SBUS SOCIEDADE BRASILEIRA DE ULTRASSONOGRAFIA

DOI: 10.29327/218041.32.37-8

ISSN 2675-4800

SCIENTIFIC ARTICLE - CASE REPORT

ABSENCE OF THE CAVUM SEPTUM PELLUCIDUM: MULTIDISCIPLINARY APPROACH AND DIAGNOSTIC CHALLENGES IN FETAL MEDICINE

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ABSTRACT

Introduction: The cavum septum pellucidum (CSP) is a cavity filled with cerebrospinal fluid, located between two thin sheets of the septum pellucidum. Its visualization is essential in the screening for anterior midline brain malformations, particularly due to its close relationship with the corpus callosum and the limbic system. The absence or alteration of the CSP is associated with various conditions, such as septo-optic dysplasia (SOD), agenesis of the corpus callosum, holoprosencephaly, and schizencephaly. Its persistence in adults, although often without implications, may be linked to neuropsychiatric disorders.

Case Report: A 22-year-old nulligravida patient presented with absence of CSP visualization and mild ventriculomegaly detected on ultrasound at 23 weeks. Complementary examinations included neurosonography and fetal echocardiography, which revealed no other anomalies. At birth, the newborn showed normal conditions and appropriate development up to 10 months of age, with no signs of neurological impairment. Neurological follow-up and magnetic resonance imaging are still pending.

Discussion: Although most cases of isolated CSP absence have a favorable outcome, it is important to consider that additional anomalies may be detected after birth, leading to unfavorable outcomes, such as alterations in neuropsychomotor development and hormonal deficiencies. Careful evaluation and postnatal follow-up are essential to identify potential complications and provide appropriate counseling to parents.

Conclusion: The prenatal diagnosis of isolated absence of the septum pellucidum may have a more favorable prognosis compared to cases associated with other anomalies. However, postnatal follow-up is crucial, as there may be associations not detected during fetal life, such as septo-optic dysplasia and other neurological deficiencies, which makes parental counseling a challenge.

KEYWORDS: CAVUM SEPTUM PELLUCIDUM, NEUROSONOGRAPHY, BRAIN MALFORMATIONS, AGENESIS OF THE SEPTUM PELLUCIDUM, SEPTO-OPTIC DYSPLASIA, PROGNOSIS.

INTRODUCTION

The cavum septum pellucidum (CSP) is a cavity filled with cerebrospinal fluid (CSF), situated between the two thin sheets of the septum pellucidum. It is bounded superiorly by the corpus callosum, inferiorly by the roof of the third ventricle and the anterior fornix, and laterally by the frontal horns of the lateral ventricles.

During embryonic development, the septum pellucidum forms between the 6th and 8th weeks of gestation and can be identified on obstetric ultrasound from the 17th week onwards. Its presence and morphology are important markers in the screening for brain malformations, as the CSP is visualized in axial views of the fetal brain as an anechoic, well-defined structure between the lateral ventricles. It is considered one of the main markers of the integrity of the anterior midline of the brain, essential for the proper development of the limbic system and the corpus callosum, with which it maintains a close embryological relationship. Although CSP agenesis is often associated with corpus callosum agenesis, it is not a pathognomonic sign[1-3].

The fusion of the septum pellucidum sheets typically occurs after birth, with the closure of the cavity around the first six months of life. However, persistence of the CSP can be observed in a significant percentage of the adult population, reaching up to 30%, and is often considered an anatomical variant without severe clinical implications in most cases. Nevertheless, an enlarged or persistently widened CSP has been associated with psychiatric disorders, such as schizophrenia and bipolar spectrum disorders, as well as other neuropsychiatric conditions[4,5].

Belhocine et al.[6], through a retrospective study using magnetic resonance imaging, diagnosed 34 out of 14,000 (0.02%) children with septum pellucidum agenesis[5]. However, isolated agenesis of the septum pellucidum is considered

a rare condition, with an estimated prevalence of 2 to 3 per 100,000 live births.

The absence of the CSP can be observed in association with complex anomalies, such as septo-optic dysplasia (SOD), a malformation characterized by the absence of the septum pellucidum, optic nerve hypoplasia, and hypothalamic/pituitary dysfunction[7,8]. Lepinard et al[8]. were the first to report a prenatal diagnosis of septo-optic dysplasia—Morsier syndrome. With the advancements in human genetics, a mutation in the HESX1 homeobox gene located on chromosome 3p14 has been associated with SOD[9]. These brain anomalies are generally associated with deficits in neuropsychomotor development and severe hormonal dysfunctions, which have significant prognostic implications[1,3,4,6-8]. Neuroimaging studies reveal that the absence or alterations of the CSP, particularly in the context of corpus callosum agenesis or septo-optic dysplasia, indicate brain developmental disorders that require more detailed investigation with fetal magnetic resonance imaging (MRI) to clarify the diagnosis and facilitate appropriate therapeutic planning[7,10].

DIAGNOSIS

The septum pellucidum is a structure composed of two thin sheets that delimit an anechoic space known as the cavum septum pellucidum (CSP) and is part of the anterior complex of the central nervous system (CNS). This structure can be visualized by ultrasound from the 17th week of gestation, progressively disappearing after the 37th week[1]. The CSP is identified in the transventricular, median sagittal, and transcaudate planes during the second-trimester morphology ultrasound, and its shape is predominantly square in axial views (in about 73% of cases) and triangular in 27% of cases—see figure 1.

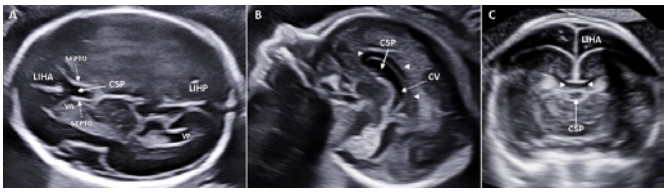

Figure 1. A - Transventricular view (LIHA: anterior interhemispheric line; CSP: cavum septum pellucidum; VA: anterior ventricle; VP: posterior ventricle; LIHP: posterior interhemispheric line). B - Median sagittal view (arrowhead: corpus callosum; CV: cavum vergae). C - Coronal transcaudate view.

The normal width of the CSP varies according to gestational age. Using a biparietal diameter (BPD) of 50 mm (20 weeks) and 80 mm (30 weeks), the CSP measures approximately 3.9 mm and 5.8 mm, respectively[11]. Measurements above the 95th percentile may be associated with aneuploidies, such as trisomy 18, 21, and chromosome 22 microdeletion[11,12]. The CSP should be present in 100% of fetuses between the 18th and 37th weeks, especially when the BPD ranges from 44 to 88 mm. It is essential to differentiate it from the anterior columns of the fornix, which are visualized as three echogenic lines and do not contain cerebrospinal fluid, and from the persistence of the cavum vergae (CV), which usually disappears after the 26th week of gestation. Proper differentiation between these structures is crucial for diagnosis and gestational follow-up. Figure 2 displays, in an inferior axial view, the hyperechogenic lines that belong to the anterior fornix (A) and, in a superior axial anechoic image, the cavum vergae (B).

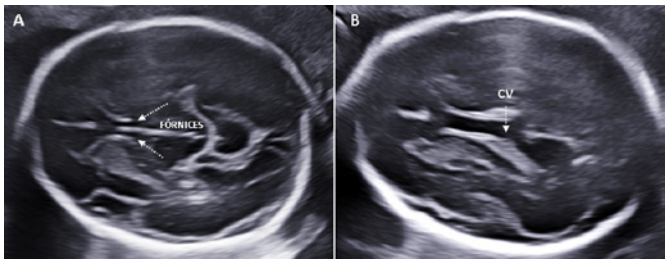

Figure 2. Axial sections of the cephalic pole. A - Inferior: fornices (three hyperechogenic lines). B - Superior: cavum vergae (CV), median and superior region.

The proper evaluation of the CSP is a crucial component of routine ultrasound examination, as its absence or alterations may indicate severe brain malformations, often associated with changes in the development of the corpus callosum and the midline of the brain.

The cavum septum pellucidum disappears in a defined sequence, with the cavum of the velum interpositum being the first to disappear, followed by the cavum vergae, both around the 26th week of gestation; this is followed by the CSP, which disappears after the 37th week. The absence of the CSP can occur in isolation, without associated brain or extracerebral anomalies, or it may be related to mild to moderate ventriculomegaly (measured as the posterior atrium being less than 15 mm). However, in some cases, its absence is associated with significant brain malformations, including holoprosencephaly, severe ventriculomegaly, agenesis or dysgenesis of the corpus callosum, schizencephaly, and septo-optic dysplasia[2,6,13].

Figure 3 illustrates the sagittal and anterior view of the cavum septum pellucidum (CSP), cavum velum interpositum (CVI), and cavum vergae (CV)[14].

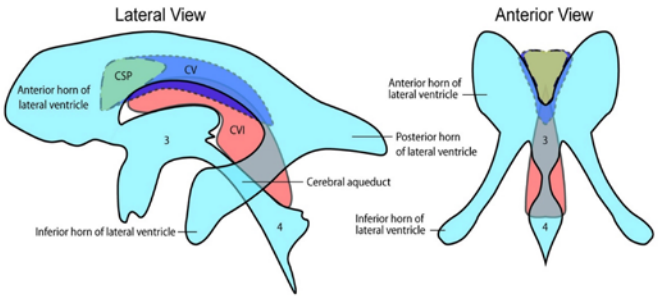

Figure 3 – The image illustrates the sagittal and anterior view of the types of cavum. (CSP = cavum septum pellucidum, CV = cavum vergae, and CVI = cavum velum interpositum)[14].

CASE REPORT

A 22-year-old nulliparous patient was referred by the SUS for follow-up in the postgraduate program of Fetal Medicine at Clínica Gennus, associated with the Faculdade de Ciências Médicas of Minas Gerais. Her personal and family history showed no diagnosed neurological diseases, with normal laboratory tests and previous ultrasounds within the normal range.

Ultrasound performed on 08/05/2023 at Clínica Gennus: Absence of visualization of the cavum septum pellucidum (CSP) in the axial, sagittal, and coronal sections, and identification of mild ventriculomegaly (Figures 4-6). No other associated structural anomalies were observed, particularly in the posterior fossa, posterior midline, and optic chiasm.

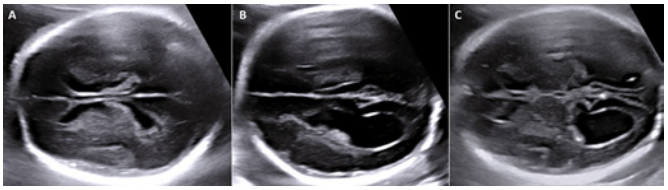

Figure 4. Axial image of the cephalic pole at three levels showing the absence of the cavum septum pellucidum and ventriculomegaly.

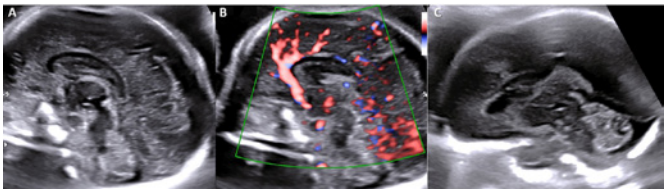

Figure 5. A. Median sagittal image of the cephalic pole showing the absence of the cavum septum pellucidum. B. Color Doppler showing the pericalosal artery.

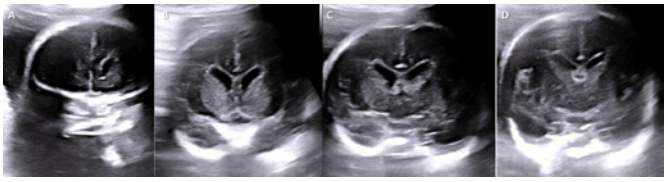

Figure 6. Coronal image of the cephalic pole at three levels showing the absence of the cavum septum pellucidum.

Complementary Evaluations:

To clarify the absence of the CSP and mild ventriculomegaly, the following were performed:

Endovaginal Neurosonography: Confirmed the findings of ventriculomegaly and absence of the cavum septum pellucidum. The optic chiasms, structures of the posterior midline, and posterior fossa were investigated, identified, and found to be normal (Figure 7).

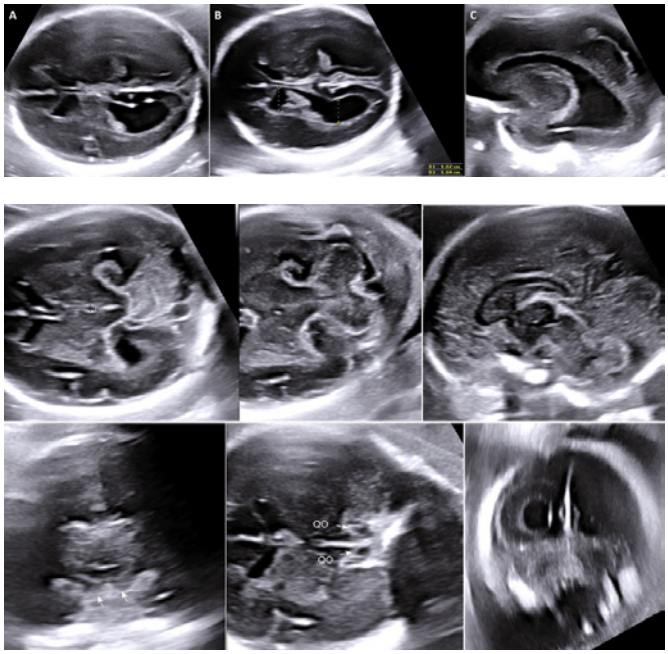

Figure 7. Fetal Neurosonography. A, B, C: Evaluation of ventriculomegaly. Images of the posterior midline and posterior fossa. Arrows indicate the optic chiasm.

Fetal Echocardiography: Normal, with no evidence of structural heart diseases.

Prenatal Management: During prenatal care, cytogenetic studies (karyotype) or fetal magnetic resonance imaging (MRI) were not performed, despite the findings of alterations in the central nervous system.

Delivery and Neonatal Evolution: Male newborn, delivered vaginally on 11/12/2023, at 40 weeks and 2 days of gestation. Birth weight: 3,220 g. Length: 49 cm.

Neonatal Conditions: Discharged on the second day of life, without apparent complications.

Postnatal Evolution: By 10 months of age, the infant showed adequate development in cognitive, sensory, visual, and motor aspects, with no signs of neurological impairment. However, neurological follow-up and magnetic resonance imaging (pending through the SUS) were recommended, especially due to the absence of the septum pellucidum and the mild ventriculomegaly detected during the prenatal period.

DISCUSSION

The isolated absence of the cavum septum pellucidum (CSP) is a condition that, in most cases, presents a favorable prognosis, with normal development and good outcomes. However, as highlighted in the literature, there is a risk of detecting additional cerebral anomalies after birth, which can negatively impact neurological development. Among the postnatal complications are alterations in neuropsychomotor development, visual impairments such as blindness, and hormonal dysfunctions [7].

Borkowski-Tillman et al.[3] highlight that, despite advancements in imaging techniques, it is difficult to guarantee with absolute certainty the isolated absence of the CSP during the prenatal period, pointing to the possibility of other undetected malformations during gestation. The authors analyzed 47 fetuses, with 17/47 (15%) considered to have isolated CSP defects. Approximately 14 babies underwent neurological follow-up, and all were normal. On the other hand, at least 50% of fetuses with associated anomalies showed abnormal results[3].

Studies also show that even in cases where CSP agenesis appears to be isolated during the prenatal period, additional anomalies may be diagnosed later [4,6,7].

Damaj et al.[4] conducted a study with 17 cases of isolated CSP agenesis, where 14 out of 17 exhibited normal neurological development. However, in 3 out of 17 (18%) patients displayed behavioral problems, 2 out of 17 (28%) experienced language delays, and 3 out of 17 (18%) were diagnosed with septo-optic dysplasia.

Di Pasquo et al.[15] conducted a cohort followed by a meta-analysis, revealing that in 14% of cases (9 out of 70) of isolated CSP agenesis, an additional anomaly was detected after birth. Genetic testing was performed on 30 cases, resulting in two abnormal outcomes (9%) – microdeletion 1p14 and a variant of uncertain significance (VUS) at 10p13. Among the 79 fetuses monitored, 14 out of 79 (19%) presented with septo-optic dysplasia (SOD). Among the 46 infants who underwent neurological follow-up and did not have SOD, 3 out of 46 (6.5%) were diagnosed with severe neurological deficits. Furthermore, 60 fetuses were considered normal when the ophthalmological tract was analyzed by ultrasound and MRI; however, 6 out of 60 (9.1% - false negative) presented with SOD in the postpartum period. This evidence demonstrated that an apparently normal visualization of the optical pathways in prenatal imaging does not exclude the possibility of septo-optic dysplasia. Table 1 illustrates the findings of postnatal septo-optic dysplasia from this meta-analysis, reinforcing the importance of follow-up even when examinations appear normal in prenatal imaging.

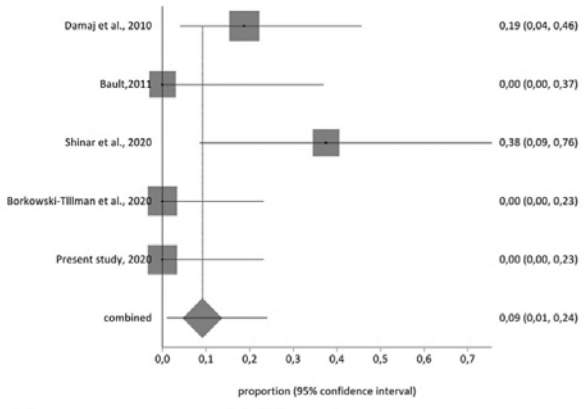

Table 1. Displays the proportion of cases of septo-optic dysplasia in fetuses that showed normal prenatal evaluation of the optic tracts, nerves, or chiasms.

Therefore, postnatal follow-up is crucial to monitor the development of these children, especially in cases of absent CSP, and should involve a multidisciplinary team, including neurologists, endocrinologists, and ophthalmologists.

CONCLUSION

The identification of the cavum septum pellucidum is essential in routine obstetric ultrasound starting from the 17th week of gestation, in axial cuts of the central nervous system. It is important not to confuse the CSP with the fornix or with the persistence of the cavum vergae.

Its absence is a significant marker of anterior cerebral midline defects. When the CSP is not visualized, it is essential to conduct a detailed evaluation of the CNS, including the optic pathways, through neurosongraphy, magnetic resonance imaging (MRI), and 3D/4D ultrasound. MRI between 28 and 32 weeks and after birth is highly recommended, as well as the performance of invasive tests, such as karyotyping or microarray, in cases with associated anomalies.

After analyzing these findings, we included in our fetal neurosonography examination the evaluation of the optic nerve, in addition to the investigation of the optic chiasm. Alonso et al.[16] described a method for identifying and measuring the chiasm, nerve, and optic tract using abdominal ultrasound. Through an axial image of the fetal head in the transventricular plane, the probe is moved caudally, and color Doppler is activated to identify the circle of Willis for orientation. Figure 8 illustrates how to identify the fetal optic chiasm, nerve, and tract.

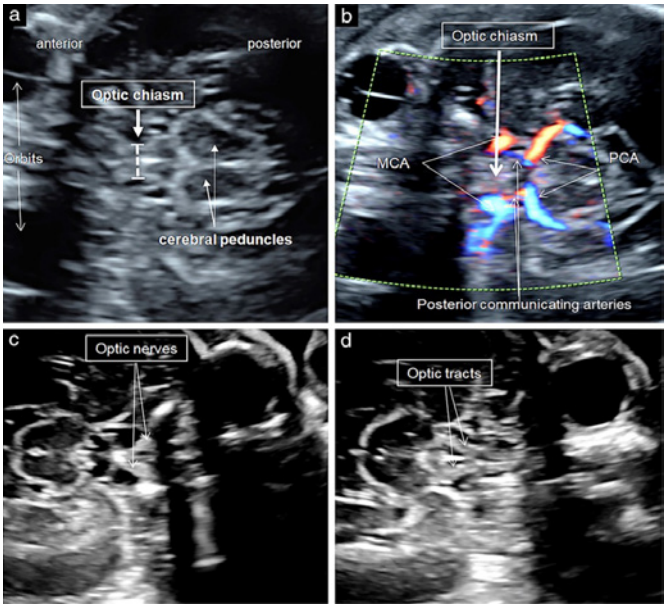

Figure 8. (a) Transabdominal ultrasound image of the fetal head at 26 weeks of gestation, demonstrating an adequate view to evaluate and measure the optic chiasm. At least the anterior orbit should be visible anteriorly and the cerebral peduncles posteriorly; laterally, the cerebrospinal fluid appears as an anechoic space around the echogenic X-shaped optic chiasm. Calipers are placed at the center of the X-shaped structure, surrounded by an anechoic cerebrospinal fluid. (b) Transabdominal ultrasound image of the fetal head at 29 weeks of gestation at the level of the optic chiasm. Color Doppler is activated to show that the center of the optic chiasm corresponds to the origin of the middle cerebral artery (MCA), which arises from the internal carotids, and the relationship of the optic chiasm with the posterior cerebral arteries (PCA) and the posterior communicating arteries that form the circle of Willis. (c, d) Transabdominal ultrasound images of the fetal brain at 28 weeks of gestation, demonstrating normal optic nerves (c) and normal optic tracts (d) [16].

Although the type of delivery depends on specific obstetric indications, postnatal follow-up is necessary in all cases of isolated agenesis of the CSP, with an emphasis on neurological, endocrinological, and ophthalmological monitoring. Prenatal counseling in these cases poses a challenge, as additional malformations, such as septo-optic dysplasia and behavioral or hormonal changes, may arise after birth, compromising the initial prognosis.

Unlike other CNS anomalies, such as agenesis of the corpus callosum, which have more established diagnostic and prognostic criteria, the isolated absence of the septum pellucidum still lacks clear guidelines for accurate counseling. This necessitates rigorous follow-up and effective communication with the parents to prepare them for potential future complications.

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Scientific Editor - Heverton Pettersen
Spelling Check: Dario Alvares
Received: 02/10/24. Accepted: 10/10/24. Published: 06/11/24.
Updated: 02/12/24.