The brain shadowing sign: a clue finding for early suspicion of craniosynostosis?

Authors: Andrea Dall’Asta¹,², Gowrishankar Paramasivam², Christoph Lees²,³,⁴, Tullio Ghi¹, Tiziana Frusca¹

Affiliations:

¹Department of Obstetrics and Gynecology, University of Parma, Parma, Italy

²Centre for Fetal Care, Queen Charlotte’s and Chelsea Hospital, Imperial College Healthcare NHS Trust, London, United Kingdom

³Department of Surgery and Cancer, Imperial College London, London, United Kingdom

⁴Department of Development and Regeneration, KU Leuven, Leuven, Belgium

Running title: Early suspicion of craniosynostosis.

Address for correspondence:

Prof. Tullio Ghi, MD, PhD, Department of Obstetrics and Gynecology, University of Parma, Parma, Italy. Via Antonio Gramsci 14, 43126 Parma, Italy

Phone +390521033676

E-mail contact: tullio.ghi@unipr.it
Authorship declaration

All the Authors have contributed to the work and take responsibility for the content.

Acknowledgements

None.

Ethics

Informed consent for publication was obtained by the involved subjects prior to publication.

Disclosure statement

The Authors state no conflict of interest in relation to this work.

Funding

None.

Word count (references excluded): 997

Figure count: 2

Keywords: antenatal ultrasound, Fetal Medicine, skull sutures, prenatal diagnosis
Bulleted statements

Established facts

- Isolated craniosynostosis is detected only sporadically at prenatal ultrasound.

Novel insights?

- The “brain shadowing sign” can be noted also at screening ultrasound and may lead to early suspicion of craniosynostosis.

- The identification of the “brain shadowing sign” should warrant ultrasound follow up monitoring.
Abstract

Antenatal imaging of craniosynostosis mainly relies on the demonstration with 2D ultrasound of the abnormal contour of the calvarium, of the loss of hypoechogenicity of the synostotic sutures and on indirect signs of premature closure of the skull sutures, however isolated craniosynostosis is detected only sporadically at prenatal ultrasound. In this manuscript we present the first case to our knowledge in which the “brain shadowing sign”, a recently described indirect sign of craniosynostosis, noted at 24 weeks in a structurally normal fetus was the first clue for the diagnosis of isolated bilateral coronal craniosynostosis, which became evident at late gestation.
Case Report

A 35 year-old para 1 woman was referred for anomaly scan due to raised nuchal translucency (4.2 mm) at first trimester combined screening test. CGH-array on chorionic villous sampling was negative. At 20 weeks fetal anatomy appeared normal as were the cavum septum pellucidum (CSP) and the fetal profile (Figures 1a,b), however the patient was not discharged due to low-lying posterior placenta. At the 24 weeks’ follow up scan normal placental insertion was documented, however when repeating fetal biometry it was difficult to obtain a proper transthalamic axial view as the clear visualization of the CSP could not be obtained bilaterally due to acoustic shadowing which persisted despite repeated tilting movements of the probe. On the same view the anterior part of the brain could not be visualized due to shadowing, even though no obvious abnormality of the skull shape was noted (Figure 1c). Similar findings were reported at follow up scan at 28 weeks (Figure 1d), while the diagnosis of bilateral coronal craniosynostosis was confirmed at 32 weeks, when the skull shape was consistent with the diagnosis of brachycephaly (cephalic index, i.e. ratio between the biparietal diameter and the occipito-frontal diameter, measuring 90.3) (Figure 1e) and the midsagittal view of the fetal profile appeared abnormal as per turricephaly (Figure 1f). The antenatal diagnosis of bilateral coronal craniosynostosis with widening of the metopic suture was confirmed using three-dimensional ultrasound as shown in Figure 2. Targeted genetic tests for the most common genetic syndromes associated with craniosynostosis was performed on stored villi and came negative. The diagnosis of non-syndromic isolated bilateral coronal craniosynostosis was confirmed postnatally and the baby underwent corrective surgery in the first month of life.

Discussion

Craniosynostosis is a congenital developmental disorder causing the premature fusion and closure of one or more of the skull sutures and leads to a variable distortion of the head shape [1]. Non-
syndromic craniosynostosis most commonly involves only one suture and is not associated with additional abnormalities, while syndromic craniosynostosis is usually accompanied by other anomalies within the context of genetic syndromes such as Crouzon, Apert, Pfeiffer and Saethre-Chotzen [1].

The antenatal diagnosis of craniosynostosis is challenging even for expert investigators [2,3]. Prenatal imaging mainly relies on the demonstration of the abnormal contour of the calvarium and the loss of hypoechogenicity of the synostotic sutures on 2D ultrasound. Additionally, indirect signs which can be noted at 2D ultrasound include abnormal cephalic index, cranial shape and/or face morphology [2]. 3D US represents a potential complementary tool for the rendered visualization of the skull sutures and for the measurement of the bony gaps on multiplanar mode [1,4]. Nevertheless, in most instances the diagnosis is suggested by the detection of additional findings in the context of syndromic craniosynostosis. In the largest published case series ultrasound examination of the skull sutures proved to be very accurate in women at high risk of recurrent syndromic craniosynostosis based on positive family history, while among low risk cases referred due to suspected skull deformity or facial dysmorphism at second or third trimester ultrasound, the diagnosis of craniosynostosis was confirmed only in 4 out of 24 cases. Among these, 2 fetuses eventually showed multiple abnormalities and 1 case of apparently isolated craniosynostosis was eventually classified as syndromic, the remaining case being a false positive. Therefore, within a non-selected and low risk population the specificity of antenatal ultrasound for the diagnosis of craniosynostosis is very low.

Isolated craniosynostosis is detected only sporadically during prenatal ultrasound and, if so, almost invariably in the third trimester [2]. The observation that shadowing of the fetal brain may represent an indirect sign of craniosynostosis was previously reported by Haratz et al. [3] on a case series of
24 fetuses with antenatal diagnosis of craniosynostosis. In this cohort the diagnosis was made before 26 weeks only in 7 cases, however none of them had isolated craniosynostosis; if considering a gestational age cut off of 28 weeks, only 2 out of 11 cases had isolated craniosynostosis. In the case we present the “brain shadowing sign” was noted at 24 weeks in a structurally normal fetus and represented the first clue for craniosynostosis, which became evident at later gestation. Therefore, intracranial shadowing may represent an early sign of premature fusion of the cranial sutures even in the absence of abnormal skull shape. Conversely, it is of note that “unusual echogenicity” represents an indirect sign of conditions in which the bone density is pathologically reduced, such as in osteogenesis imperfecta [5].

Insonation through open coronal and lamboid cranial sutures and fontanels is an essential requirement for the sonographic assessment of the brain. We do not envisage that the “brain shadowing sign” will allow a straightforward detection of all cases of craniosynostosis, especially given that different sutures other than the coronal and the lamboid ones may be affected, however we believe that an important message for sonographers is that unexpected acoustic shadowing of the intracranial structures is worth being followed up as it may be an early sign of congenital craniosynostosis even in the absence of obvious skull deformities. Given the relatively late presentation of the dysmorphisms diagnostic for craniosynostosis, the “brain shadowing sign” may improve the overall antenatal detection of isolated craniosynostosis as in most Countries low risk women are not submitted to screening ultrasound in the third trimester.

Craniosynostosis may interfere with the molding of the skull and preclude a normal birth [6]. Furthermore, infants affected by craniosynostosis are at increased risk of having concomitant complex abnormalities of the upper airway and elevated intracranial pressure [7] and may require
ventilatory support or neurosurgical intervention early after birth, thus justifying the need for prenatal diagnosis and counseling.

In conclusion, the “brain shadowing sign” may be the first sign of craniosynostosis and its identification should warrant US follow up. This sign, which can be noted also at screening US, has the potential to improve the antenatal detection of isolated craniosynostosis, thus allowing a multidisciplinary approach in the antenatal period and optimal care to the affected infants.
REFERENCES


Figures:

Figure 1 – Longitudinal two-dimensional (2D) ultrasound imaging of the presented case of isolated bilateral coronal craniosynostosis. At 20 weeks, normal appearance of the skull shape, of the cavum septum pellucidum (CSP), of the brain (a) and of the facial profile (b). At 24 weeks, suboptimal visualization of the CSP and the anterior portion of the brain (c), which was confirmed at 28 weeks (d). In e) confirmation of the abnormal intracranial findings and diagnosis of brachycephaly, which was associated with abnormal facial profile consistent with turricephaly (f).
Figure 2 – Three-dimensional (3D) ultrasound (US) imaging of the coronal (a,c) and the metopic (b,d) sutures in the presented case of isolated bilateral coronal craniosynostosis at 32 weeks (a,b) and in a normal case (c,d) with paired gestation. In a) 3D US allows to demonstrate the obliteration of the coronal suture and the fronto-parieto-temporal fissure (arrows), which is associated with the widening of the metopic suture (b, arrows). In the normal case the coronal suture and fronto-parieto-temporal fissure are not synostotic (c, arrows) and there is normally thin-appearing metopic suture (d, arrows).

3D imaging of normal and abnormal skull sutures was performed using Crystal Vue rendering technology.