



Fetal optic nerve sheath measurement as a non-invasive tool for assessment of increased intracranial pressure

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KEYWORDS: fetal brain; fetal neurosonography; intracranial pressure; optic nerve; prenatal diagnosis

ABSTRACT

Objectives To describe the sonographic technique for assessment of the fetal optic nerve sheath and to report on three fetuses with intracranial lesions and enlarged optic nerve sheath diameter (ONSD) compared with normal controls matched for gestational age (GA).

Methods In this cross-sectional study ONSD was measured sonographically in three fetuses (aged 23, 24 and 35 gestational weeks) with intracranial findings associated with increased intracranial pressure (ICP; dural thrombosis and intracranial tumors) as well as 42 healthy controls matched for GA ± 1 week (aged 22–25 and 34–36 weeks). For fetal eye assessment, transabdominal and transvaginal routes and high-resolution transducers were used for optimal visualization depending on fetal position. Measurements were made using an axial view at the level of the orbits, with the fetal face positioned towards the transducer. The ONSD was measured 1.5 or 2 mm behind the papilla (depending on GA) in all fetuses. Mean ± 2 SD ONSD of controls were calculated for each GA and compared with data from the three fetuses with intracranial pathology.

Results In the 42 normal fetuses, ONSD increased from 1.2 mm at 23 weeks to 2.6 mm at 36 weeks. The measurements at 36 weeks correlated well with those observed in newborns. ONSD measurements of the three cases were above mean $+ 2$ SD of values obtained from healthy controls at the same GA and also exceeded values of fetuses that were 1 week older.

Conclusions Fetal ONSD measurement is feasible using a technique similar to that used in adults and children. ONSD enlargement was observed in all three fetuses with intracranial lesions and may be an early tool with which to diagnose increased ICP. Copyright © 2011 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Intracranial pressure (ICP) is increased in children with hydrocephalus, intracranial tumors and pseudotumor cerebri, and may be associated with increased mortality and poor neurological outcome¹. Experimental and clinical studies in adults and children have found that increased ICP leads to enlargement of the optic nerve sheath diameter (ONSD), and that this finding precedes papilledema^{2–6}. Ultrasonographic measurement of ONSD^{7,8} has been used as a reliable method for detection of increased ICP, with results similar to those obtained using magnetic resonance imaging (MRI), both in experimental⁷ and in clinical^{9,10} settings. Abnormal ONSD is usually present when ICP rises above 20 mmHg^{7,8,10}. Yet, although ONSD measurement by ultrasound is easy, cheap and effective for detecting raised ICP in children and adults^{8,11}, it has never been used in evaluation of the fetus.

The aims of this study were to describe the sonographic technique for assessing the fetal optic nerve sheath in normal fetuses, to report on three fetuses with space-occupying intracranial lesions and enlarged ONSD, and to compare these with normal fetuses matched for gestational age.

METHODS

In this cross-sectional study, a single observer with expertise in fetal neurosonography measured once the ONSD in each of three fetuses with space-occupying intracranial lesions that may increase the intracranial pressure due to mass effect or impaired venous brain drainage and in 42 healthy fetuses in the second and third trimester (controls). The three fetuses, aged 23, 24 and 35 gestational weeks, were referred for suspected brain lesions and controls were all referred for routine scans. Inclusion criteria for controls were: (1) gestational age matched to one of

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Table 1 Numbers of fetuses enrolled according to gestational age (GA)

GA (weeks)	Controls (n)	Cases (n)
22	5	—
23	11	1 (Case 3)
24	9	1 (Case 1)
25	4	—
34	6	—
35	5	1 (Case 2)
36	2	—
Total	42	3

the affected fetuses ± 1 week, confirmed by date of last menstrual period and first-trimester sonography; (2) normal nuchal translucency thickness and second-trimester scan; (3) follow-up sonographic exams without growth or morphologic abnormalities. Gestational ages of fetuses included in the study are given in Table 1.

The technique for sonographic assessment of the optic nerve in its retrobulbar part (anterior visual tract) and for measurement of the ONSD has been described and incorporated into clinical practice for children and adults^{6,12,13}, using linear high-frequency probes. We used the same premise for the evaluation of the fetal eye, but using volumetric abdominal and transvaginal high-frequency probes (4–8 and 5–9 MHz, respectively; Voluson 730 and E8, GE Medical Systems, Zipf, Austria). The preferred means of visualizing the fetal eye is in an axial plane at the level of the lens, with the face positioned towards the transducer or at an angle of $< 45^\circ$ from the midline¹⁴. This plane provides a transverse view of the globe and the structures of the retrobulbar area in which the optic nerve sheath complex (the optic nerve sheath, subarachnoid space (SAS) and the optic nerve) can be visualized (Figure 1). The images obtained are very similar to those depicted in postnatal ophthalmic sonography, although with lower resolution, allowing only visualization of the whole complex and not of each structure separately. Since the optic nerve sheath moves with eye movements it may be visualized in any part of the retrobulbar space. Ideally, ONSD measurements should be performed when the lens is positioned centrally. A transabdominal or transvaginal route may be used, optimal visualization depending on fetal position.

Once the appropriate view was obtained, the ultrasound beam was focused on the retrobulbar area and the output intensity and ultrasound gain adjusted to attain the optimum level of contrast between the hypoechoic optic nerve complex and the retrobulbar fat. The optic nerve sheath appeared as a sharply defined homogeneous low-reflection band extending posterior from the base of the bulb¹³. For its measurement, maximum zoom was used and cursors were placed on the outer contours of the optic nerve complex, 1.5 mm posterior to the papilla before 28 weeks and 2.0 mm posterior to the papilla after 28 weeks (Figure 1). The measurement was performed perpendicularly to the optic nerve sheath borders.

Mean diameters ± 2 SD were calculated separately for each gestational week. Values found for normal fetuses



Figure 1 Optic nerve sheath diameter (ONSD) of 2.1 mm (Caliper 2), measured 2 mm posterior to the papilla (Caliper 1) in a 33-week fetus. L, lens; RBF, retrobulbar fat; V, vitreous.

were compared to the ONSD of the three affected fetuses, matched for the same gestational age ± 1 week.

RESULTS

In the 42 normal fetuses, the mean ONSD increased from 1.2 mm at 22 weeks to 2.6 mm at 36 weeks. The measurements at 36 weeks were comparable to those observed in newborns¹⁵. ONSD values at 22–25 weeks and 34–36 weeks are shown in Figure 2.

Among the fetuses with a space-occupying intracranial lesion, in Case 1 (Figure 3), the neurosonographic examination at 24 weeks of gestation revealed a rounded, echogenic supracerebellar mass mimicking an intracranial tumor that was surrounded by a hypoechogenic, triangular-shaped zone. Sagittal images showed that the lesion was located in the region of confluence of the dural sinuses (torcular Herophili), with enlargement of the interhemispheric space consistent with an extremely dilated superior sagittal sinus; the posterior part of the longitudinal sinus was also abnormal. The brain, cerebellum and posterior fossa appeared normal and there were no signs of cardiac failure. Color Doppler showed absence of signal inside the mass or along the venous sinuses, confirming the diagnosis of thrombosis of the torcular. The ONSD of the right fetal eye was 2.1 mm (Figure 3e). Follow-up examination 3 weeks later (at 27 weeks) showed an increase in the size of the clot but the longitudinal and superior sagittal sinuses were less dilated. The ONSD was smaller but still enlarged (1.8 mm). MRI at 30 weeks demonstrated continuous resorption of the clot at the torcular and the presence of hypointense foci in the right extra-axial opercular

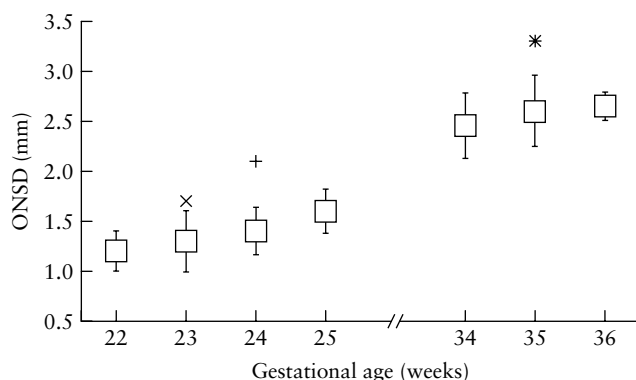


Figure 2 Normal mean $\pm$ 2 SD fetal values for optic nerve sheath diameter (ONSD) at 22–25 and 34–36 gestational weeks. Values of three fetuses with space-occupying intracranial lesions (Cases 1 (+), 2 (*) and 3 (x)) are shown, matched for gestational age; all three were above the normal mean + 2 SD.

region, along with cerebrospinal fluid (CSF) flow-void sign (area of decreased signal related to CSF flow in narrowed areas of the ventricular system). These findings were compatible with meningeal vein dilatation, but a vascular malformation (arteriovenous malformation or arteriovenous fistula) could not be ruled out.

Case 2 (Figure 4) was referred at 35 weeks of gestation for fetal hydrocephalus. The neurosonographic examination demonstrated a large tumor with solid and cystic components involving almost the whole right brain hemisphere. The right lateral ventricle was indistinguishable and the left lateral ventricle was severely dilated. Only a thin stripe of brain parenchyma could be seen. Color Doppler showed hypervascularity inside the solid portions of the tumor. Fetal MRI confirmed the diagnosis. The ONSD of the right eye was 3.3 mm (Figure 4e). The fetus was delivered 2 weeks later and postnatal evaluation confirmed the presence of a brain tumor and hydrocephalus requiring a ventriculoperitoneal shunt at the age of 5 days.

Case 3 (Figure 5) attended for a routine second-trimester ultrasound examination at 23 weeks, following a normal 15-week examination. The scan demonstrated a very large echogenic mass located in the midline, which was compressing, but had not invaded, the cerebral hemispheres. The 45 $\times$ 56-mm mass originated in the sellar region, passing through and enlarging the circle of Willis and reaching close to the cranial vault. A few small cysts and some calcifications could be seen within the mass, which was richly vascularized. The lateral ventricles were not dilated and the corpus callosum was visible, although deviated upwards by the tumor. The tumor occupied more than 50% of the cranial volume, resulting in an enlarged head circumference. No other malformations were seen in the other fetal systems and fetal growth was normal at this stage. The differential diagnosis was between craniopharyngioma (due to its location and sonographic characteristics) and fetal teratoma or glioma (more common). Ocular sonography showed fetal nystagmus (Videoclip S1) and the ONSD measured 1.7 mm (Figure 5e). After multidisciplinary counseling, the family opted for termination of the pregnancy but declined autopsy.

When comparing the ONSD measurements of these three fetuses with those of normal fetuses matched for gestational age $\pm$ 1 week, we found that all measurements were above 2 SD of the normal range (Figure 2).

DISCUSSION

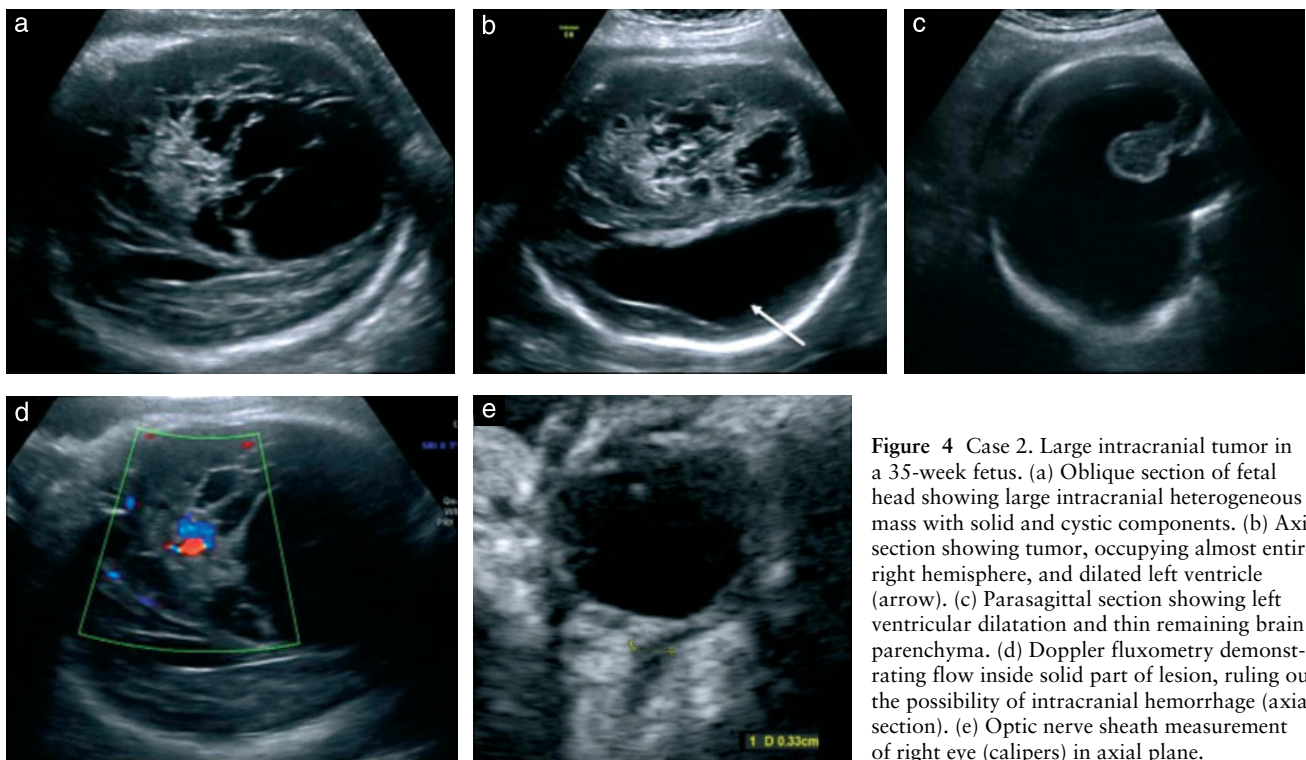
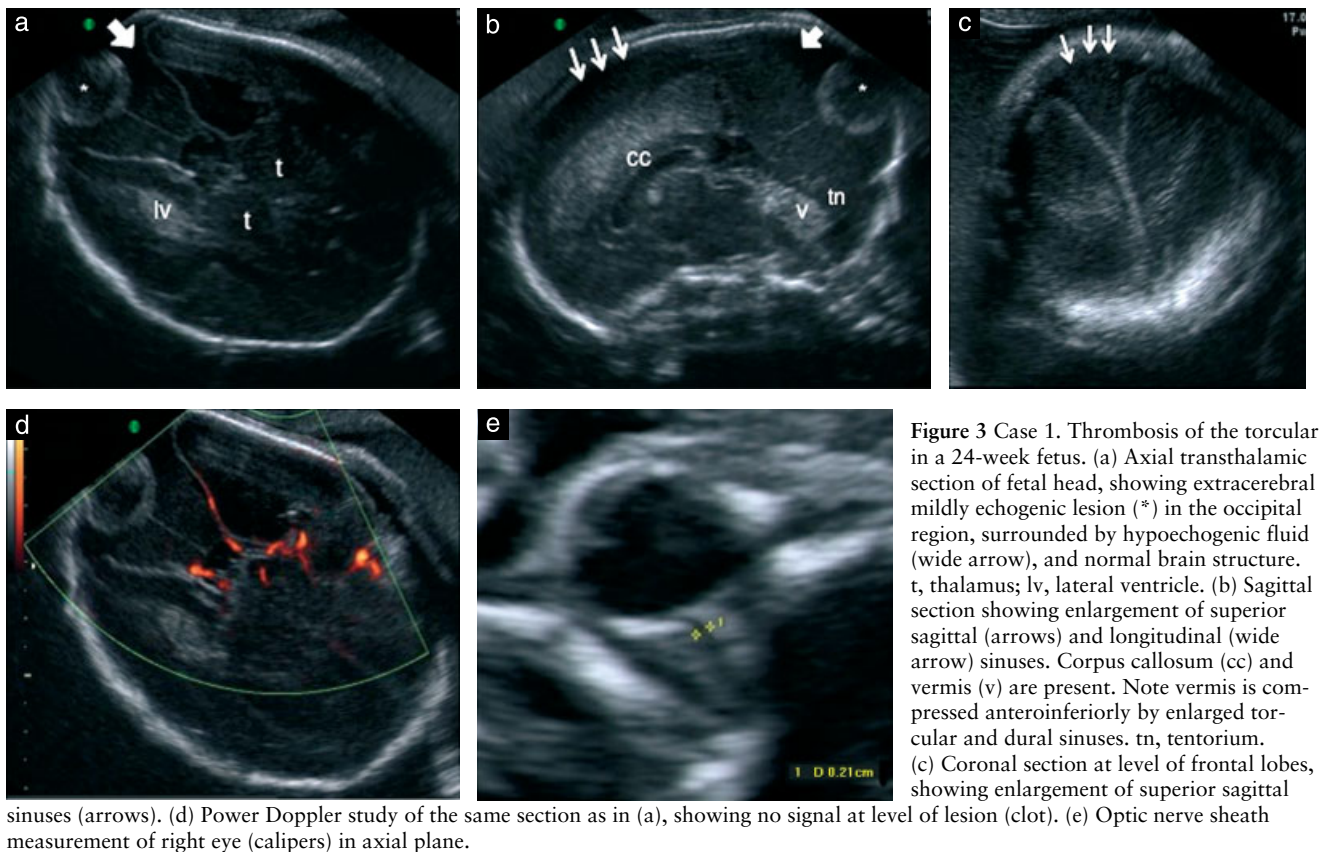
Ontogenetically, the optic nerve is a part of the central nervous system, surrounded by a meningeal sheath and a trabeculated SAS, with slow flow of CSF within it⁴. The optic nerve sheath is distensible in its retrobulbar segment and anatomically continuous with the meninges, surrounded by perioptic fat². The perioptic SAS communicates with the intracranial cavity and intracranial CSF pressure changes can be transmitted along the optic nerve sheath, modifying its diameter^{4,5,7}. Increased ICP forces the inflow of CSF into the perineural space, increasing the ONSD, whereas in cases of CSF hypotension ONSD is reduced^{3,16}.

Liu and Kahn⁵ studied in cadavers the pressure gradient within the optic nerve sheath related to its anatomy. The SAS trabeculations were sparser proximal to the orbit, the sheath being most distensible at that level. The authors noted that the bulbous part of the optic nerve bulged and inflated along with the ICP increase, but there was no obvious change in appearance along the remaining nerve. These findings were confirmed by an *in-vivo* study conducted on subjects undergoing intrathecal infusion tests¹⁷. Based on these observations, a position of 3 mm behind the globe was chosen for the sonographic ONSD measurement in children and adults. Insonation through the anechoic vitreous allows good depiction of the retrobulbar structures with highly reproducible ONSD values⁹.

Experimental studies in sheep confirmed that CSF transport is similar in the fetus and the adult¹⁸, and that significant cerebral vascular flow changes occur only after a four-fold increase in fetal ICP¹⁹; this means that Doppler studies can diagnose only extreme cases of increased ICP. Results of Doppler fluxometry studies in fetuses with ventriculomegaly have been controversial and provide no additional information, findings varying from a pathological flow profile in all fetuses to the absence of a uniform pattern^{20–24}.

It is known that papilledema is not usually found in neonates and young children with acute or moderate increased ICP due to open fontanels and the potential for head expansion. On the other hand, we see that acute ventriculomegaly does not cause enlargement of the head circumference in these patients and even in fetuses until it becomes severe with very high ICP levels. Increased fetal ONSD seems to be an early and sensitive marker for increased ICP long before any increment in head size or the development of papilledema^{2,6}.

To the best of our knowledge this is the first study to measure the ONSD in fetuses. Since the length of the retrobulbar portion of the optic nerve increases with gestational age, we decided arbitrarily to perform the measurement at a distance of 1.5 mm from the papilla in fetuses before 28 weeks and at 2.0 mm after 28 weeks.



Nomograms for ONSD in fetuses throughout gestation are currently being constructed by our group, to be published in the near future.

The ophthalmologic and radiologic literature has published data and established norms for ONSD as

measured by ultrasound in children^{6,25}, and means and SD matched closely with results derived from MRI studies^{10,26}. There is a positive correlation between age and ONSD, the greatest increase occurring during the first year of life. In children under 1 year, the mean ONSD is

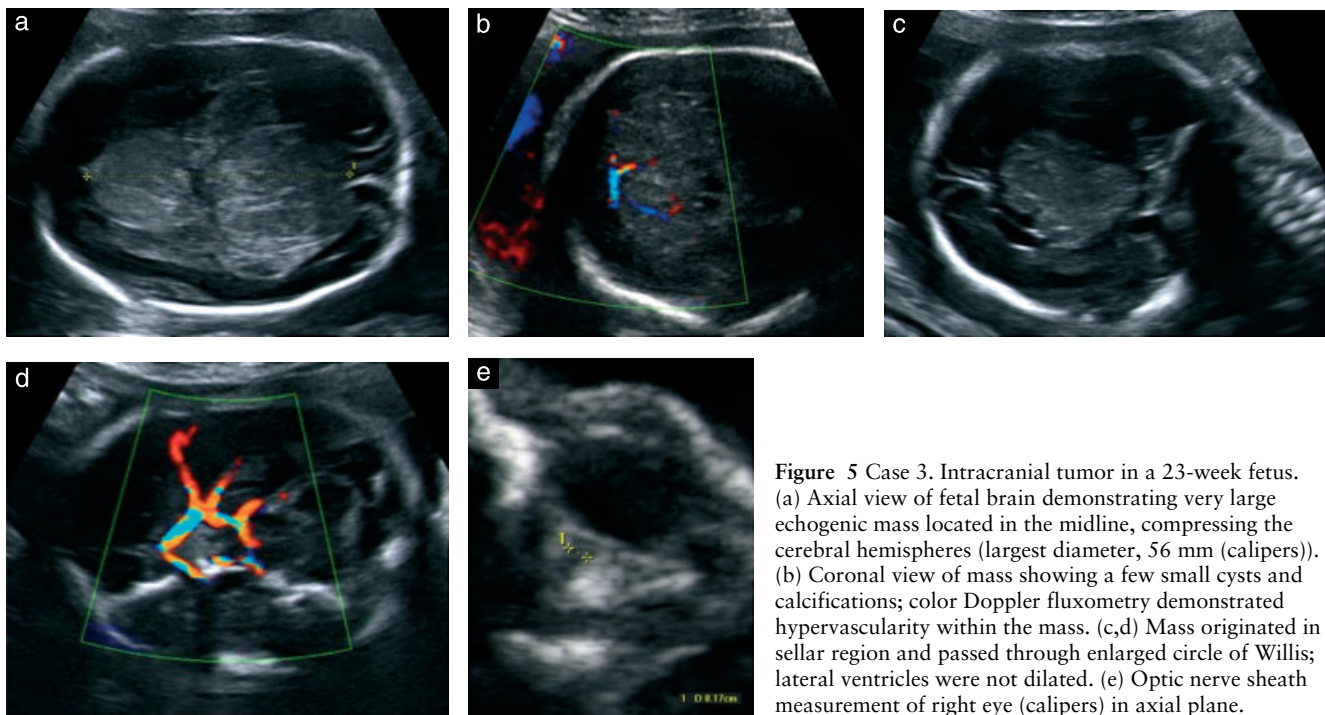


Figure 5 Case 3. Intracranial tumor in a 23-week fetus. (a) Axial view of fetal brain demonstrating very large echogenic mass located in the midline, compressing the cerebral hemispheres (largest diameter, 56 mm (calipers)). (b) Coronal view of mass showing a few small cysts and calcifications; color Doppler fluxometry demonstrated hypervascularity within the mass. (c,d) Mass originated in sellar region and passed through enlarged circle of Willis; lateral ventricles were not dilated. (e) Optic nerve sheath measurement of right eye (calipers) in axial plane.

2.9 (range, 2.2–3.4) mm and an ONSD > 4.0 mm is considered abnormal^{6,27}. Defining values higher than the mean $+ 2$ SD to be beyond the normal limits would result in a 5% false-positive rate⁸.

ONSD measurement showed a sensitivity of 83% and a specificity of 38% for increased ICP in children with hydrocephalus³, indicating that one should be cautious in interpreting negative findings. By virtue of the biologic characteristics of the optic nerve sheath, a purely linear correlation between ONSD and ICP measurements cannot be achieved for extreme ICP values, as in these cases the optic nerve sheath either reaches its maximum distensibility (elevated ICP) or adheres to the optic nerve (ICP < 10 mmHg)²⁸.

Our three affected cases had an ONSD above 2 SD of the normal measurements of fetuses matched for gestational age ± 1 week, and the ONSD decreased during the process of resolution in one of our patients, suggesting that this may be an important tool in the evaluation of cases of fetal intracranial lesions potentially leading to increased ICP.

The prognosis of fetal dural sinus thrombosis is considered good, with normal neurodevelopment in 50% of reported cases. The size of the clot, the surrounding dilatation or the number of thrombi do not seem to be predictive of poor outcome, whereas regression, isolated abnormality and absence of signs of cardiac failure are good prognostic factors²⁹. The main mechanism behind the increase in ICP is the decreased resorption of CSF and, therefore, it is possible that ONSD measurement may be useful in monitoring the reestablishment of normal CSF flow.

Although the sonographic measurement of fetal ONSD seems to be an important tool for indirect assessment of increased ICP, additional factors should be taken into account. Recent observations in optic nerve

sheath sonography³⁰ emphasize the incidence of artifacts resulting in false ONSD measurements; these should be observed and avoided. The transbulbar sound direction and the incidence of the ultrasound beam on the lamina cribrosa or the dura mater may produce acoustic shadows, giving the impression of a wider optic nerve sheath. The use of color Doppler for identification of the central retinal artery may aid in preventing over-measurement of the shadow, decreasing the false-positive rates. This observation may be especially relevant in fetal optic sonographic assessment using probes with a frequency lower than 7.5 MHz^{31,32}.

It should also be remembered that the optic nerve and the retrobulbar fat have some mobility and are related to ocular globe motion. Furthermore, the nerve transverse section is not spherical and its course may not run strictly straight, which may create meningeal sonographic shadows³³. Another important aspect, regarding brain injury, is that ONSD measurement may not be reliable enough to diagnose increased ICP in cases of optic nerve hemorrhage. There may be significant differences between left and right ONSD measurements in such cases³⁴.

In conclusion, fetal optic nerve sheath sonographic measurement is feasible using an assessment technique similar to the one performed in adults and children. We were able to demonstrate ONSD enlargement in three fetuses with intracranial lesions that could lead to increased ICP.

Our follow-up observations suggest that ONSD measurement may be useful in the decision-making process when dealing with fetal space-occupying lesions. Normal ONSD values for fetuses are yet to be published and prospective studies are needed to assess the usefulness of the ONSD compared with other currently available diagnostic tools.

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SUPPORTING INFORMATION ON THE INTERNET



Videoclip S1 (nystagmus in Case 3) may be found in the online version of this article.