Intracranial ultrasonographic findings in open *spina bifida*

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Abstract

Spina bifida aperta is one of the most frequent open neural tube defects and consists in a closure defect in the fetal spine and the subsequent skin, leaving the spinal cord vulnerable. Since folic acid supplementation has been recommended periconceptionally, the incidence of neural tube defects, including spina bifida, has been reduced dramatically. Unfortunately, spina bifida is usually diagnosed in the second trimester, more frequently between 18 and 20 weeks of gestation, according to the American College of Obstetricians and Gynecologists (ACOG), by visualizing the spinal defect, as well as well-known intracranial signs. There have been attempts in finding the right intracranial sign or measurement that can predict a future positive diagnosis of spina bifida or at least alert the sonographer to further investigate. The early diagnosis of spina bifida represents the subject of interest of this paper, as this congenital neural tube defect carries the burden of a significant morbidity. The mothers should be counseled, informed about the fetal complications of this pathology and about the therapeutic possibilities, including intrauterine fetal surgery, and they should also be given the possibility of pregnancy termination, if the patient decides in this direction.

Keywords: *spina bifida, early signs, intracranial translucency, brain stem, mesencephalon to occiput diameter*

Rezumat

Spina bifida aperta este una dintre cele mai frecvente defecte de tub neural și constă într-un defect de închidere la nivelul coloanei vertebrale fetale și, respectiv, a pielii, lăsând măduva spinării vulnerabilă. Datorită faptului că suplimentarea cu acid folic a fost recomandată periconcepțional, incidența defectelor de tub neural (inclusiv spina bifida) a fost redusă dramatic. Din păcate, spina bifida este adesea diagnosticată doar în al doilea trimestru, mai frecvent între 18 și 20 de săptămâni de gestație, conform Colegiului American al Obstetricienilor și Ginecologilor (ACOG), prin vizualizarea defectului coloanei vertebrale, precum și a semnelor intracraniene bine cunoscute. Numeroase eforturi au fost îndreptate spre a găsi markerul intracranian corect și predictiv pentru spina bifida, capabil de a avertiza ecografistul asupra existenței, vizibile sau nu la momentul scanării, a unui defect de tub neural. Diagnosticul precoce al spina bifida reprezintă subiectul de interes al articolului, deoarece acest defect congenital poartă povara unei morbidități semnificative. Gravida trebuie consiliată cu privire la complicațiile fetale ale acestei patologii și în privința posibilităților terapeutice, incluzând indicațiile și disponibilitatea intervenției chirurgicale intrauterine fetale. De asemenea, diagnosticul în trimestrul întâi de sarcină permite luarea în considerare a întreruperii sarcinii, la cererea pacientei, în condiții legale.

Cuvinte-cheie: *spina bifida, semne precoce, translucență intracraniană, trunchi cerebral, diametrul mezencefal-occiput*

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Markeri ultrasonografici intracranieni în spina bifida aperta

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Introduction

Open *spina bifida* – known as *spina bifida aperta* or myelomeningocele – represents the most common open neural tube defect, characterized by a breach in the vertebral column with a subsequent defect in the skin through which the spinal cord is exposed[1]. This neural tube defect appears as a result of the closing failure of the embryonic neural tube by the 28th day after conception[2]. The incidence of neural tube defects – with *spina bifida aperta* being the most frequent in this category – has a variability between <1 to 7 per 1000 live births, and is dependent on geographic, ethnic and nutritional factors[3-5].

The main risk factors for the majority of neural tube defects are represented by folate deficiency[7], genetic factors[8], syndromes that can be associated with neural tube defects, fever or even hyperthermia, obesity[9], and pregestational diabetes[10]. Folate deficiency can be either due to insufficient oral intake[7], defective intestinal absorption, genetic factors interfering with the normal folate metabolism or to the administration of folic acid antagonists (carbamazepine, valproic acid or methotrexate)[7,11]. Since folic acid supplementation has been introduced periconceptionally, the incidence of neural tube diseases has decreased significantly[12].

The most common screening test for myelomeningocele is represented by ultrasound examination (Figures 1 and 2). The American College of Obstetricians and Gynecologists (ACOG) recommends that a high-quality second trimester structural fetal screening test at 18 to 20 weeks of gestation should include screening for neural tube defects, including *spina bifida*[13], as this congenital anomaly is associated with certain degrees of neurological impairment and with a possible cognitive function impairment if ventriculomegaly or a genetic syndrome is involved. Besides the spinal lesion, the brain suffers certain changes, establishing the Chiari II malformation: a small posterior fossa with a

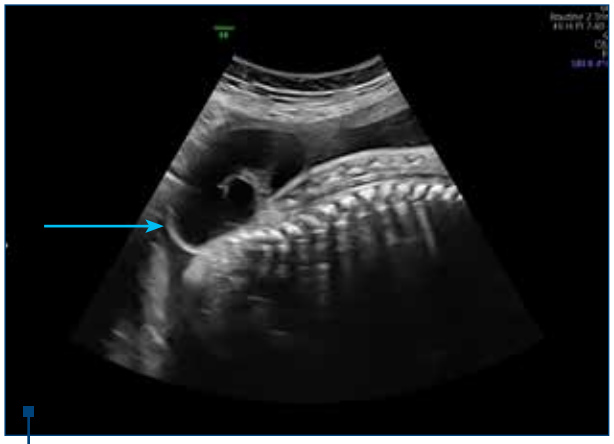

Figure 1. *Two-dimensional ultrasound image of terminal spine disruption of the continuity of the skin and vertebrae plane (arrow) in the longitudinal view of the fetal spine as positive diagnosis of spina bifida at 28 weeks + 6 days of pregnancy*

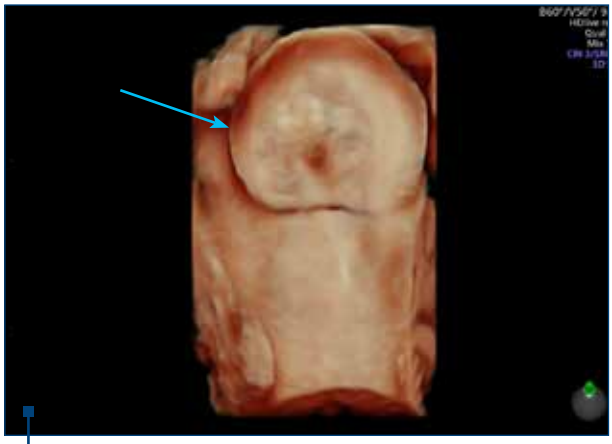

Figure 2. *Three-dimensional reconstruction image of a large spina bifida (arrow) at 28 weeks + 6 days of pregnancy*

herniation of the cerebellum and the vermian structures through the tentorial incisura and the foramen magna, resulting in an abnormal cerebellar morphology and a deformation of the brainstem structures, pons, medulla and fourth ventricle[14,15]. Although second-trimester ultrasonographic screening allows a good fetal anatomy examination and *spina bifida* diagnosis, there have been studies trying to evaluate fetuses within the first-trimester anatomy scan, but the detection rates remain lower (44%) than those in the second trimester (92% to 95%)[16].

The early diagnosis should be considered, as mothers must be informed, counseled about further investigations such as chromosomal microarray or gene sequencing, as well as fetal magnetic resonance imagining, prepared to give birth to an infant with multiple complications, probably necessitating surgery, or be given the possibility of pregnancy termination if desired.

Second-trimester ultrasonographic intracranial signs in *spina bifida*

A systematic review published in 2021 by Kunpalin et al.[15], including 15 studies, summarized the intracranial sonographic findings present in myelomeningocele: funneling of the posterior fossa, banana sign (abnormal shape and anteriorly effacing cerebellum) – Figure 3, lemon sign (inward concavity interesting the frontal bones), small transcerebellar diameter, abnormal shape of the midbrain, small biparietal diameter, perinodular heterotopia, small head circumference, gyration disorders, abnormal *corpus callosum*, ventriculomegaly, abnormal position or shape of the lateral ventricle and

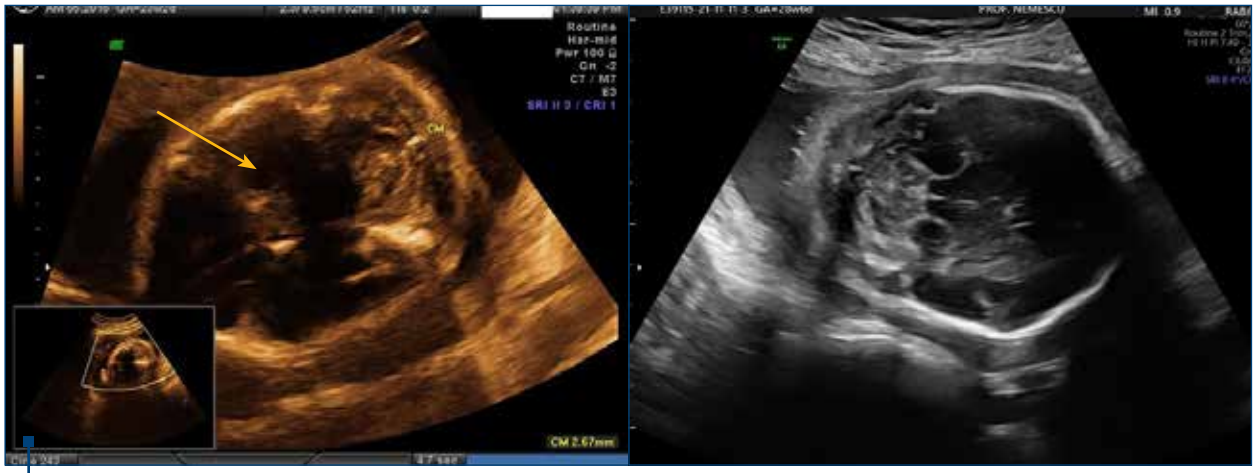

Figure 3. *Two-dimensional ultrasound images of posterior fossa plane presenting evident abnormal cerebellar morphology known as "banana sign" (yelow arrows) in a 23 weeks and 2 days (a) and 26 weeks and 6 days (b) fetuses with spina bifida aperta*

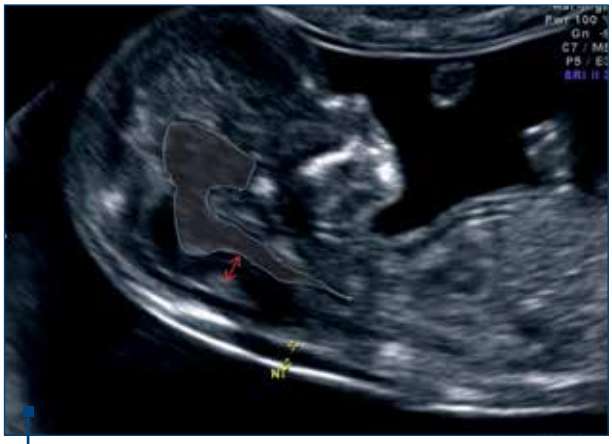

Figure 4. *Brain stem (blue area) and IT (red arrow) measurements during the first-trimester anatomical screening in a normal fetus; the section plane is the standard one used for NT measurement*

interhemispheric arachnoid cyst. In addition, there were nine studies relating modifications belonging to Chiari II malformation: scalloping of the frontal bones of the fetal head, abnormalities of the cerebellum, abnormal shape of the posterior fossa and elongated quadrigeminal plate of the midbrain, that may cause cognitive and attention deficits, stridor, poor executive skills and apnea[17].

First-trimester ultrasonographic intracranial signs in *spina bifida*

As a need to diagnose this neural tube defect with significant morbidity, certain first-trimester ultrasonographic signs that might help in the early diagnosis of *spina bifida* have been described during the first-trimester fetal anatomy screening. The pioneers in this direction were Chaoui and Nicolaides[18] in 2009, suggesting the use of a intracranial measurement called intracranial translucency (IT) – Figure 4, which is actually the fourth ventricle in the mid sagittal view, used for detecting nuchal translucency (NT). Due to caudal displacement of the brain, the fourth ventricle is compressed and no longer visible in the cases that were subsequently diagnosed during the second trimester presenting the "banana" and "lemon" signs.

A year later, a study[19] regarding the first-trimester fetal anatomy ultrasonographic examination, which compared measurements of brain stem (BS) diameter, brain stem to occipital bone (BSOB) diameter and brain stem to BSOB ratio from images of 30 cases of open *spina bifida* with a control group involving images from 1000 cases of normal fetuses, has sustained that in cases of *spina bifida aperta*, BS and the BS to BSOB ratio are high and the BSOB diameter is lower compared to normal fetuses (Figure 5). Such intracranial findings should warn the sonographer to examine more carefully the spine, and in cases of imperfect images, the examination should be delayed for two or three weeks.

In 2011, a study by Finn et al.[20] revealed that the included cases of neural tube defects presented a diameter between the aqueduct of Sylvius and the occiput below the normal range in accordance to the crown-rump length and gestational age, which, although not considered a diagnostic ultrasonographic marker, it helps the sonographer and afterwards lead to a positive diagnosis of *spina bifida* (Figure 6).

Another interesting intracranial measurement described by Nemescu et al.[21] in an article published in 2020 alerts sonographers about the possibility of early diagnosing *spina bifida*. The authors reveal the results of measurement between the mesencephalon and occiput in the axial view of the head (Figure 6), which is increased in women who have not received folic acid supplementation and could – in association with the "crash sign" (the deformed and posteriorly displaced

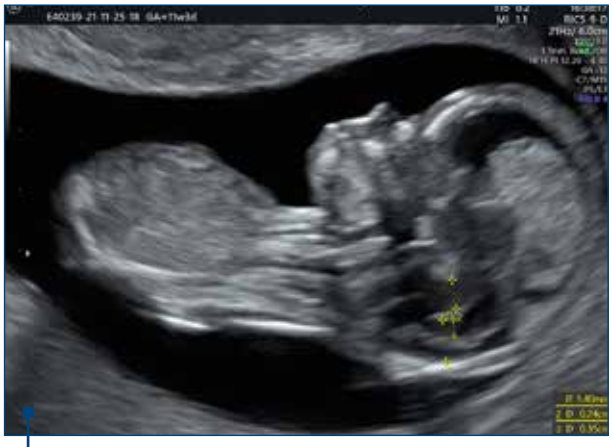

Figure 5. *The brain stem (BS) diameter (2D measurement), brain stem to occipital bone (BSOB) diameter (3D measurement), and intracranial translucency (IT) diameter in a normal fetus, on mid-sagittal fetal section during the first-trimester screening for fetal anomalies*

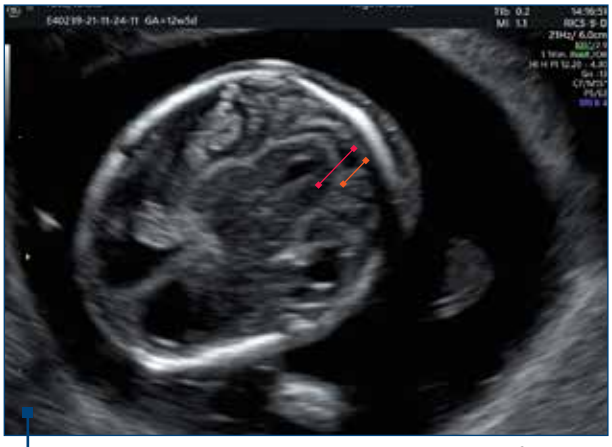

Figure 6. *The diameter between the aqueduct of Sylvius and the occiput (red line) and the measurement between the mesencephalon and occiput (orange line) in the axial view of the head*

mesencephalon against the occipital bone)[22] – aid in selecting the cases that require detailed neural tube defects examination and improve prompt diagnosis of *spina bifida*.

Discussion

Positive diagnosis of *spina bifida* is currently being made during the second-trimester anatomical ultrasound when a bulging defect that contains elevated neural plate and meninges juxtaposed laterally with the subcutaneous tissue. The normal vertebral column has three ossification centers within the vertebrae. Myelomeningocele presents as a widening of the ossification centers in the coronal plane and as a separation of the ossification centers in the transverse plane, resulting a U-shaped vertebra[23]. The sensibility and specificity in prenatal ultrasonographic diagnosis of *spina bifida* are 97-98% and 100%, respectively[24]. The diagnosis is sustained by the intracranial signs. The recent ultrasonographic measurements – intracranial translucency, brain stem, brain stem to occipital bone diameter, brain stem to BSOB ratio, aqueduct of Sylvius to the occiput diameter and mesencephalon to occiput diameter – in association with the "crash sing" have the potential of selecting the cases that require a detailed examination of the spine during the first-trimester ultrasonographic screening or in the next period, in order to refer pregnant patients with a high suspicion of *spina bifida* to supplementary investigations.

Conclusions

In conclusion, further studies are required to demonstrate the effectiveness of the highly promising first-trimester ultrasound measurements, either separate or combined, in order to select the high-risk cases of *spina bifida*. If the results validate the high sensibility and specificity, these measurements could be easily introduced in the first-trimester anatomical screening, as the ultrasound sections used for the measurements are the standard ones for determining the biparietal diameter or the nuchal translucency. Therefore, patients will be informed and counseled about the implications of this pathology with important morbidity and decide whether they will terminate the pregnancy or assume the surgical correction procedures that have to be done postnatal or even from intrauterine life in order to decrease the neurological damage due to the herniation of the cerebellum and the vermian structures through the tentorial incisura and the foramen magna. ■

Conflicts of interests: The authors declare no conflict of interests.

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