Four Steps in Diagnosing Complete Agenesis of the Corpus Callosum in Prenatal Life

Vier Schritte der vorgeburtlichen Diagnose der kompletten Corpus-callosum-Agenesie

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Key words
- fetus
- CNS
- ultrasound 2 D

Abstract

Purpose: Among congenital brain anomalies, complete agenesis of the corpus callosum (cACC) including cases of callosal hypoplasia has a prevalence of 1.8 per 10 000 in the general population. It is also one of the most challenging brain anomalies to detect during the mid-trimester ultrasound scan. Standard axial planes do not provide enough information to make the definitive diagnosis of cACC.

Materials and Methods: From our library of images and ultrasound reports, we reviewed our most recent cases of complete agenesis of the corpus callosum in the fetus at the mid-trimester scan. In our analysis we included only cases that were confirmed postnatally or by autopsy. Exams were performed between January 2010 and June 2012. All of the patients were scanned transabdominally by means of 2 D and static 3 D. From the 2 D and 3 D images we identified 4 anatomical views that consistently gave us enough information to identify cACC: axial biparietal transthalamic view (AX1); axial biparietal falx view (AX2); coronal transthalamic view (COR); mid-sagittal view (SAG).

Results: From our library 30 cases were selected with confirmed cACC postnatally or in autopsy findings. The mean gestational age at the time of referral to our center was 20.7 weeks (range 19 – 23 weeks). In all analyzed cases sufficient 2 D images were found and in 93.3 % of them informative 3 D volumes were also available for off-line review. We identified the following patterns of cACC at the mid-trimester scan: A- normal size of 3 rd ventricle + normal size of the lateral ventricles or mild ventriculomegaly; B1- dilated 3 rd ventricle + normal size of the lateral ventricles; B2- dilated 3 rd ventricle + mild or moderate ventriculomegaly; C- dilated 3 rd ventricle + severe ventriculomegaly; D- gross dilatation of 3 rd ventricle with the appearance of interhemispheric

Zusammenfassung

Ziel: Die komplette Corpus-callosum-Agenesie (cACC), eine angeborene Hirnanomalie, besitzt zusammen mit der Balken-Hyperplasie eine Prävalenz von 1,8 von 10 000 in der Gesamtbevölkerung. Es handelt sich dabei auch um die am schwierigsten zu erkennende Hirnanomalie im Zweittrimester-Ultraschallscreening. Die axialen Standardebenen bieten nicht genügend Informationen, um die Diagnose der cACC sicherstellen zu können.

Material und Methoden: Aus unserem Bildarchiv und den sonografischen Berichten werteten wir unsere jüngsten Fälle mit Zweittrimester-Ultraschall und kompletter Balkenagenesie des Feten aus. In unsere Analyse schlossen wir nur Fälle ein, die nach Geburt oder durch Autopsie bestätigt wurden. Die Untersuchungen erfolgten zwischen Januar 2010 und Juni 2012. Alle Patienten wurden transabdominal mittels 2 D und statischem 3 D untersucht. Aus den 2D- und 3D-Bildern ermittelten wir 4 anatomische Schnitte, die uns übereinstimmend genügend Informationen gaben, um eine cACC zu diagnostizieren: Der axiale biparietale transthalamische Schnitt (AX1); der axiale biparietale Falx-Schnitt (AX2), der koronare transthalamische Schnitt (COR), der mediane Sagittalschnitt (SAG).

Ergebnisse: Aus unserem Archiv wählten wir 30 Fälle mit postnataler oder durch Autopsie-Befund bestätigter cACC aus. Das mittlere Gestationsalter zum Zeitpunkt der Untersuchung unserem Zentrum betrug 20,7 Wochen (Bereich 19 – 23 Wochen). In allen analysierten Fällen gab es geeignete 2D-Bilder und in 93,3 % davon waren auch informative 3D-Volumen für eine nachträgliche Auswertung vorhanden. Wir entdeckten folgende Merkmale der cACC im Zweittrimester-Screening: A – normale Weite des 3. Ventrikels + normale Weite der Seitenventrikel oder milde Ventrikulomegalie; B1 – erweiterter 3. Ventrikel + normale

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cyst. The AX1 view revealed: absence of the cavum septum pellucidi in all cases; dilatation of the third ventricle in 86.6 % of cases; separation of frontal horns in 83.3 % of cases; ventriculomegaly in 73.3 % of cases, including 13.6 % with severe forms. The AX2 view showed separation of the interhemispheric fissure (IHF) in 90 % of cases and upward displacement of the 3 rd ventricle in 80 % of cases. The COR view confirmed separation of the interhemispheric fissure in 90 % of cases including gross separation in 7.4 % of cases; absence of CC fibers at this level and descent of the falx towards the roof of the 3 rd ventricle in all cases, and upward displacement of the 3 rd ventricle in 80 % of cases. The SAG view revealed the absence of the CSP-CC complex in all cases and dilatation of the 3 rd ventricle in 86.6 % of cases.

Conclusion: 1. We suggest a stepwise ultrasound diagnostic approach for cACC and variations of this condition. 2. We suggest a classification of characteristic patterns found in fetuses with proven cACC based on findings presented in axial views.

Weite der Seitenventrikel; B2 – erweiterter 3. Ventrikel + milde oder moderate Ventrikulomegalie; B2 – erweiterter 3. Ventrikel + schwere Ventrikulomegalie; D – stark erweiterter 3. Ventrikel und Auftreten einer interhemisphärischen Zyste. Der AX1-Schnitt zeigte: In allen Fällen fehlte das Cavum septi pellucidi; Dilatation des 3. Ventrikels bei 86,6 %; Trennung der Vorderhörner bei 83,3 %; Ventrikulomegalie bei 73,3 % der Fälle, darunter bei 13,6 % der Fälle schwere Formen. Der AX2-Schnitt zeigte eine Trennung der interhemisphärischen Fissur (IHF) bei 90 % und eine Anhebung des 3. Ventrikels bei 80 % der Fälle. Der COR-Schnitt bestätigte die Trennung der interhemisphärischen Fissur bei 90 % der Fälle einschließlich einer groben Trennung bei 7,4 % der Fälle; ein Fehlen der CC-Fasern auf dieser Ebene und einen Abstieg der Falx zum Dach des 3. Ventrikels in allen Fällen und eine Anhebung des 3. Ventrikels bei 80 % der Fälle. Der SAG-Schnitt zeigte das Fehlen des CSP-CC-Komplexes in allen Fällen und die Dilatation des 3. Ventrikels bei 86,6 % der Fälle.

Schlussfolgerung: 1. Wir empfehlen eine schrittweise sonografisch-diagnostische Herangehensweise bei der cACC und den verschiedenen Ausprägungen dieser Erkrankung. 2. Wir schlagen eine Klassifizierung der im Feten mit bestätigter cACC vorgefundenen charakteristischen Marker vor, die auf den Befunden aus den axialen Schnitten basieren.

Introduction

Among congenital brain anomalies, complete agenesis of the corpus callosum (cACC) including cases of callosal hypoplasia has a prevalence of 1.8 per 10,000 in the general population [1]. The incidence of callosal agenesis increases in the group of mentally disabled patients to 3 % [2]. cACC is also one of the most challenging brain anomalies to detect during the mid-trimester ultrasound scan. Standard axial planes do not provide enough information to make the definitive diagnosis of callosal agenesis [3, 4]. The most recognized sonographic feature of cACC in the mid-trimester scan is the lack of visualization of the cavum septi pellucidi since the corpus callosum and cavum septi pellucidi are both derived from the same structure – lamina reuniens [5]. Nevertheless starting at 22 weeks non-visualization of the cavum septi pellucidi may not be consistent with the diagnosis of cACC [6]. Absence of the corpus callosum changes the shape of the lateral ventricles, which is the consequence of Probst bundles formation [7]. Another described common finding is ventriculomegaly with a “tear drop” appearance of the lateral ventricles. In general, callosal abnormalities are found in 13 % of ventriculomegaly cases [8]. When ventriculomegaly is absent there is a higher risk that cACC may be missed. However, this anomaly has a complex presentation in the fetal brain including: interhemispheric separation in coronal and axial views; forward and upward extension of the third ventricle in axial, coronal and sagittal views; lack of visualization of the cavum septi pellucidi–corpus callosum complex (CSP-CC) in the median view; third trimester formation of radiating folds instead of cingulate sulcus in the parasagittal views; colpocephaly in axial views; widely separated frontal horns in coronal views [3, 9 – 11]. Despite clear diagnostic signs of cACC in the mid-trimester exam, the majority of authors do not report this diagnosis until later in pregnancy [12 – 14]. In the recent study the mean gestational age was 24.5 +/- 1.3 weeks [6]. Furthermore, the MRI-based papers demonstrate inconsistency between ultrasound and MRI not only in terms of additional findings, but also in the primary diagnosis [14 – 16]. Moderate or severe ventriculomegaly on ultrasound happened to present cACC on MRI, or suspected cACC and callosal hypogenesis in sonography demonstrated normal corpus callosum on MRI. These inconsistencies arise from a very high operator dependency in ultrasound and the technical advantages of MRI. Therefore, we concentrated in our study on effective recognition of cACC in the mid-trimester scan. On the other hand in the third trimester, the ultrasound picture of cACC is more evident and at this stage of pregnancy the sign of radial cortical sulcation can be implemented in the diagnostic process [3]. In the authors’ opinion, the diagnosis of callosal agenesis can be done easier at mid-gestation if the operator uses a targeted approach for this anomaly. The objectives of this paper are as follows:

to suggest a stepwise ultrasound diagnostic approach for cACC, which has not been previously proposed to the best of our knowledge; to describe variations of this condition with their ultrasound picture at the mid-trimester scan including cases without ventriculomegaly, with severe ventriculomegaly, and with an interhemispheric cyst that change the presentation of the typical ultrasound signs of cACC. The authors classified these variations into characteristic patterns according to the size of the third ventricle, the level of ventriculomegaly, and their influence on the presence of the secondary findings.

Methods

From our library of images and ultrasound reports, we retrospectively reviewed our cases of complete agenesis of the corpus callosum diagnosed in the fetus at the mid-trimester scan (19 – 23 weeks). In our analysis we included only cases that were confirmed postnatally or by autopsy. Exams were performed between January 2010 and June 2012. All of the patients were scanned transabdominally by means of both 2 D and static 3 D methods using a Voluson E6 BT10 ultrasound scanner equipped with a volumetric 4 – 8 MHz hybrid probe (GE Healthcare, Zipf, Austria). None of the patients was scanned transvag-

inally in this study. In all scans, we standardized our basic 2 D settings using high frequencies with harmonics, level 5 speckle reduction and level 1 cross beam compounding. The 2 D approach was based on collecting still frames presenting the views described below and axial cine loops covering sections from the base of the skull to the top of the head. At our institution 3 D ultrasound of the fetal brain for image archiving is a routine practice. All 3 D acquisitions were similarly standardized using an axial acquisition from the oblique transcerebellar view (insonation angle to the mid-line of approx. 70 degrees; position of the cerebellum on the screen closer to the transducer than the cavum septi pellucidi) as an original plane with a volume angle of 60 degrees and a maximum quality factor. This acquisition technique is based on the mastoid fontanelle window, which reduces shadowing behind the parietal and frontal bones [17]. Acquired 3 D volume datasets were reviewed using 4DView software v.10.5 (GE Healthcare, Austria) with multiplanar views in three orthogonal planes and enhanced 2 mm slice imaging for better tissue differentiation (static Volume Contrast Imaging (VCI)). No dynamic VCI in the C plane was applied in this study because it is a function of 4 D imaging demonstrating an inferior quality in comparison to the static 3 D technique. Before review, unified orientation of the 3 D datasets was performed based on a horizontal positioning of the mid-line of the brain in the A and B planes. To do this, the reference point was placed at the mid-line of the brain in the A plane. Next, the A plane was rotated around the Z-axis until a horizontal position of the mid-line was achieved. Finally, the B plane was rotated around the Z-axis in order to obtain a horizontal position of the mid-line. These maneuvers automatically produce a median view of the brain in the C plane. From the 2 D and 3 D images we identified 4 anatomical views that consistently gave us enough information to identify cACC. Two of these views are from an axial plane, AX1-biparietal transthalamic view and AX2-biparietal falx view. The other 2 views that we found most helpful were a transthalamic coronal view (COR) and a median sagittal view (SAG). In this study, we concentrated on callosal agenesis not on partial ACC and this was the reason for not implementing the transcaudate coronal view in our protocol. **Fig. 1 – 4** are examples of described views shown with normal anatomy. The levels that these views were obtained from are also shown.

In **Table 1** the sonographic features related to cACC that may be seen during analyses of each view are summarized.

The diagnosis of cACC was made in SAG and COR views from 2 D images by demonstrating the absence of the corpus callosum structure. In 3 D datasets it was evaluated if the observations in reconstructed SAG and COR views were consistent with the 2 D findings. Additionally, we checked if any of the secondary signs of cACC were present in the described sections (Table1). The abnormal proximity of the interhemispheric fissure (IHF) resulting in the separation between the hemispheres was termed as the interhemispheric fissure sign [18 – 20]. We evaluated the presence

Table 1 The checklist of the features related to cACC that may be seen in each view used in this paper.

view	sonographic features
AX1	absence of cavum septui pellucidi
	dilatation of the third ventricle
	separation of frontal horns of lateral ventricles
	ventriculomegaly
AX2	interhemispheric separation
	upward displacement of the third ventricle
COR	interhemispheric separation
	absence of corpus callosum fibers
	descent of the falx towards the roof of the third ventricle
	upward displacement of the third ventricle
SAG	absence of cavum septui pellucidi-corpus callosum complex
	size and shape of the 3rd ventricle

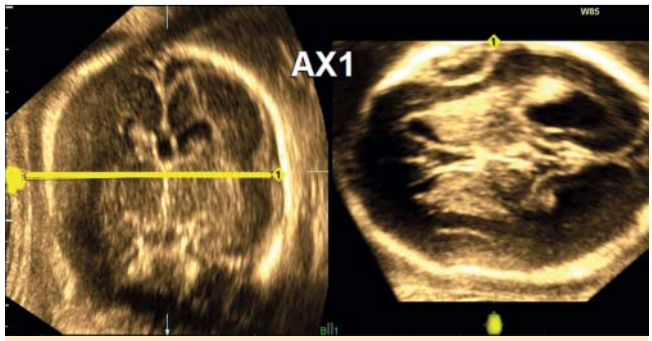

Fig. 1 AX1 – Axial biparietal transthalamic view (an axial biparietal view taken at the level of the thalami).

Abb. 1 AX1 – Axial biparietaler transthalamischer Schnitt (ein axialer biparietaler Schnitt im Bereich des Thalamus).

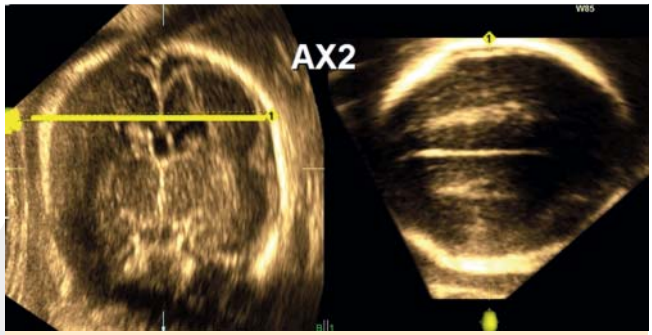

Fig. 2 AX2 – Axial biparietal falx view (an axial biparietal view taken through the lower 1/3 of the cerebral falx just superior to the cavum septum pellucidi). One line representing tightly adjoined hemispheres and the falx is seen in the normal brain.

Abb. 2 AX2 – Axialer biparietaler Falx-Schnitt (ein axialer biparietaler Schnitt durch das untere Drittel der Falx cerebri kurz oberhalb des Cavum septi pellucidi). Eine Linie zeigt die eng verbundenen Hemisphären und die Falx cerebri ist im normalen Gehirn zu sehen.

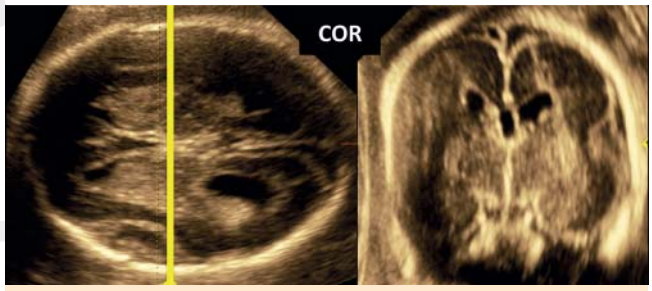

Fig. 3 COR – Coronal transthalamic view (a coronal view taken at the upper level of the thalami).

Abb. 3 COR – koronarer transthalamischer Schnitt (ein koronarer Schnitt im oberen Bereich des Thalamus).

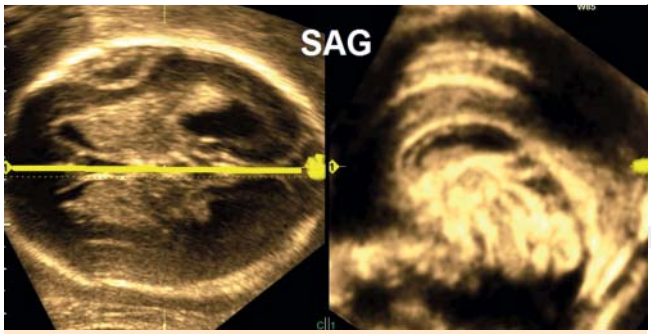

Fig. 4 SAG- Median view (a sagittal view taken at the midline level).

Abb. 4 SAG – medianer SAG-Schnitt (ein sagittaler Schnitt auf Höhe des Medians).

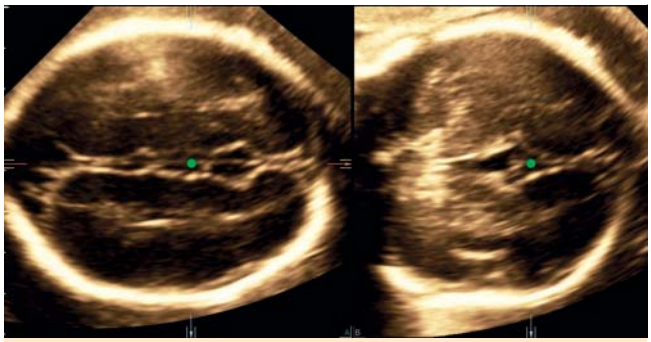

Fig. 5 A case of callosal agenesis. In the biplanar display format (A plane-axial and B plane-coronal): on the left a positive interhemispheric fissure sign (3 lines, the falx and the 2 separated medial borders of the hemispheres, instead of one line representing tightly adjoined hemispheres and the falx) seen along the entire AX2 view; on the right a reference coronal view is shown. Note the position of the reference point (green dot).

Abb. 5 Fall einer Balkenagenesie. In der biplanaren Darstellung (A Ebene – axial und B Ebene – koronar): links ist über den gesamten AX2-Schnitt das Zeichen einer positiven interhemisphärischen Fissur zu sehen (3 Linien, die Falx cerebri und die 2 geteilten medianen Grenzen der Hemisphären; anstelle einer Linie, welche die eng zusammengefassten Hemisphären und die Falx cerebri darstellen); rechts ist ein koronarer Schnitt als Referenz gezeigt. Zu beachten ist die Lage des Referenzpunktes (grüner Punkt).

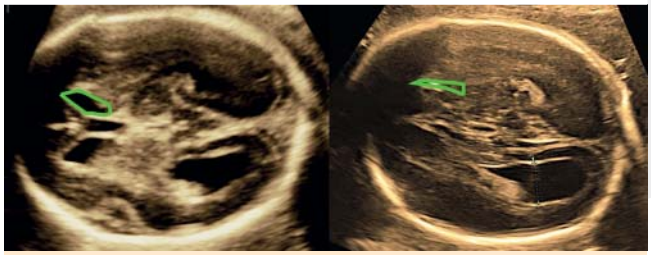

Fig. 6 On the left a case that is negative for 'the separation between the frontal horns' sign. Note the appearance of the frontal horns. On the right, a positive case is shown, confirmed with complete callosal agenesis. Note the small, pointed and medially indented frontal horns.

Abb. 6 Links ist ein Fall zu sehen, der einen negativen Befund für das Merkmal „Trennung zwischen den Vorderhörnern" zeigt. Zu beachten ist die Gestalt der Vorderhörner. Rechts ist ein positiver Fall gezeigt, der die komplette Balkenagenesie bestätigt. Zu beachten sind die kleinen, spitzen und median eingekerbten Vorderhörner.

or absence of this sign subjectively without performing any measurements at the level of AX2 (**Fig. 5**).

We also checked for separation between the frontal horns, which was defined as their lateral position with concave appearance of medial borders (**Fig. 6**). This sign was evaluated subjectively at the level of AX1.

Cases that presented with ventriculomegaly were classified as mild (10 – 12 mm), moderate (12.1 – 15 mm) and severe (more than 15 mm) dilatation of the lateral ventricle at the atrium. The third ventricle was interpreted as dilated if the diameter was above the 50th percentile -1.5 mm before 27 weeks of gestation [21].

Color Doppler mapping was not included in our study, as the diagnosis of cACC should always be based on B-mode characteristics. Moreover, due to the variety of anterior cerebral artery branches anatomical variants, we decided to decrease the risk of misinterpretation by not implementing any vascular mapping modalities [22].

Results

From our library 30 cases diagnosed at mid-gestation on ultrasound with callosal agenesis without extracerebral anomalies were selected with confirmed cACC postnatally (21 subjects) or in autopsy findings (9 subjects). 29 cases were isolated cACC, and 1 was complex cACC together with vermian hypoplasia as a result of toxoplasmosis infection. The mean gestational age at the time of diagnosis at our center was 20.7 weeks (range 19 – 23 weeks). In all analyzed cases sufficient 2 D images were found and in 93.3 % of them informative 3 D volumes were also available for off-line review. Each sonographic feature from 2 D and 3 D data including AX1, AX2, COR and SAG views was interpreted as present, absent or not determined. 2 D findings were found consistent with 3 D observations except in two cases due to the difficult scanning conditions. In these cases only 2 D images and cine loops were evaluated. Sonographic findings in our study group seen at selected anatomical views are summarized in **Table 2**.

Among our analyzed subjects, 4 characteristic patterns of cACC were identified and are listed in **Table 3**. We divided pattern B into 2 groups based on the amount of dilatation of the lateral ven-

Table 2 Percentage of 30 cases where the sonographic feature was seen during review of AX1, AX2, COR and SAG views.

view	% of cases where the sonographic feature was seen during review
AX1	100 % absence of cavum septui pellucidi
	86.6 % dilatation of the third ventricle
	83.3 % separation of frontal horns of lateral ventricles
	73.3 % ventriculomegaly
AX2	90 % interhemispheric separation
	80 % upward displacement of the third ventricle
COR	90 % interhemispheric separation
	100 % absence of cavum septui pellucidi-corpus callosum complex
	100 % descent of the falx towards the roof of the third ventricle
	80 % upward displacement of the third ventricle
SAG	100 % absence of cavum septi pellucidi-corpus callosum complex
	86.6 % dilatation of the 3rd ventricle

Table 3 Four patterns of ultrasound findings in cACC in axial views.

pattern		characteristics
A		normal size of 3rd ventricle + normal size of the lateral ventricles or mild ventriculomegaly (N = 4)
B	B1	dilated 3rd ventricle + normal size of the lateral ventricles (N = 4)
	B2	dilated 3rd ventricle + mild or moderate ventriculomegaly (N = 17)
C		dilated 3rd ventricle + severe ventriculomegaly (N = 3)
D		gross dilatation of 3rd ventricle with the appearance of an interhemispheric cyst (N = 2)

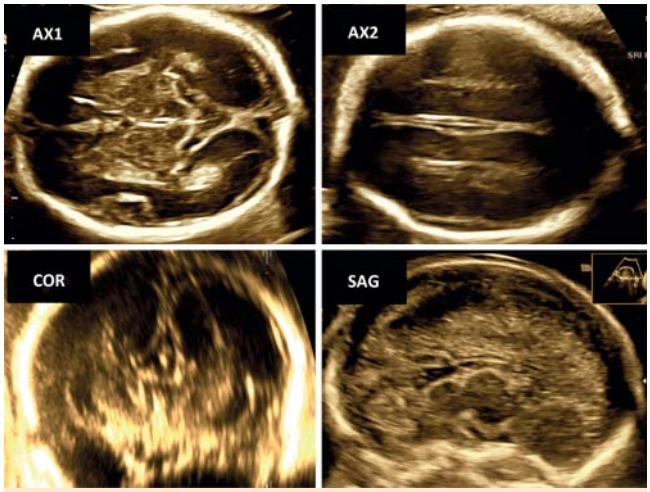

Fig. 7 A fetus at 20 weeks presenting with pattern A (normal size of 3 rd ventricle and normal size of the lateral ventricles or mild ventriculomegaly) in the four described views. This pattern represented 13.3 % of our 30 cases. In this pattern the AX1 view reveals no dilatation of the 3 rd ventricle. The AX2 view reveals a separation of the hemispheres. The COR view reveals that the cerebral falx descends towards the roof of the 3 rd ventricle with evident separation between the hemispheres and increase of the distance between the lateral ventricles. The SAG view shows a normal size of the 3rd ventricle. Note the absence of the CSP-CC complex.

Abb. 7 Ein Fetus der 20. Woche zeigt das Muster A (normale Weite des 3. Ventrikels und normale Weite der Seitenventrikel oder milde Ventrikulomegalie) in den vier beschriebenen Schnittebenen. Dieses Muster macht 13,3 % unserer 30 Fälle aus. Bei diesem Muster zeigt der AX1-Schnitt keine Dilatation des 3. Ventrikels. Der AX2-Schnitt bringt die Trennung der Hemisphären zum Vorschein. Der COR-Schnitt zeigt, dass die Falx cerebri zum Dach des 3. Ventrikels absteigt bei deutlicher Trennung zwischen den Hemisphären und einer Vergrößerung des Abstandes zwischen den Seitenventrikeln. Der SAG-Schnitt zeigt den 3. Ventrikel in Normalgröße. Zu beachten ist das Fehlen des CSP-CC-Komplexes.

tricles and found that B2, a mild to moderately dilated 3rd ventricle along with mild to moderately ventriculomegaly, was by far our most common group representing 56.6 % of our 30 cases while pattern B1 only represented 13.3 %. We decided to distinguish pattern C that is characterized by severe ventriculomegaly from pattern B (mild or moderate ventriculomegaly) due to the differences in the interhemispheric fissure appearance and the absence of frontal horn separation. These features are striking in this pattern and very different from pattern B. Due to the variety of mid-gestational patterns of agenesis of the corpus callosum in our analyzed series, like cases were grouped together in order to describe their common features.

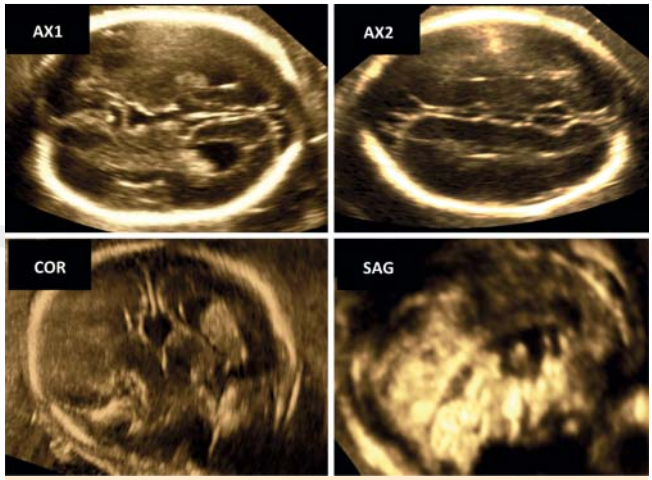

Fig. 8 A fetus at 22 weeks presenting with pattern B (dilated 3 rd ventricle and normal size of the lateral ventricles or mild to moderate ventriculomegaly) in the four described views. The AX1 view demonstrates dilatation of the 3 rd ventricle and mild ventriculomegaly. The AX2 view reveals separation of the hemispheres. The COR view reveals that the cerebral falx descends towards the roof of the 3 rd ventricle, dilatation of the 3 rd ventricle and separation between the hemispheres. The SAG view shows clear dilatation of the 3 rd ventricle. Note the absence of the CSP-CC complex.

Abb. 8 Ein Fetus der 22. Woche zeigt das Muster B (dilatierter 3. Ventrikel und normale Weite der Seitenventrikel oder milde bis moderate Ventrikulomegalie) in den vier beschriebenen Schnittebenen. Der AX1-Schnitt weist eine Dilatation des 3.Ventrikels und milde Ventrikulomegalie nach. Der AX2-Schnitt erkennt die Trennung der Hemisphären. Der COR-Schnitt zeigt, dass die Falx cerebri zum Dach des 3. Ventrikels absteigt, eine Dilatation des 3. Ventrikels und eine Trennung der Hemisphären. Der SAG-Schnitt zeigt eine deutliche Erweiterung des 3. Ventrikels. Zu beachten ist das Fehlen des CSP-CC-Komplexes.

The images below (**Fig. 7 – 10**) demonstrate cases of the 4 patterns described in **Table 3**.
The details of our study group, including the follow-up, are listed in **Table 4**.

Discussion

In our study we concentrated on the recognition of cACC in the fetuses at mid-trimester scan. We suggest a classification of characteristic patterns found in fetuses with proven cACC based on findings presented in axial views.
Our analysis is consistent with the observations of previous investigators and confirms that cases of suspected cACC, seen in standard axial views, should be further evaluated by means of a detailed scan also using coronal and sagittal views [2, 9, 10]. These cases include fetuses presenting with an absence of the cavum septi pellucidi, ventriculomegaly, or an interhemispheric cyst. Examiners should be aware that a sectional plane taken at the level of the collumna fornicis may mimic the normal appearance of the cavum septi pellucidi. However, this level shows a septated rectangle instead of an empty one [23].
We suggest a stepwise ultrasound diagnostic approach for cACC due to the several variations of this condition in the mid-trimester, when the spectrum of ultrasound findings is not as evident as later in gestation. Mid-trimester diagnosis enables parents to decide on pregnancy continuation, especially in countries where

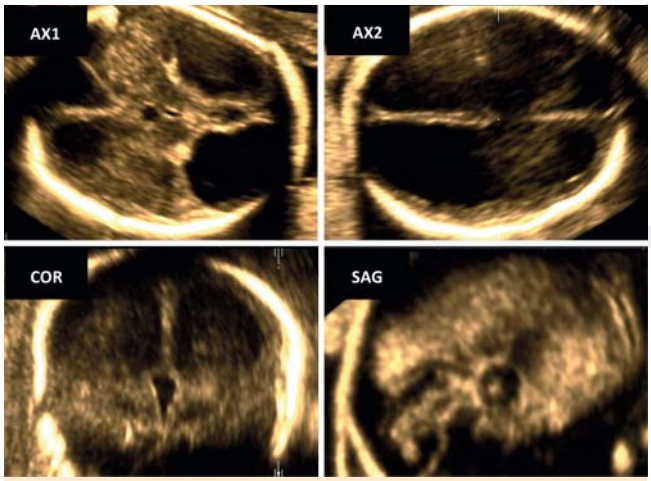

Fig. 9 A fetus at 21 weeks presenting with pattern C (dilated 3 rd ventricle and severe ventriculomegaly) in the four described views. This pattern represented 10 % of our 30 cases. The AX1 view demonstrates dilatation of the 3 rd ventricle and severe ventriculomegaly. The AX2 view reveals no separation of the hemispheres due to the increased pressure from the high fluid volume within the lateral ventricles pushing the hemispheres against each other. The COR view reveals that the cerebral falx reaches the roof of the 3 rd ventricle with dilatation of the 3 rd ventricle. The SAG view shows clear dilatation of the 3 rd ventricle. Note the absence of the CSP-CC complex.

Abb. 9 Ein Fetus der 21. Woche zeigt das Muster C (dilatierter 3.Ventrikel und schwere Ventrikulomegalie) in den vier beschriebenen Schnittebenen. Dieses Muster macht 10 % unserer 30 Fälle aus. Der AX1-Schnitt weist eine Dilatation des 3.Ventrikels und schwere Ventrikulomegalie nach. Der AX2-Schnitt zeigt keine Trennung der Hemisphären aufgrund des erhöhten Drucks des großen Flüssigkeitvolumens in den Seitenventrikeln, der die Hemisphären aneinander drückt. Der COR-Schnitt zeigt, dass die Falx cerebri das Dach des 3. Ventrikels erreicht bei Dilatation des 3. Ventrikels. Der SAG-Schnitt zeigt eine deutliche Erweiterung des 3. Ventrikels. Zu beachten ist das Fehlen des CSP-CC-Komplexes.

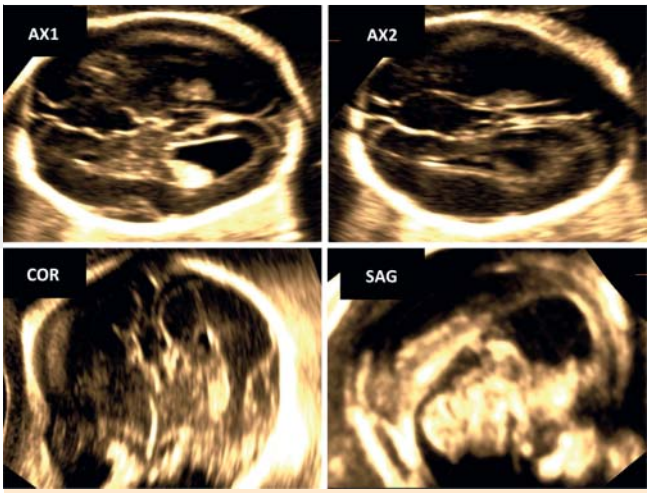

Fig. 10 A fetus at 21 weeks presenting with pattern D (gross dilatation of the 3 rd ventricle with the appearance of interhemispheric cyst) in the four described views. This pattern represented our lowest number of cases at 6.6 %. The AX1 view shows severe dilatation of the 3 rd ventricle and ventriculomegaly. The AX2 view reveals a severely dilated 3 rd ventricle that is displaced upwards. The COR and SAG views also reveal the grossly dilated 3 rd ventricle. Note the absence of the CSP-CC complex in the SAG view.

Abb. 10 Ein Fetus der 21. Woche zeigt das Muster D (stark erweiterter 3. Ventrikel und Auftreten einer interhemisphärischen Zyste) in den vier beschriebenen Schnittebenen. Dieses Muster ist mit 6,6 % bei unseren Fällen am geringsten vertreten. Der AX1-Schnitt weist eine starke Dilatation des 3. Ventrikels und Ventrikulomegalie nach. Der AX2-Schnitt zeigt einen stark erweiterten 3. Ventrikel, der angehoben ist. Die COR- und SAG-Schnitte zeigen einen stark dilatierten 3. Ventrikel. Zu beachten ist das Fehlen des CSP-CC-Komplexes im SAG-Schnitt.

termination of pregnancy is legally not allowed above viability. Step 1 is an evaluation of the AX1 view. In the majority of cases among fetuses where cACC is present, this axial biparietal view shows only secondary signs of the condition such as the absence of the cavum septi pellucidi, ventriculomegaly and dilatation of the 3rd ventricle. Step 2 is done with an additional tilt of the probe superior to the AX2 view, which demonstrates the lower 1/3 of the falx just superior to the cavum septi pellucidi in an axial plane. We recommend obtaining this view prior to the coronal or sagittal one as it is relatively easy to visualize and provides the examiner with quick information on the appearance of the IHF. When cACC is present, except in the case of severe ventriculomegaly, this view shows 3 lines, the falx and the 2 separated medial borders of the hemispheres, instead of one line representing tightly adjoined hemispheres and the falx.

In our opinion this is a very characteristic feature of cACC that can be of great assistance in correctly identifying this brain malformation, which was also raised by other authors [3]. In a normal brain the IHF is separated from the third ventricle by the corpus callosum, the cavum septi pellucidi, anterior commissure, fornix, and the lamina terminalis. If the corpus callosum and the cavum septi pellucidi are absent, the hemispheres lose their support and detach from each other [19]. This sign was present in all cases of cACC that we have examined except in cases of severe ventriculomegaly as seen in pattern C. With severe ventriculomegaly the increased volume within the lateral ventricles maintains the normal appearance of adjacency of the hemispheres and no separation between the frontal horns of the lateral ventricles. In pattern D the apparent interhemispheric cyst makes visualization of the IHF difficult.

The 3rd step in the evaluation of cACC is a 90 degree rotation to the transthalamic coronal view. We found this to be the most reliable view during the diagnostic process as primary features of cACC are found in this view. Seen here is the descent of the falx towards the roof of the 3rd ventricle, lack of corpus callosum fibers seen at this level, secondary dilatation of the third ventricle, in most cases, and interhemispheric separation as the IHF becomes closer to the 3rd ventricle, if the ventriculomegaly is not severe. The roof of the third ventricle is usually intact and in 80 % of cases extends upward to a variable degree. In 52 % of cases it reaches the falx and may be indented or deviated by it [10]. The importance of the IHF in cACC was firstly raised in a CT study describing its relationship to the third ventricle [19]. Interhemispheric fissure sign was recognized as a very accurate, present in 100 % of cases, feature of cACC [9, 19, 20, 24, 25]. The usual hyperechogenic tip at the distal end of the falx seen in coronal views, representative of a callosal sulcus in the normal fetal brain, is not visualized in ACC due to the separation of the IHF.

The 4th step in the evaluation of cACC is the acquisition of a median view. It has the same diagnostic value as the coronal view. However it needs to be mentioned that it is very operator dependent and due to the variety of cACC patterns analysis of this view is not always straightforward. As an example, we demonstrate in ▶ **Fig. 11**, a case that may mimic a normal appearance of the CSP-CC complex in the median view, but reveals the typical appear-

ance for cACC in the coronal view. In our opinion the SAG view should be used in combination with the COR view.

The SAG view confirms the absence of the CSP-CC complex and shows various degrees of 3rd ventricle dilatation in most of the cases. As described above, our stepwise approach is a simple, logical and reliable tool that confirms or excludes cACC during midtrimester sonography. We believe that this approach will help examiners with less experience to diagnose callosal agenesis more effectively. Later in gestation or postnatally, the median section can be accompanied by parasagittal views presenting the absence of a cingulated gyrus and the presence of an atypical radiating appearance of the median sulci that converge toward the third ventricle. Difficulties in the ultrasound prenatal diagnostics of cACC arise from the complexity of this condition in which we describe four patterns with various degrees of size and shape of the third ventricle. The presentation of these patterns is influenced by the presence of ventriculomegaly. We emphasize that ventriculomegaly is not a constant finding in cACC and a normal size of the lateral ventricles increases the risk of missing the anomaly. It has been confirmed in many studies that cACC is detected in 13 – 17 % of fetuses referred due to ventriculomegaly [3, 8]. A confusing issue is the presence of an interhemispheric cyst (IHC). According to Barkovich classification, in type I of IHC, diverticula of the 3rd or lateral ventricles form cysts that are located in between the hemispheres [26]. This finding makes neurosonography more challenging and may be easily mistaken for arachnoid cysts, if coronal and sagittal views are not examined. That erroneous prenatal diagnosis may influence the effectiveness of counseling. The findings in our cases show that careful investigation, according to our proposed approach, reduces the risk of missing the anomaly. The classification that we propose will not improve the diagnostic efficiency of callosal agenesis, but allows understanding of the heterogeneous prenatal ultrasound picture of cACC at mid-gestation, which is, in our opinion, one of the main reasons for diagnostic dilemmas.

3 D ultrasound imaging of the brain is an extremely reliable data archiving method and allows for precise reconstruction of the

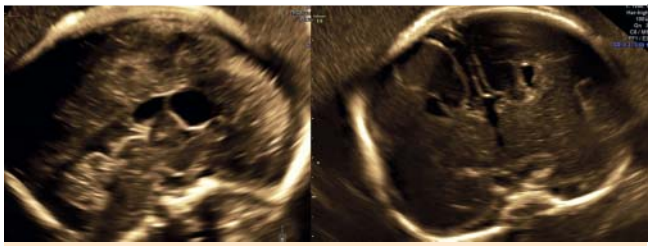

Fig. 11 A fetus at 23 weeks diagnosed with cACC. The SAG view shows the cystic dilatation of the 3 rd ventricle recesses that imitates the normal pattern of the CSP-CC complex (left). The COR view on the other hand is conclusive for cACC (right).

Abb. 11 Ein Fetus der 23. Woche mit cACC. Der SAG-Schnitt zeigt die zystische Dilatation in den Recessi des 3. Ventrikels, die das Normalmuster des CSP-CC Komplexes nachahmt. Andererseits spricht der COR-Schnitt für eine cACC (rechts).

Table 4 The details of our study group, including the follow-up.

case	pattern	gestational age at diagnosis	outcome	follow-up
1	A	21	TOP	isolated cACC on autopsy
2	A	22	term delivery	normal development at 15 months
3	A	20	term delivery	normal development at 8 months
4	A	21	CS at term	seizures
5	B1	19	TOP	isolated cACC on autopsy
6	B1	19	term delivery	normal neurodevelopment at 10 months
7	B1	21	term delivery	normal neurodevelopment at 12 months
8	B1	22	TOP	isolated cACC on autopsy
9	B2	20	TOP	isolated cACC on autopsy
10	B2	19	term delivery	seizures, severe neurodevelopmental delay
11	B2	20	TOP	Isolated cACC on autopsy
12	B2	20	term delivery	mild neurodevelopmental delay
13	B2	20	premature delivery at 36 weeks	severe neurodevelopmental delay
14	B2	21	term delivery	normal neurodevelopment at 6 months
15	B2	23	term delivery	severe neurodevelopmental delay
16	B2	20	CS at term	seizures, mild neurodevelopmental delay
17	B2	21	TOP	isolated cACC on autopsy
18	B2	22	term delivery	seizures
19	B2	23	term delivery	seizures, mild neurodevelopmental delay
20	B2	20	term delivery	mild neurodevelopmental delay
21	B2	20	CS at term	severe neurodevelopmental delay
22	B2	21	CS at term	severe neurodevelopmental delay
23	B2	23	term delivery	seizures, severe neurodevelopmental delay
24	B2	20	CS at term	mild developmental delay
25	B2	20	TOP	isolated cACC on autopsy
26	C	21	TOP	cACC + severe VM + vermian hypoplasia on autopsy
27	C	21	TOP	cACC + severe VM on autopsy
28	C	19	CS at term	neonatal demise
29	D	22	CS at term	mild neurodevelopmental delay
30	D	22	CS at term	severe neurodevelopmental delay

important coronal and median sections of the fetal brain, even with the fetus in difficult positions. This technique assures the operator that the A, B and C reference planes are displayed in orthogonal fashion, which simplifies and standardizes precise multiplanar analysis [27]. In 2 D imaging the multiplanar approach is possible, but is limited due to fetal positions where it is difficult to maneuver the transducer to capture and relate necessary views one to another. Also, 3 D neurosonography is a reliable tool for detailed corpus callosum measurements, like the length of its structure and the height of its particular parts [28]. For these reasons we advocate using 3 D acquisition in all cases suspected of cACC. Like any other imaging method, it requires a learning curve, which is particularly focused on avoiding shadowing behind the parietal and frontal bones before acquisition is initiated.

Conclusion

A mid-trimester stepwise approach minimizes the risk of missing cACC taking into account several patterns of this condition. To the best of the author's knowledge, these variations have not been described before in the literature. We hope that the four recognition patterns described by us will be considered when cACC is suspected and will widen the diagnostic perspective of sonographers and physicians dealing with screening or counseling at tertiary centers.

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