing simultaneously the facial profile, may be optional (Figure 5B) (Supplementary Material Video 3) [2, 6, 19]. This approach is often feasible transabdominally, subjected to maternal habitus and fetal position. Obtain a standard mid-sagittal view of the fetal profile, angulate the transducer in order to use the acoustic window of the frontal suture and the anterior fontanel, thus demonstrating the CC, fine side-to-side movements may be needed in order to achieve an ideal image of the CC (Figure 5B) (Supplementary Material Video 3). The transfrontal view allows clear visualization of the midline structures of the fetal brain comparable with that obtained through the anterior or bregmatic fontanelle [19].

- Adequate demonstration of the CC in the second trimester can often be achieved by standard transabdominal ultrasonography. However, in cephalic fetal presentation, a transvaginal scan provides better resolution. In breech presentation, a transfundal approach is the only possibility [18].
- It is important to know that the position of the fetal head is dynamic and may be gently manipulated during sonography by the transducer or the physician's free hand [18].
- If the fetal position is not adequate to obtain a median view of the fetal brain, please repeat the evaluation in 15–30 min until the fetus changes position. If after a reasonable time the fetal position could not be appropriately obtained to assess this anatomical target, a note on the report should be written in order to reevaluate it in a week.

8) Thalami

Under normal condition two thalami separated from each other in the midline are detectable (Figure 1A).

Recommendation

- The presence of two thalami separated from each other in the midline should be assessed at the anatomy scan by axial scans (trans-thalamic plane).

9) Insula

The Sylvian fissure (SF) is among the most well-studied anatomical structures of the fetal cortex and demonstrate a typical pattern of development through gestation. In the early second trimester, the SF appears on the US axial view as a smooth-margined, shallow notch on the lateral side of the cerebral hemisphere (Supplementary Material Video 1). Over the course of the subsequent weeks of pregnancy, the morphology of this structure changes, showing a more prominent indentation with distinct angularity (Figure 2A) [20].

Recommendation

- The presence of a normal developed SF could be assessed for its shape at the mid-trimester anatomy scan by axial scans (trans-ventricular plane as well as transthalamic plane). That doesn't mean that we can rule out every abnormality.

10) Cerebellum

Under normal condition in the axial plane the cerebellum appears as a butterfly shaped structure (Figure 6A) (Supplementary Material Video 4) formed by the round

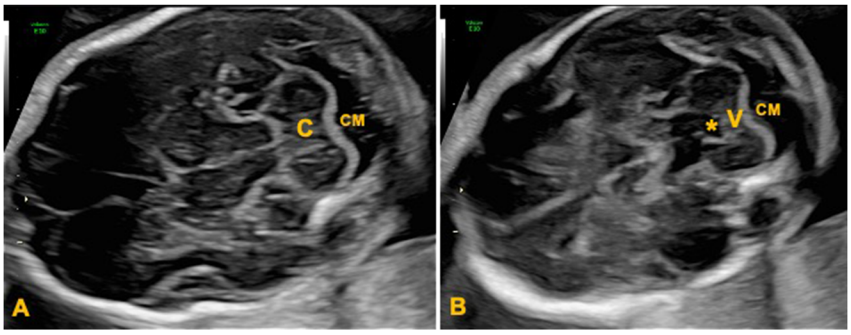

Figure 6: Transcerebellar planes.
(A) The plane includes the cerebellum (C) and behind the cerebellum, the cisterna magna (CM). (B) Moving slightly downwards the fourth ventricle (*) becomes visible, with the vermis (V) and the cisterna magna (CM) behind it.

cerebellar hemispheres joined in the middle by the slightly more echogenic cerebellar vermis.

Recommendations

- The presence of normal cerebellar hemispheres joined in the middle by the cerebellar vermis should be assessed at the anatomy scan by axial scan (trans-cerebellar plane).
- The measurement of the transverse cerebellar diameter should be performed at the anatomy scan by axial scan (trans-cerebellar plane).

11) Cerebellar vermis

Under normal condition the cerebellar vermis appears as a slightly more echogenic structure located between the cerebellar hemispheres in an axial scan. At the time of mid-trimester scan the cerebellar vermis completely covers the fourth ventricle resulting in a narrow passage between the cisterna magna and the fourth ventricle (foramen Magendie).

While the normal appearance of the cerebellar hemispheres, fourth ventricle and cisterna magna is expected to be seen by axial scan (trans-cerebellar plane), on this plane only a narrow segment of the vermis is seen. Serial axial planes with slight angulations between them performs better than a single axial plane to demonstrate the portions of the cerebellar vermis (Figure 6B) (Supplementary Material Video 4). Therefore, the direct evaluation of the cerebellar vermis in all its components in a single plane requires the median/mid-sagittal plane [21].

Recommendation

- The midsagittal/median view should be performed to directly demonstrate the cerebellar vermis in terms of presence or absence (or extreme hypoplasia).

Technical issues

- The median/midsagittal plane is obtained aligning the transducer with the large midline acoustic window, formed from anterior to posterior by the frontal or metopic suture, the bregmatic fontanel, the sagittal suture and the posterior fontanel. Even if all these approaches are possible, more details of the cerebellar vermis could be obtained by posterior insonation through the sagittal suture and the posterior fontanel (Figure 7). However, considering that the frontal or metopic suture is patent at the time of the anatomy scan, it is possible to use it as an acoustic window, showing simultaneously the facial profile and the midline structures of the brain including cerebellar vermis (Figure 5B) (Supplementary Material Video 3) [2, 6, 19]. This approach is usually feasible transabdominally.
- Adequate demonstration of the cerebellar vermis in the second trimester can often be achieved by standard

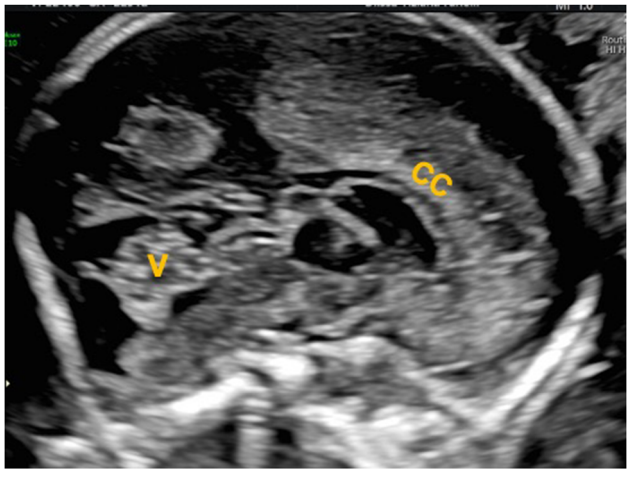

Figure 7: Posterior median/midsagittal plane through the sagittal suture.
With this approach both corpus callosum (CC) and cerebellar vermis (V) may be visualized, but more details of the cerebellar vermis could be obtained.

transabdominal ultrasonography. However, in vertex fetal presentation, a transvaginal scan provides better resolution. In breech presentation, a transfundal approach is the only possibility.
- It is important to know that the position of the fetal head is dynamic and may be gently manipulated during sonography by the transducer or the physician's free hand.
- If the fetal position is not adequate to obtain a median view of the fetal brain, please repeat the evaluation in 15–30 min until the fetus changes the position. If after a reasonable time the fetal position could not be appropriately obtained to assess this anatomical target, a note on the report should be written in order to reevaluate it in a week.

12) Cisterna magna

Under normal condition the cisterna magna or cisterna cerebello-medullaris is a fluid filled space posterior to the cerebellum (Figure 6) (Supplementary Material Video 4). It contains thin septations, that are normal structures. An abnormal cisterna magna, enlargement or obliteration, has been associated with CNS anomalies.

Recommendation

- The presence of a normal cisterna magna should be assessed at the anatomy scan by axial scan (transcerebellar plane).
- The measurement of the cisterna magna should be performed at the anatomy scan by axial scan (transcerebellar plane).

Technical issues

- The use of an angled semi-coronal plane may cause the false appearance of an enlarged cisterna magna.
- While at the time of the second trimester anatomy scan the normal developmental remnant of the Blake's pouch already disappears, at times a thin walled, anechoic fluid filled outpouching in the shape of a small "balloon" is seen in the cisterna magna. This is normal and should not be confused with any malformation of the posterior fossa [22].
- The antero-posterior diameter of the cisterna magna is the distance between the vermis and the inner border of the occipital bone, and it should not exceed 10 mm.

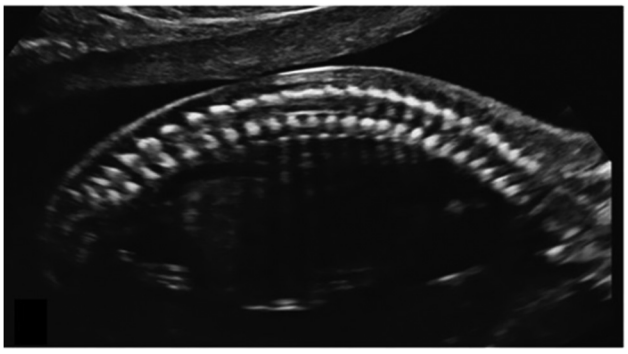

Figure 8: Midsagittal view of the fetal spine, showing a normal S-shaped line without any abnormal curvatures and the skin above the spine appears continuous without interruption.

- In case of an apparently large cisterna magna, it is important to proceed to a median/midsagittal plane of the posterior fossa to evaluate the normal anatomy and position of the cerebellar vermis.

13) Spine

Under a normal condition the spine appears as an S-shaped line without any abnormal curvatures and the skin above the spine appears continuous without interruption (Figure 8).

Recommendation

- The presence and regularity of the whole spine (including the sacrum) and integrity of the skin should be assessed at the anatomy scan by a sagittal scan.

Technical issues

- In most of open spina bifida there are abnormal cerebellar and cisterna magna findings, therefore if a pathology of the spine is seen a renewed evaluation of the posterior fossa is a prudent practical move to do.

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