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Sonographic spectrum of first-trimester fetal cephalocele: review of 35 cases

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KEYWORDS: cephalocele; fetal ultrasound; first-trimester screening; Meckel–Gruber syndrome; open neural tube defects; prenatal diagnosis

ABSTRACT

Objective *To describe the sonographic features of fetal cephalocele diagnosed at the time of first-trimester ultrasound screening for aneuploidy.*

Methods *This was a retrospective review of cases of cephalocele diagnosed in the first trimester at four fetal medicine referral centers. Once diagnosis was suspected, a transvaginal ultrasound examination was offered to improve depiction of the cranial defect and enhance examination of fetal anatomy, with special attention given to the location, size and content of defects. To assure consistency in diagnosis, representative pictures and videoclip sequences of the cranial defect were obtained and reviewed by at least two authors. Cases were classified and compared with the assessment made at diagnosis.*

Results *Of the 35 affected fetuses identified, 33 were of a singleton pregnancy and two were of twin pregnancies in which the other fetus was unaffected. The lesion was classified as a cranial meningocele in 13 (37%) cases and as an encephalocele in 22 (63%). The bone defect was occipital in 27 (77%), frontal in three (9%), parietal in three (9%) and non-classifiable in two (6%). Twelve (34%) were considered as small in size, 11 (31%) as medium and 12 (34%) as large. There were no reported cases of aneuploidy; however, four (11%) cases were associated with Meckel–Gruber syndrome, two (6%) with a disruptive syndrome and one (3%) with skeletal dysplasia. Eight (23%) pregnancies were lost to follow-up. Parents opted for termination of pregnancy in 21 of the 27 remaining cases and, of the six ongoing pregnancies, four patients miscarried or the fetus died* in utero *during the second trimester, one liveborn infant died shortly after delivery and one underwent neonatal surgery for an isolated cranial meningocele and is currently doing well.*

Conclusions *First-trimester sonographic diagnosis of cephalocele is accomplished easily with a detailed examination of the skull contour at the time of routine assessment of the axial and sagittal views of the head for measurement of the biparietal diameter and nuchal translucency, respectively. However, the sonographic features are highly variable. A significant proportion of cases are associated with genetic or disruptive syndromes. Prenatal diagnosis of cephalocele in the first trimester was associated with a high rate of termination of pregnancy and early intrauterine fetal demise. Only one fetus in this series survived and is neurologically intact; therefore, the prognosis of this condition remains poor.* Copyright © *2014 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Cephaloceles are relatively rare open neural tube defects characterized by protrusion of brain tissue or meninges through a congenital cranial defect. These defects are classified, according to their content, into those containing only meninges (cranial meningocele), brain tissue (encephalocele) or brain and part of the lateral ventricles (encephalocystocele)[1,2]. The prenatal sonographic diagnosis of this condition is, in most cases, straightforward, particularly if the defect is medium or large in size[2,3]. Indeed, there is a plethora of reports in the ultrasound literature describing the sonographic findings, antenatal course and pregnancy outcome in pregnancies complicated by a cephalocele diagnosed in the second and third trimesters[2–8]. In contrast, reports of cases diagnosed in the first trimester are scarce and are usually single case reports or small case series[9–12].

With the widespread incorporation of sonographic screening for aneuploidy at 11 – 13 weeks of gestation into clinical practice[13,14], an increasing number of

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cases of cephalocele are expected to be diagnosed at this early gestational age. Nevertheless, there is still limited information regarding the sonographic features, associated findings and clinical implications in fetuses diagnosed as having cephalocele in the first trimester. The aim of this report was to describe these characteristics based on a large number of fetuses with cephalocele diagnosed in the first trimester.

METHODS

This was a retrospective review of fetuses with cephalocele diagnosed in the first trimester of pregnancy at four fetal medicine referral centers. In all cases, sonographic examinations were performed for clinical reasons following the recommendations of the UK Fetal Medicine Foundation[13,14], by operators with extensive experience in first-trimester sonographic screening and under protocols approved by the corresponding local institutional review boards.

The diagnosis of cephalocele was considered when a defect in the skull associated with protrusion of meninges or brain tissue was identified in both the axial and sagittal sections of the fetal head on routine ultrasound examination for aneuploidy screening. At our institutions, the axial view is obtained routinely at the first-trimester scan in order to measure the biparietal diameter and visualize the choroid plexuses[15], and the sagittal view is obtained for nuchal translucency (NT) measurement and nasal bone assessment[16]. Once the diagnosis of cephalocele was considered, the parents were offered transvaginal ultrasound for improved depiction of the cranial defect and to enhance examination of the fetal anatomy. Special attention was given to the location, size and content of the defect, and to differentiate large encephaloceles from acrania and cranial meningoceles from cystic hygroma colli by demonstration of the fetal skull and the bony defect, respectively[2]. Cephaloceles diagnosed in association with disruptive syndromes, such as body stalk anomaly or amniotic band syndrome, were also included in the analysis. Once the diagnosis was confirmed, available pregnancy management options were discussed extensively with the parents. If the parent decided to continue the pregnancy, serial ultrasound scans were offered. In addition, fetal karyotyping was offered and performed prenatally or postnatally according to the parental wishes.

To assure consistency in the diagnosis, representative pictures and videoclip sequences, if available, of the cranial defect were reviewed by at least two of the authors (W.S. and S.M.). The cases were classified independently according to the location (occipital, parietal or frontal), content (cranial meningocele or encephalocele) and size (large if $> 30\%$, medium if $10–30\%$ and small if $< 10\%$ of the cranial content), and compared with the assessment made at the time of diagnosis. If different opinions were given among reviewers or operators, the final assessment was established by consensus.

Information regarding maternal demographics, first-trimester sonographic findings, subsequent antenatal course and pregnancy outcome was obtained from the ultrasound reports and medical records, from the referring obstetricians or from the patients themselves. Owing to the retrospective nature of this review, ethical permission for this study was waived by the corresponding institutional review boards.

RESULTS

A total of 35 cases from 34 patients diagnosed between 2002 and 2014 were analyzed; one patient had two consecutive affected fetuses within the study period. Two (6%) cases occurred in a twin pregnancy (one monochorionic–monoamniotic[17] and one dichorionic)

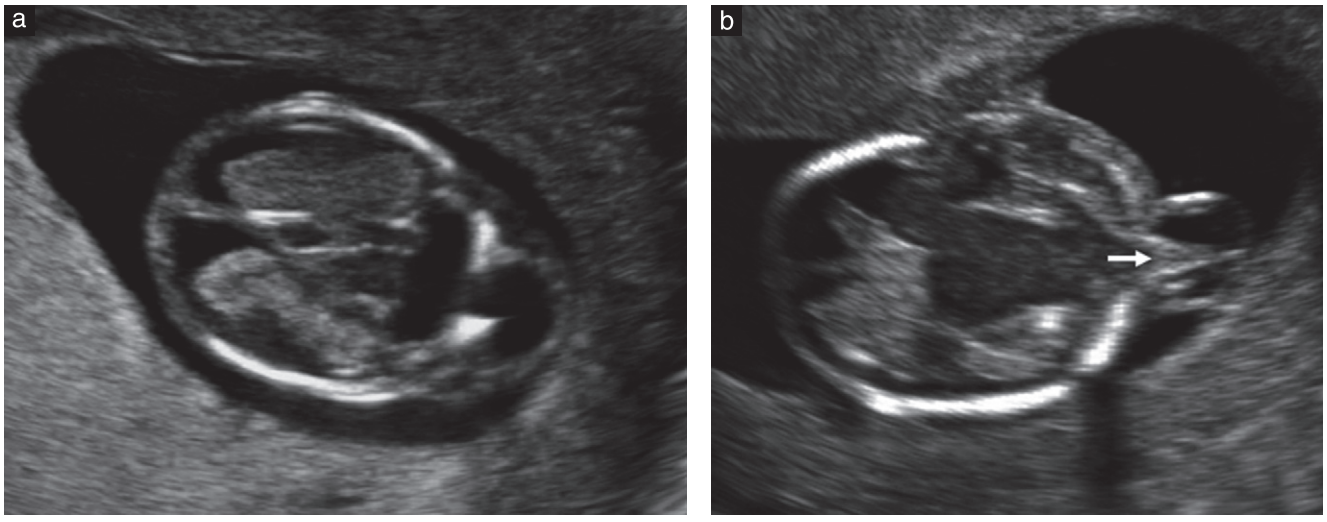

Figure 1 Axial transvaginal ultrasound images of fetal head showing a cranial cephalocele at 13 + 4 weeks (a) and an encephalocele at 12 + 6 weeks (b). Note enlarged cisterna magna, enlarged third ventricle and absent brain tissue within the defect in (a). Arrow depicts brain tissue within the defect in (b).

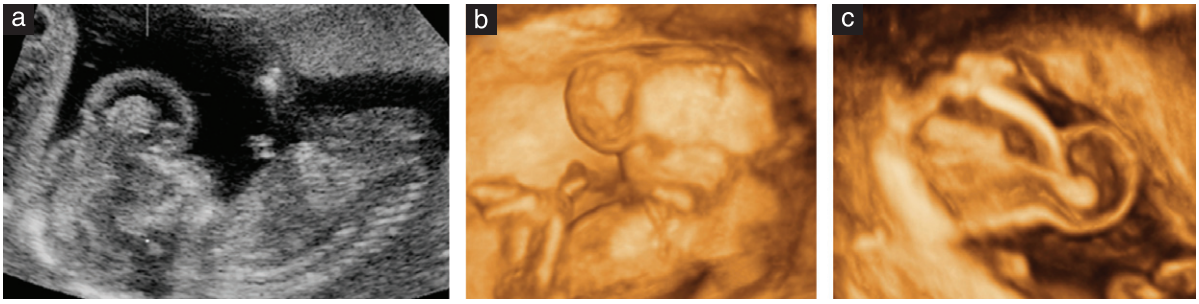

Figure 2 Frontal encephalocele in a fetus at 11 + 2 weeks: two-dimensional ultrasound showing a large cranial defect with protrusion of brain tissue (a); sagittal (b) and axial (c) three-dimensional sonographic views of the fetal head showing a cranial defect containing brain tissue.

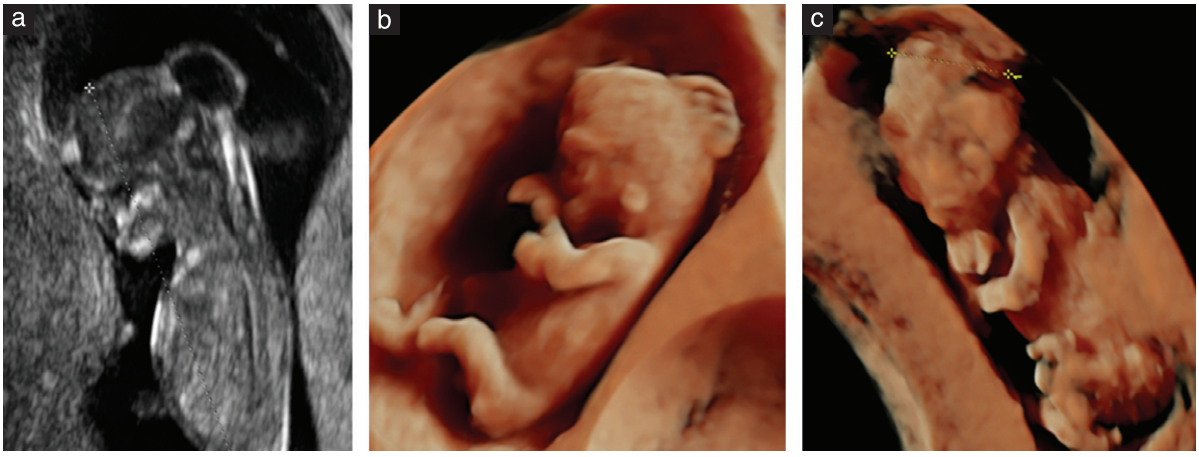

Figure 3 Fetal two-dimensional ultrasound (a) and three-dimensional ultrasound using the HDlive technique (b) showing a medium-sized occipital cranial cephalocele at the time of first-trimester referral. (c) The defect was larger and contained brain tissue at ultrasound examination 2 weeks later.

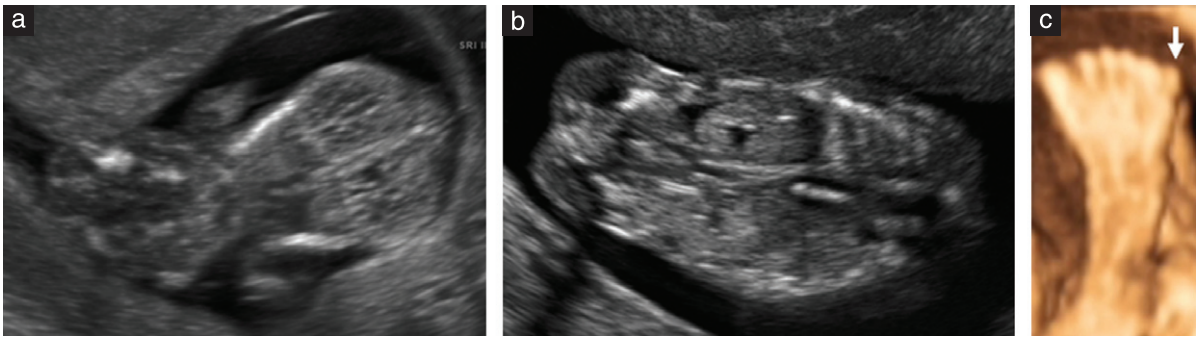

Figure 4 First-trimester ultrasound images of a fetus with: cephalocele associated with Meckel–Gruber syndrome (note bilateral polycystic kidneys) (a); isolated cephalocele showing normal kidneys (b); and postaxial polydactyly, with the arrow depicting an extra toe (c).

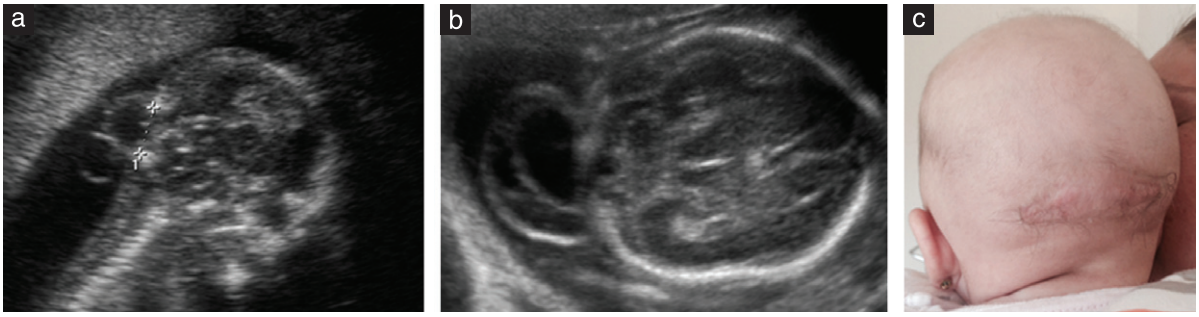

Figure 5 (a) Ultrasound image of cranial cephalocele, diagnosed at 13 + 2 weeks, with calipers depicting a cranial defect (courtesy of Dr Paula Vargas). (b) Axial view of fetal head showing the defect at 16 weeks. (c) Posterior aspect of the head after surgical repair in the only survivor in this series.

in which only one of the fetuses was affected and the other was normal anatomically. Information on the first-trimester sonographic findings was available for all 35 cases, but eight (23%) pregnancies were lost to follow-up or the records were missing. Demographic data were not obtained in six (17%) cases because of missing medical records. Of the remaining 29 cases, the median maternal age was 29 (range, 21–40) years, the median gestational age at evaluation in our centers was 12 (range, 11–14) weeks, and the median crown–rump length was 63 (range, 45–80) mm. All patients had an otherwise uncomplicated antenatal course. However, one patient was receiving antidepressive medication at the time of the scan and two had an obstetric history of fetuses with Meckel–Gruber syndrome.

Thirteen (37%) cases of cephalocele were classified as cranial meningocele and 22 (63%) as encephalocele (Figure 1). The defect was located in the occipital area in 27 (77%) cases, in the parietal area in three (9%), in the frontal area in three (9%) (Figure 2) and was part of a disruptive lesion and involved several areas of the skull in two (6%) cases, and was therefore assessed as non-classifiable. The defect was classified as large in 12 (34%) cases, medium in 11 (31%) and small in 12 (34%). There was good agreement ($n = 33$; 94%) between the operator and the reviewers regarding the location, size and content of the cephalocele. In three cases, a follow-up scan was performed in the first trimester; changes in defect appearance, both in content and size, were documented in all three cases, despite the short period of time between examinations (Figure 3). All three of these pregnancies were terminated.

Five (14%) cases were associated with NT thicknesses $> 95^{th}$ percentile for gestational age. Of note, in some cases of occipital cephalocele, NT thickness was difficult to measure because of the defect extending significantly into the cranial aspect of the neck, hampering accurate measurement. Nevertheless, chromosomal analysis was performed in 17 of the 27 cases with complete information, and no cases of aneuploidy were reported. There were four (11%) cases associated with Meckel–Gruber syndrome (Figure 4), two (6%) with a disruptive syndrome and one (3%) with a skeletal dysplasia. Of the remaining 28 cases with non-recognizable syndromes, five had additional malformations, including congenital heart defects in two and one each of congenital diaphragmatic hernia, enlarged posterior fossa and omphalocele. All cases of large encephalocele were associated with microcephaly.

Among the 27 cases for which follow-up was available, 21 were terminated after counseling of the parents. Of the six ongoing pregnancies, four resulted in miscarriage or fetal demise during the second trimester, one liveborn infant died shortly after delivery and one underwent neonatal surgery for an isolated cranial meningocele and is currently doing well at 8 months of age (Figure 5). In four of the six ongoing pregnancies, the sonographic follow-up showed an increase in the size and an alteration in the content of the cephalocele as pregnancy advanced. Finally, there was no recollection of false-negative cases, as determined by the second-trimester scan or at delivery, in any of the referral centers.

DISCUSSION

This is the largest series of fetal cephalocele diagnosed in the first trimester reported to date. Until now, most information on the condition at this early stage in gestation has been obtained from single case reports or small series. The relatively large number of cases reported in this study was possible by reviewing the collected experience from four fetal medicine referral centers, which provided us with the opportunity of compiling and analyzing data that can be useful to characterize this condition in early pregnancy.

Our study demonstrates that most cases of cephalocele contain brain tissue (63%), are located preferentially in the occipital region (77%) and, more often than not, present as an isolated anomaly on the first-trimester scan (66%). However, a major limitation of this study was the lack of information regarding antenatal course and associated findings that were undetectable during the first trimester because of the high rate of pregnancy termination and early intrauterine fetal demise in this population. Special consideration should be given to the observation obtained from the few cases in which a sonographic follow-up was available; in a large proportion of these cases, an increase in size and change in content of the defect was documented with advancing gestation. This information should be included in parental counseling, as it may influence prognosis and therefore subsequent management options.

There were no cases of aneuploidy in our series; however, as the use of microarray-based comparative genomic hybridization is becoming the standard of care in many fetal medicine centers, this technique could help in the identification of submicroscopic chromosomal imbalances that may be associated with the underlying cause in some cases. Of note, four fetuses in this series had Meckel–Gruber syndrome, an autosomal-recessive condition characterized by the triad of occipital cephalocele, bilateral polycystic kidneys and axial polydactyly[2,18]. The risk of recurrence of these cases is 25%; therefore, careful evaluation of the kidneys should be performed every time an occipital cephalocele is detected, to rule out this genetic condition. Because the severe oligohydramnios associated with fetuses affected by Meckel–Gruber syndrome frequently impairs detailed anatomic evaluation in the second trimester[2], the diagnosis of the syndrome is easier in the first trimester when there remains sufficient amniotic fluid surrounding the fetus[18]. Two other cases of cephalocele were detected in association with a disruptive syndrome: one with body stalk anomaly and the other with amniotic band syndrome, conditions closely related to early amniotic rupture sequence and therefore associated with a poor prognosis. The main first-trimester sonographic features observed in these cases include additional disruptive malformations, such as facial clefting, anterior abdominal wall defects, kyphoscoliosis and limb

amputations[19,20]. Our series also included three (9%) cases of frontal cephalocele, which is a rare location for this condition in the Caucasian population[2,3]. Prognosis in these cases is almost invariably poor because consequences of the skull defect and brain protrusion in this area are devastating. In cases with frontal cephalocele in our series, one patient decided to continue the pregnancy but the neonate died soon after delivery and the other two opted for an early termination of pregnancy.

In our centers, there was no recollection of false-negative cases, as demonstrated by the second-trimester scan or examination of the newborn at the time of delivery. Therefore, it can be inferred that, with a detailed examination of the fetal skull contour, all cases of cephaloceles are potentially amenable to an early prenatal diagnosis. This is particularly true in cases of medium- and large-sized cephaloceles because small cephaloceles are obviously more difficult to detect. The main differential diagnoses in the latter case were a scalp cyst, cranial lymphangioma and hemangioma, which are developmental abnormalities that usually present later on in pregnancy[2].

In summary, cephaloceles can be diagnosed readily in the first trimester of pregnancy during the 11–13-week scan. The sonographic appearance is similar to that described for affected cases in the second trimester, although diagnosis of Meckel–Gruber syndrome can be facilitated in the first trimester as a result of the normal volume of amniotic fluid present. Because of the poor prognosis associated with cephaloceles, an early prenatal diagnosis can lead to earlier, and therefore safer, termination of pregnancy.

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