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Clinical practice guidelines and recommendations by World Association of Perinatal Medicine and Perinatal Medicine Foundation: Reporting suspected findings from Fetal Central Nervous System examination

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Abstract

These guidelines follow the mission of the World Association of Perinatal Medicine, in collaboration with the Perinatal Medicine Foundation, which brings together groups and individuals worldwide, with the aim to improve prenatal detection of Central Nervous System anomalies and the appropriate referral of pregnancies with suspected fetal anomalies. In addition, this document provides further guidance for healthcare practitioners with the goal of standardizing the description of ultrasonographic abnormal findings.

Keywords: Guidelines, anomaly scan, fetal central nervous system, fetal anomalies, ultrasound

Introduction

Fetal central nervous system (CNS) abnormalities are relatively common.[1] Although some patients are at high risk for fetal CNS abnormalities, either because of a family history or due to exposure to teratogens such as congenital infections[2], the vast majority of fetal CNS abnormalities occur in patients without any fetal or familial/maternal risk factors for these anomalies. Therefore, the evaluation of the fetal CNS during the routine mid-trimester US scan, traditionally performed between 20 to 24 weeks of gestation, plays a central role in the prenatal diagnosis of these abnormalities, representing the gold standard for their detection.[1] However, the evaluation of fetal anatomy in the first trimester of pregnancy, including CNS, has drastically evolved in the past decade. This is the reason why the evaluation of the fetal head and spine have been recommended between 11 + 0 to 14 + 0 weeks' gestation by the guidelines of the World Association of Perinatal Medicine (WAPM) recently published.[3] Furthermore, certain CNS anomalies can develop or being recognized only later on during the third trimester or even after delivery. Consequently, in cases where a third trimester scan is performed for any indication, some assessment of the fetal CNS is warranted.

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Whenever possible, when a suspected congenital anomaly is detected, patients should be referred to specialized centers for expert evaluation (referral scan) and a definitive diagnosis.[4] This evaluation includes a detailed examination of the CNS commonly referred to as "fetal neurosonography".[5,6] However, to the best of our knowledge, the standardization of reporting suspected findings during routine scans has not been implemented yet. An appropriate interpretation and standardized description of abnormal US findings may have a significant impact not only on the management of referrals, but also on the training of obstetricians. Ultimately, adopting a standardized approach can help to reduce the burden of false positive cases. Hence, the scope of these guidelines is to establish a consensus regarding the description and interpretation of the US abnormal findings in each trimester suggestive of the most common CNS anomalies. All anatomical structures and measurements of the fetal brain and spine recommended in the WAPM Practice Guidelines on fetal CNS examination between 11 + 0 to 14 + 0 weeks' gestation and at the mid-trimester US scan[1,3] were listed and the most common descriptions of the US abnormal findings were reported for each item. Group members were asked to reach a consensus on the description of each finding to establish a standardized reporting, and to point out which signs may appear late in pregnancy requiring a third trimester evaluation. For each US abnormal finding, agreement among members was assessed. Only items for which consensus exceeding 75% agreement among members are reported in this document. If no initial agreement was reached, members were asked to vote again after discussion. Reference studies were reviewed and evaluated to assess evidence quality according to the method outlined by the U.S. Preventive Services Task Force.[7]

CNS examination in routine practice

All the recommendations were: Evidence level III, Strength of recommendation Level C.

1.First trimester examination of the CNS in routine practice

Recommendation

- The suspicious findings concerning the fetal CNS at the routine first trimester examination should be reported as listed in Table 1.

1) Skull Ossification

Under normal conditions, the fetal skull appears as an oval-shaped hyperechoic bony structure (Fig. 1).[3]

Technical issues: Recognition of small cranial meningoceles by antenatal ultrasound may be challenging. In addition, basal cephaloceles protruding through the base of skull are inaccessible to antenatal sonography (Fig.1C).

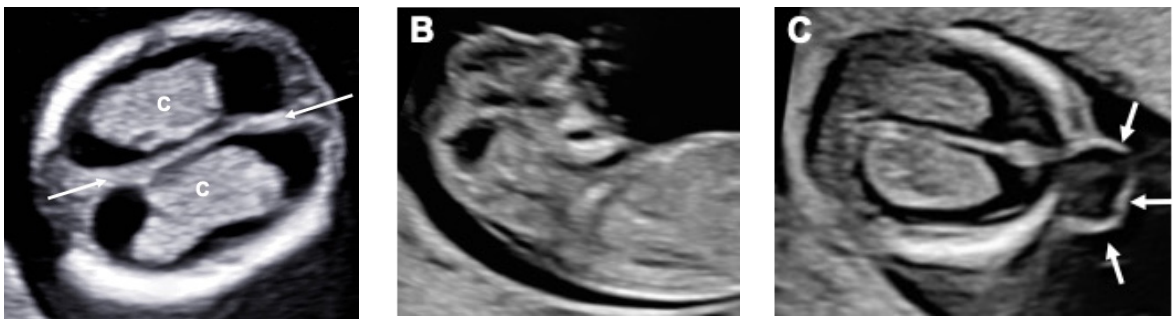

Fig.1 A) Normal fetal head and brain at 13 weeks' gestation. The hyperechoic oval-shaped skull is visible. The cerebral hemispheres are separated by the interhemispheric fissure (arrows). Lateral ventricles (*) containing choroid plexuses (**C)** are also visible. **B)** Cranial bone defect: the cranial vault is absent (acrania). **C)** Cranial bone defect: a skull defect is localized in the frontal region (cephalocele) with a cystic formation (arrows) protruding through the defect.

2) Cerebral Hemispheres

The two hemispheres, similar in size, are separated by a straight, uninterrupted midline echo (interhemispheric fissure) on the axial planes. The choroid plexuses should fill the two lateral ventricles on the sides of the midline (butterfly sign on axial view) occupying roughly half or more of the ventricle length/area (Fig. 1A).[3]

Technical issues:In the first trimester only severe forms, alobar and semilobar varieties, are usually detected (Fig.2).

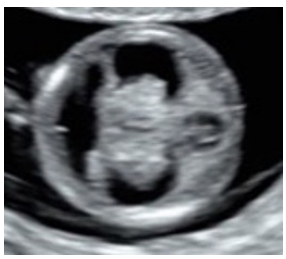

Fig.2 Incomplete separation of cerebral hemispheres: transverse view of the head showing the fusion of the thalami and the presence of a single midline ventricle (alobar holoprosencephaly).

Table 1. Suspicious findings to be reported at the first trimester examination

Suggested description	Main related anomalies
Head and Skull	
Cranial bone defect (Fig 1B,**C)**	Acrania- Exencephaly - Anencephaly sequence; Cephalocele
Incomplete separation of cerebral hemispheres (Fig. 2)	Holoprosencephaly
Cranial Posterior Fossa (CPF)	
Two instead of three spaces are detectable in the CPF (Fig. 3B)	Open Spina Bifida; Cystic posterior fossa anomalies
Anechoic spaces in the CPF are not similar in size (Fig.3C)	Open Spina Bifida; Cystic posterior fossa anomalies
Spine	
The spine appears irregular	Scoliosis
An interruption of the cutaneous contour is detected (Fig.4B)	Open Spina bifida
A cystic mass is detected (Fig.4B)	Open Spina bifida

3) Cranial Posterior Fossa

On the sagittal view of the fetal brain, the anechoic round-shaped diencephalon is visible and the cranial posterior fossa structures are just posterior to it, including the brainstem, the 4th ventricle and the cisterna magna, appearing as three anechoic spaces, roughly similar in size (Fig.3).[3]

Technical issues: On a routine basis, the width of each of the three spaces should be qualitatively evaluated, as these spaces are normally expected to be similar in size. However, measurement of the spaces and ratio between the width of the brainstem and the space behind it (BS/BSOB) could be helpful when the three spaces seem abnormal.[8] With high-frequency transvaginal probe, the brainstem does not appear anechoic but shows echogenicity similar to that of the brain tissue.

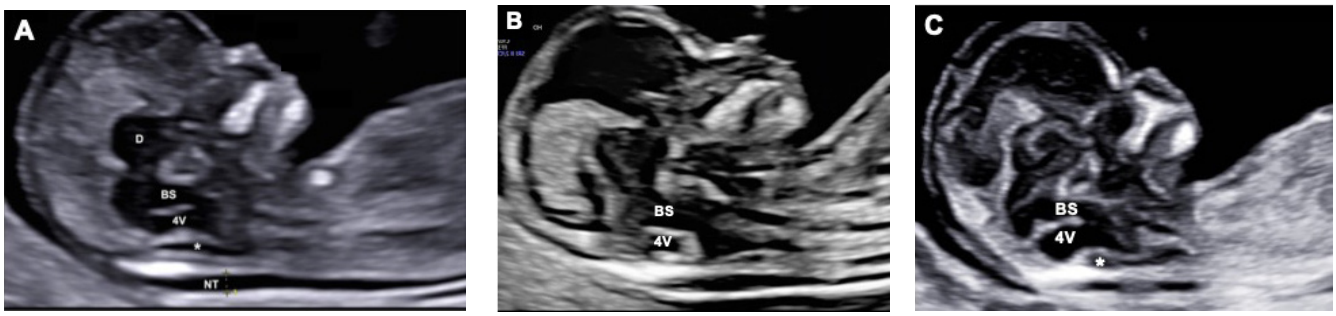

Fig.3 Sagittal view of the fetal head and brain. **A)** Normal aspect of the posterior fossa: the brainstem (BS), the 4th ventricle (4V), and the cisterna magna (*) appear as three anechoic spaces, roughly similar in size (D: the diencephalon). **B)** Sagittal view of the fetal head and brain: Two instead of three spaces are detectable in the posterior fossa in this fetus with open spina bifida. **C)** Sagittal view of the fetal head and brain: Anechoic spaces in the posterior fossa are not similar in size: the 4V is bigger than the other ones in this fetus with a cyst of the posterior fossa.

4) Fetal Spine

The fetal spine typically appears as linear structure, composed of a continuous sequence of vertebrae, covered by the uninterrupted skin (Fig. 4). The spine could bend according to the fetal movements, but no disruptions or interruptions of the vertebral lines or overlying skin should be visualized in normal conditions.

Technical issues: To reliably assess the spine, the fetus should lie in a dorso-anterior position. The main limitation to achieve a reliable evaluation of the spine is the persistent supine fetal lie. In most cases, given enough time, the fetus will turn over during the examination. In the first trimester, a normal appearance of the spine cannot rule out all cases of open spina bifida, as some defects may not be sufficiently evident at this early stage. Caution should be exercised when evaluating the sacrum since the lower sacral vertebras are still not calcified.

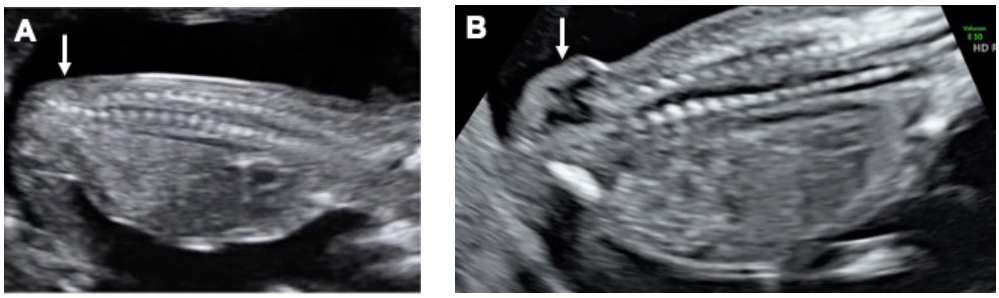

Fig.4 Midsagittal view of the fetal spine. **A)** Normal aspect of the fetal spine in the 1st trimester: it appears as linear structure, composed of a continuous sequence of vertebrae, covered by the uninterrupted skin (arrow). **B)** Midsagittal view of the fetal spine: An interruption of the cutaneous contour and a cystic mass are detected in this fetus with open spina bifida.

2. Second and third trimesters examination of the CNS in routine practice

Recommendation

- The suspicious findings concerning the fetal CNS at the mid-trimester examination should be reported as listed in Table 2.

1) Skull Ossification

Under normal conditions the skull has a regular oval shape with no bony defects (distortion or disruption) by trans-thalamic or trans- ventricular planes (Fig.5).[1] The measurement of biparietal diameter (BPD) and head circumference (HC) should be in the normal range (± 2SD), according to the chosen growth charts.

Technical issues. A detailed neurosonographic examination should be performed for fetuses with HC greater than 2 standard deviations below or above the mean[9,10], when the skull shape is abnormal or when US beam penetrance is reduced. Several ultrasonographic abnormal findings of the skull may appear later in gestation. As a consequence, the absence of some of these abnormal signs at the mid-trimester scan does not rule out late-onset abnormalities of the shape and size of the fetal skull. Molding of the fetal head, particularly in early gestation, may be responsible for an abnormal skull shape. In case the skull shape deviates from oval, reducing transducer pressure is advisable.

In case of a BPD or HC outside the normal ranges, the chosen growth chart should be specified on the report. Fetal positioning can significantly affect the skull's shape, with advanced gestational age and oligohydramnios also playing a role.[11] In particular, a significantly smaller BPD (dolichocephaly or elongated anteroposterior axis of the skull) could be found in breech fetuses, suggesting that HC can be considered a more reliable measurement, as less affected than BPD by head shape variations and fetal presentation.

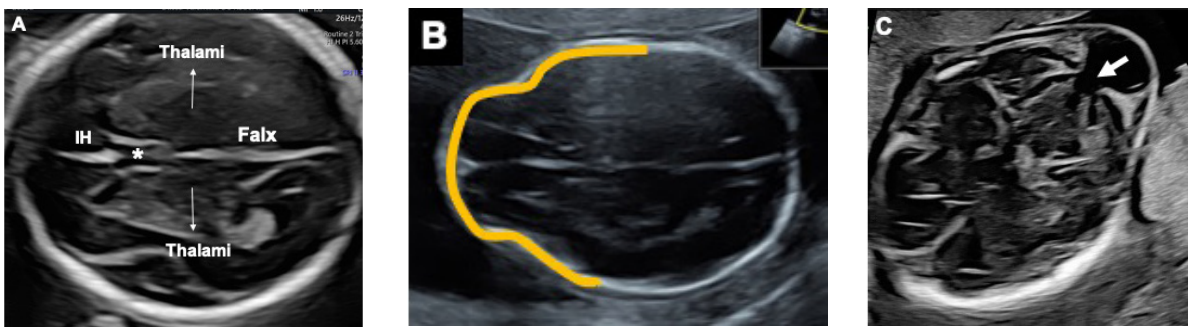

Fig.5 Trans-thalamic plane. **A)** Normal aspect of the skull with a regular oval shape and no bony defects. **B)** Trans-thalamic plane: Abnormal shape of the fetal head (not oval): this is the typical lemon sign in a fetus with open spina bifida. **C)** rans-thalamic plane: Cranial bone defect: cystic formation protruding through a skull defect (arrow), localized in the occipital region (cephalocele).

2) Cerebral Hemispheres

Under normal conditions the cerebral hemispheres appear symmetrical and separated on the trans-ventricular plane (Fig. 5A).

Technical issues: The axial planes provide an adequate visualization of the hemisphere distal to the transducer. One of the major disadvantages of using this axial plane is the poor visualization of the hemisphere proximal to the transducer.[1] Due to this technical issue, asymmetry of

the cerebral hemispheres could be difficult to be assessed using these planes. The cerebral hemispheres are completely separated by a hyperechoic straight line representing the interhemispheric fissure and the falx. The only normal interruption is at the level of the cavum septum pellucidum (CSP).

Increased distance between cerebral hemispheres (Fig. 6) has been described as an indirect sign of either complete agenesis of the corpus callosum (ACC)[12] or brain atrophy.[6] However, if not accompanied by other indirect signs these findings are frequently overlooked.

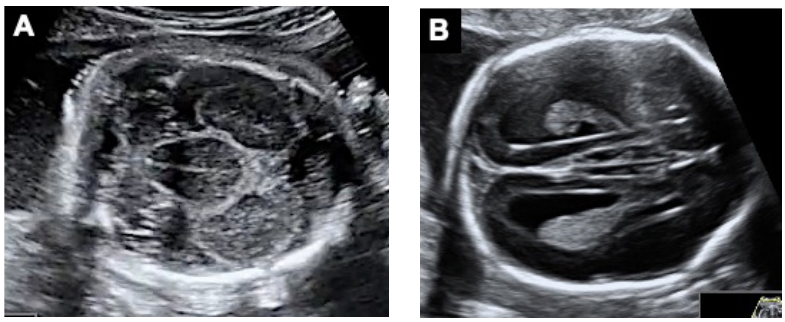

Fig.6 A) Incomplete separation of cerebral hemispheres and the interhemispheric fissure is absent: axial scan at the level of the thalami showing absence of midline structures and fused thalami in a fetus with alobar holoprosencephaly. **B)** Increased distance between cerebral hemispheres: this is an indirect sign of the complete agenesis of corpus callosum showing an increased separation of the hemispheres with the bodies of the lateral ventricles parallel to each other and shifted laterally.

3) Falx (interhemispheric fissure)

Under normal conditions the hemispheres appear separated by a clearly visible interhemispheric fissure and falx on the trans-ventricular plane (Fig. 5A and 7A).

Technical issues: Distortion of the interhemispheric fissure is commonly subtle (Fig. 7B) and challenging to assess based solely on axial views. Consequently, at the mid-trimester anomaly scan its evaluation could be limited.

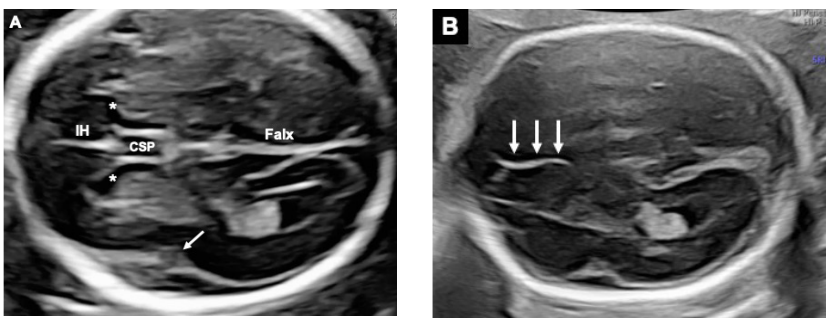

Fig.7 A) The trans-ventricular plane in a normal fetus: the interhemispheric fissure (SI), cavum septi pellucidi (CSP), two frontal horns (*), falx and insula (arrow) can be assessed. **B)** Distortion of the interhemispheric fissure (arrows)

4) Lateral ventricles: occipital horns (atrium)

Under normal conditions the occipital horns of the lateral ventricles appear as sonolucent structures with the echoic choroid plexuses filling the ventricular bodies and atria (Fig. 7A). Measurement of the atrial width of the lateral ventricle distal to the transducer is part of the second-trimester anatomy scan. It should not exceed 10 mm, independently from gestational age.

Technical issues: The poor visualization of the lateral ventricle proximal to the transducer (Fig. 8A) inevitably limits the detection rate of unilateral ventriculomegaly. The detection of unilateral ventriculomegaly affecting the proximal ventricle usually relies on its qualitative assessment, as the measurement is generally suboptimal. In cases where a subjective impression suggests a proximal ventricle significantly larger than the distal one (Fig. 8B), the patient should be referred for fetal neurosonography.[13,14] However, the predictive accuracy is suboptimal, with a significant number of false positive and negative cases. The teardrop shape of the lateral ventricles (colpocephaly) (Fig. 8C) has been described as an indirect sign of

complete ACC.[12] However, if not accompanied by other indirect signs, complete ACC might be overlooked. Furthermore, the teardrop shape becomes more evident with advancing gestational age[14], which may partially explain the limited detection of ACC if not directly assessed on the midsagittal view.

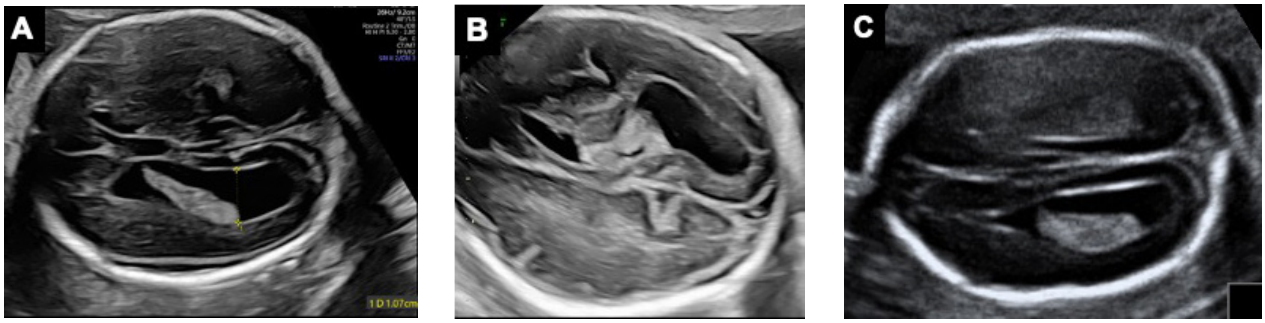

Fig.8 A) The atrial width of the distal ventricle is increased (≥ 10 mm) in a fetus with mild ventriculomegaly. **B)** The atrial width of the proximal ventricle appears significantly larger than the distal one in a fetus with unilateral ventriculomegaly affecting the proximal ventricle. **C)** The lateral ventricle has a teardrop shape (colpocephaly): this is an indirect sign of the complete agenesis of corpus callosum.

5) Lateral ventricles: frontal horns

Under normal conditions the anterior portion of the lateral ventricles (frontal or anterior horns) appears as two comma-shaped, fluid-filled structures separated medially by the CSP (Fig. 7A).

Technical issues: Under normal conditions the shape of the anterior horns (AH) is comma-shaped in the vast majority of cases, but it may be triangular as well.[15] A square shape of the AH (Fig. 9) may be an important clue of abnormal cortical development. The optimal assessment of the frontal horns orientation requires a coronal view. Therefore, although an abnormal shape or distance between the AH could be associated to CNS anomalies (such as ACC), it has not been included among the abnormal US signs to report.

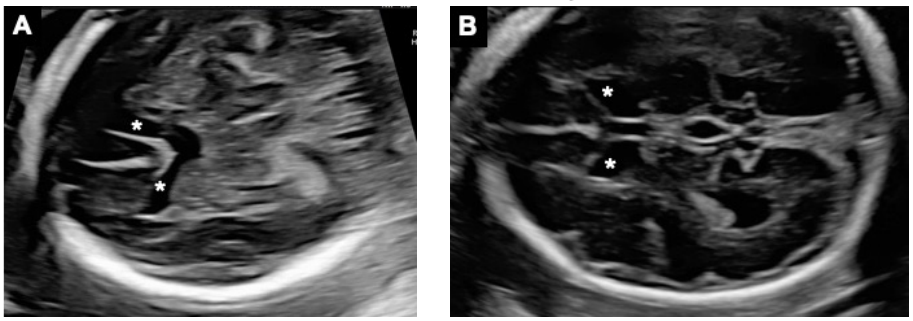

Fig.9 A) The frontal horns (*) appear fused due to the agenesis of the CSP. **B)** The shape of the frontal horns (*) doesn't look normal: the square shape of the frontal horns is visible in this fetus with cortical anomaly.

6) Cavum septum pellucidum

Under normal conditions the CSP is detected as a fluid-filled cavity between two thin membranes located between the frontal horns of the lateral ventricles (Fig. 7A).

Technical issues: A common mistake is to consider the columns of the fornix as the CSP, possibly missing many CNS anomalies.[16,17] When the CSP is present, the columns of the fornix are seen on a plane just below the CSP. Although the hypoechoic appearance of the columns of the fornix may resemble the CSP, the identification of a parallel "line" in the center of this hypoechoic structure helps to differentiate between the fornix and CSP. The columns of the fornix appear as two hypoechoic structures with a central interface reflection (Fig. 10), whereas the CSP is a rectangular box-like structure located between the AH (Fig. 7A). Another artifact is due to the US beam crossing the walls of the frontal horns, normally in close proximity, and generating linear echoes that mimic the presence of a CSP within the ventricular cavity.[16,18]

Abnormal shape and size of the CSP has been described as potentially associated to cerebral[19] and genetic anomalies.[20,21] However, the evaluation of the CSP shape is extremely subjective and measurement of the CSP is not part of the mid-trimester routine anatomy scan.[1]

Moreover, these abnormal findings, when isolated, have unclear significance and have been described as a normal variant. Thus, consensus among experts has not been reached and abnormal shape and size of the CSP should not be reported at the mid-trimester routine US scan.

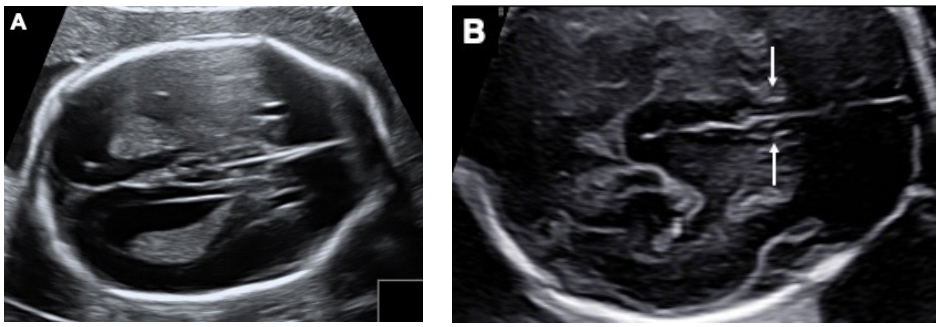

Fig.10 A) The CSP is not visible in the trans-ventricular plane in this case of complete agenesis of the corpus callosum. **B)** TA plane just slightly inferior to the trans-ventricular one: the columns of the fornix are visible (arrows)

7) Corpus Callosum (CC)

The CC appears as a hypoechoic midline structure at US by median/mid-sagittal plane of the fetal brain. Under normal conditions the CC is present with all its components, going front to back: rostrum, genu, body and splenium (Fig. 11).

Technical issues: At the mid-trimester scan, the CC should be entirely visualized but its measurement is not required. When a median/mid-sagittal plane of the fetal brain is properly obtained, the patient should be referred if the CC subjectively appears shorter due to the lack of some of its components. The evaluation of the CC thickness is not required at the mid-trimester routine US evaluation as the significance and prognosis of an isolated thick CC remains unknown due to the lack of definitive data.[22] Agreement among experts has not been reached on this issue, and abnormal thickness of CC should not be reported at the mid- trimester routine US scan. The visualization of the pericallosal artery on the mid-sagittal view by color Doppler could be a useful hint of the presence of the CC.

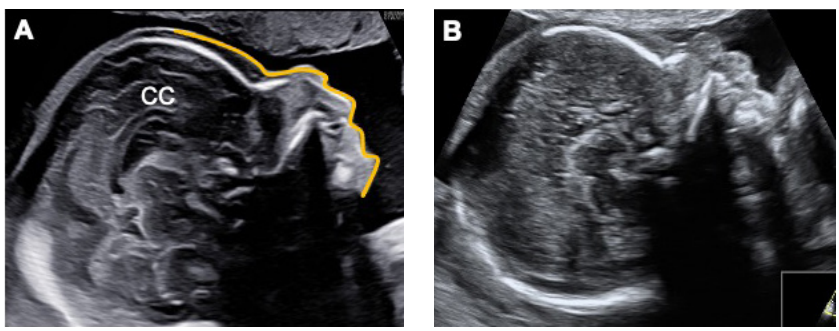

Fig.11 A) Trans-frontal view in a normal fetus showing simultaneously and the facial profile, the corpus callosum (CC). **B)** The corpus callosum is not visible in this case of complete agenesis of the corpus callosum.

8) Thalami

Under normal conditions two thalami separated from each other in the midline are detectable (Fig. 5A).

Technical issues: Since the third ventricle (Fig. 12) is in many cases very thin frequently the thalami appeared "fused", however holoprosencephaly never involves only the thalami.

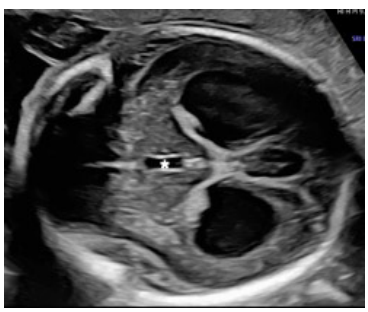

Fig.12 Trans-thalamic plane showing an anechoic structure (*) between the two thalami in this fetus with triventricular hydrocephalus

9) Insula

In the early second trimester, the Sylvian fissure (SF) appears as a smooth-margined, shallow notch on the lateral side of the cerebral hemisphere (Fig. 7A). Over the course of the subsequent weeks of pregnancy, the morphology of this structure changes, showing a more prominent indentation with distinct angularity.

Technical issues: SF operculization is a fetal brain gyration feature easily assessed prenatally by ultrasound.[23] Even if the SF is always visible on the standard trans-thalamic plane, in case of abnormal cortical development the SF shape changes at around 20 weeks of gestation may be very subtle[24], as abnormal SF opercularization usually becomes more evident after 24 weeks' gestation. In case of abnormal SF shape, a multiplanar approach to the fetal brain, which is not part of the second trimester anatomy scan, should be considered for a reliable assessment of the SF and cortex.

10) Cerebellum

Under normal conditions on the axial plane the cerebellum appears as a butterfly shaped structure (Fig. 13) formed by the round cerebellar hemispheres joined in the middle by the more echogenic cerebellar vermis. The cerebellar hemispheres should be homogeneous and symmetrically round-shaped[25], with smooth borders.

Technical issues: At the mid-trimester scan the cerebellar vermis completely covers the fourth ventricle, clearly separated from the cisterna magna. However, if the US beam includes the lower part of the cerebellum with an excessive caudal angulation, the plane will cut through the inferior part of the fourth ventricle rather than the vermis. The juxtaposition of the fluid-filled vallecula cerebelli with the adjacent cerebellar hemispheres creates the impression of a continuum between the cisterna magna and the fourth ventricle, mimicking hypoplasia/partial agenesis of the vermis.

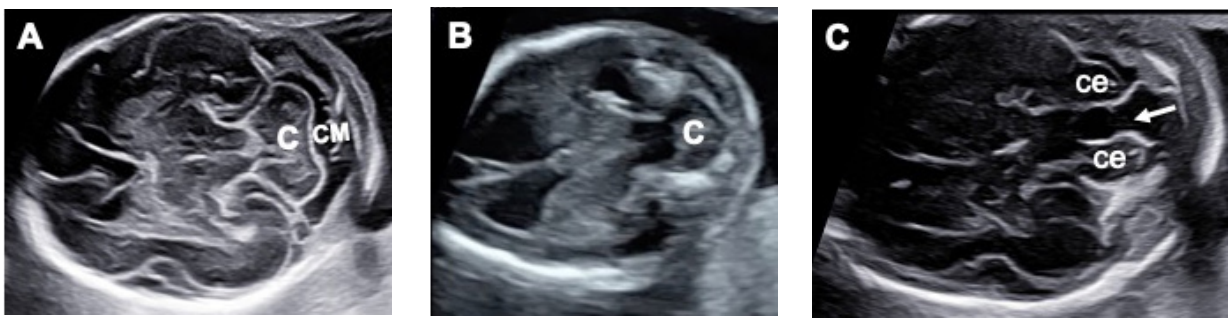

Fig.13 A) Normal trans-cerebellar plane showing the cerebellum (C) as a butterfly shaped structure and behind the cerebellum, the cisterna magna (CM). **B)** The shape of the cerebellum (C) doesn't look normal ("banana sign") and the cisterna magna obliterated in this case of open spina bifida. **C)** A cleft (arrow) is present between the hemispheres (ce) and the cerebellar vermis does not completely cover the fourth ventricle in this fetus with a cyst of the posterior fossa.

11) Cerebellar Vermis

Under normal conditions the cerebellar vermis appears as a more echogenic structure located between the cerebellar hemispheres on an axial scan (Fig.14A). On the median/mid-sagittal plane the entire cerebellar vermis is visible, completely covering the fourth ventricle and appearing in direct contact with the brainstem (Fig. 14B).

Technical issues: Using high-frequency ultrasound transducers improves the ability to differentiate the 4th ventricle choroid plexus (4V-CP) from the inferior border of the vermis. 4V-CP appears more echogenic than the vermis and attaches to the vermis' inferior part, directly in contact with the brainstem.[26]

The presence of a communication between the 4th ventricle and the cisterna magna in the midsagittal plane is relatively common during the 2nd trimester due to the still incomplete rotation of the vermis.

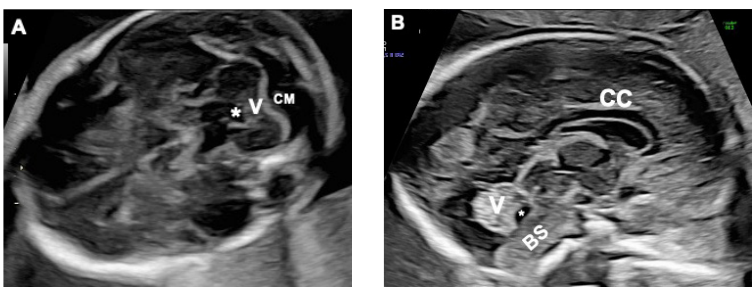

Fig.14 A) The normal aspect of the cerebellar vermis (V) in an axial plane: it appears as a more echogenic structure located between the cerebellar hemispheres. The fourth ventricle (*) is visible, with the vermis (V) and the cisterna magna (CM) behind it. **B)** The normal aspect of the cerebellar vermis (V) in the median/midsagittal plane: it completely covers the fourth ventricle and appeared to be in direct contact with the brainstem (BS). (*: the fourth ventricle; CC, corpus callosum)

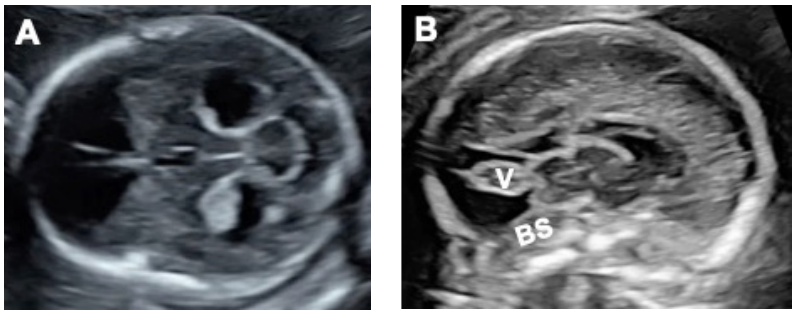

Fig.15 A) Abnormal aspect of the cerebellar vermis in an axial plane: the cerebellar vermis is absent and cerebellar hemispheres are fused in this case of Rhombencephalosynapsis. **B)** Abnormal aspect of the cerebellar vermis in the midsagittal view of the posterior fossa showing an upward displacement of the vermis (V) and an open fourth ventricle, communicating with the cisterna magna. The vermis (V) is not in direct contact with the brainstem (BS).

12) Cisterna Magna (CM)

Under normal conditions the cisterna magna or cisterna cerebello-medullaris (CM) is a fluid filled space posterior to the cerebellum (Fig.14A). The antero-posterior diameter of the cisterna magna should not exceed 10 mm.

Technical issues: Thin septations in the CM are normal structures (Fig.16) and should not be confused with any malformations of the posterior fossa.[27] The use of an angled semi-coronal plane may create the false appearance of an enlarged cisterna magna.

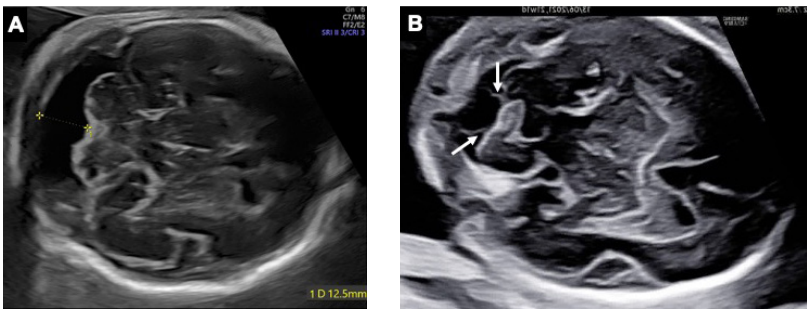

Fig.16 A) The antero-posterior diameter (yellow dashed line) of the cisterna magna is > 10 mm in this fetus with a megacisterna magna. **B)** Thin septations (arrows) in the cisterna magna are normal structures.

13) Spine

Under normal conditions the spine appears as an S-shaped line without any abnormal curvatures, and the skin above the spine appears continuous without interruption (Fig.17A).

Technical issues: Even if one of the most common spinal abnormalities, the open spina bifida, is usually detected by the typically associated intracranial US signs, a longitudinal section of the fetal spine should always be obtained to rule out other spinal malformations, including closed spina bifida, vertebral abnormalities (Fig.17B) and sacral agenesis. To reliably assess the spine, the fetus should lie in a dorso-anterior position. The main limitation to achieve a reliable evaluation of the spine is the persistent supine fetal lie. In most cases, given enough time, the fetus will turn over during the course of the examination. Diagnosing sacral agenesis may be challenging even for experts due to the physiological non-ossification of the caudal spine in the mid trimester.[28]

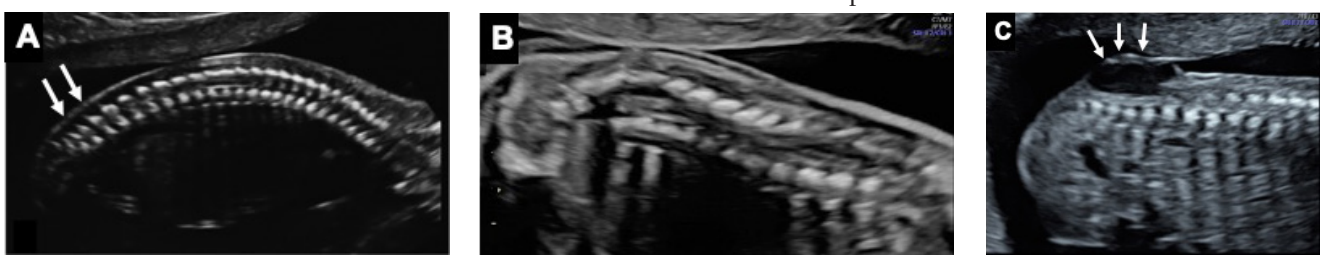

Fig.17 A) Normal aspect of the fetal spine in the midsagittal view: the spine appears as an S-shaped line without any abnormal curvatures and the skin above the spine appears continuous without interruption. **B)** The spine appears irregular. **C)** A cystic mass (arrows) is detected at the caudal end of the spine in this case of spina bifida.

Table 2. Suspicious findings to be reported at the mid-trimester examination

Suggested description	Main related anomalies
Head and Skull	
Abnormal shape of the fetal head (not oval) (Fig. 5B)	Secondary to cerebral/ neural tube defects (ie: Open Spinal Defect); Craniosynostosis*
Abnormal density of the skull (low grade of mineralization)	Hypophosphatasia; Achondrogenesis; Osteogenesis Imperfecta type II
Cranial bone defect (Fig 5C)	Acrania- Exencephaly - Anencephaly sequence; Cephalocele
Abnormal size of fetal head (small)	Microcephaly*
Abnormal size of fetal head (large)	Macrocephaly *; Hydrocephalus*; Space-occupying lesions*
Cerebral Hemispheres	
Cerebral hemispheres appear asymmetric	Hemimegalencephaly*
Incomplete separation of cerebral hemispheres (Fig. 6A)	Holoprosencephaly
Increased distance between cerebral hemispheres (Fig. 6B)	Complete agenesis of the corpus callosum; Brain atrophy
Interhemispheric fissure	
The interhemispheric fissure is absent or partially visible (Fig. 6A)	Holoprosencephaly
Distortion of the Interhemispheric Fissure (Fig. 7B)	Midline Anomalies; cortical anomalies*; Other anomalies (tumors or massive brain hemorrhage)*
Occipital Horns	
The atrial width of the distal ventricle is increased (≥ 10 mm) (Fig. 8A)	Unilateral ventriculomegaly
The atrial width of the proximal ventricle appears significantly larger than the distal one (or vice-versa) (Fig. 8B)	Unilateral or bilateral ventriculomegaly
The lateral ventricles have a teardrop shape (Fig.8C)	Complete agenesis of the corpus callosum
Echogenic collections appear in atria/occipital horns	Hemorrhage; infections*
Abnormal content (debris, synechia or septa) is present in atria/ occipital horns	Hemorrhage; infections
Anterior Horns	
The frontal horns appear fused (Fig. 9A)	Cavum septum pellucidum agenesis; Lobar holoprosencephaly
The shape of the frontal horns doesn't look normal (Fig. 9B)	Cortical anomalies
Echogenic collections appear in the frontal horns	Hemorrhage; infections*
Abnormal content is detected in the frontal horns	Hemorrhage; infections*
Cavum Septum Pellucidum	
The CSP is not visible (Fig. 9A, 10A)	CSP agenesis; Lobar Holoprosencephaly; Complete agenesis of the CC; Obliterated CSP[16]
Corpus Callosum	
The CC is not visible (Fig.11B)	Complete agenesis of CC
The CC is not visible in all its components	Partial agenesis of CC
Thalami	
The thalami appear fused (Fig. 6A)	Holoprosencephaly
An anechoic structure is visible between the two thalami (Fig.12)	Ventriculomegaly; Aqueductal stenosis*
Sylvian Fissure	
The shape of the SF doesn't look normal for the gestational age	Cortical anomalies*
Cerebellum	
The shape of the cerebellum doesn't look normal (Fig.13B)	Open Spina Bifida; Rhombencephalosynapsis

The hemispheres appear asymmetric	Hemorrhage; Infections; Partial agenesis; PHACES syndrome[25]
A cleft is present between the hemispheres (Fig.13C)	Cystic posterior fossa anomalies
Increased fluid in the posterior fossa is present (Fig.13C)	Cystic posterior fossa anomalies
The cerebellar vermis does not completely cover the fourth ventricle (Fig.13C)	Cystic posterior fossa anomalies
The TCD is too small (Fig. 13B)	Open Spina Bifida; Cerebellar hypoplasia
Cerebellar Vermis	
The cerebellar vermis is not visible (Fig.15A)	Dandy-Walker malformation; Joubert Sydrome; Rhombencephalosynapsis
The cerebellar vermis is absent and cerebellar hemispheres are fused (Fig.15A)	Rhombencephalosynapsis
The cerebellar vermis is only partially visible	Dandy-Walker malformation; Vermian hypoplasia
The cerebellar vermis appears upwards rotated (Fig. 15B)	Dandy-Walker malformation; Vermian hypoplasia; Blake's Pouch Cyst
Cisterna Magna	
The CM is obliterated (Fig.13B)	Open Spina Bifida
The CM appears communicating with the 4th ventricle (Fig.13C)	Dandy-Walker malformation; Vermian hypoplasia; Blake's Pouch Cyst
The antero-posterior diameter of the CM is ≥ 10 mm (Fig.16A)	Megacisterna magna*
Spine	
The spine appears irregular (Fig.17B)	Hemivertebra; Scoliosis; Diastematomyelia
An interruption of the cutaneous contour is detected (Fig.17C)	Open Spina Bifida
A cystic mass is detected (Fig.17C)	Open /Closed Spina Bifida
The sacrum is not visible	Agenesis of sacrum; Caudal regression syndrome

* These abnormal signs could appear in the 3rd trimester. CSP, cavum septum pellucidum; CC, corpus callosum; TCD, trans-cerebellar diameter.

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