

Cephalocele detection *in utero*: sonographic and clinical features

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ABSTRACT

Sonographic and clinical features of 26 fetal cephaloceles were reviewed retrospectively. The most frequent reason for referral was elevated maternal serum α -fetoprotein levels. The smallest lesion identified was 0.4×0.5 cm (frontal, at 20 weeks); the largest was 9.0×10.0 cm (frontal, at 27 weeks). Twenty-four of 26 cephaloceles were detected on prenatal ultrasound examination; in 13 of these, more than 50% of the intracranial contents were exteriorized. Fifteen of 24 cephaloceles detected prenatally had a sulcal pattern (identified between 16 and 36 weeks' gestation); five were solid without a sulcal pattern (identified between 13 and 21 weeks' gestation), three were cystic, and one underwent a change in appearance from solid at 21 weeks to cystic at 26 weeks. Other cranial features were evaluated and included visible skull defect, seen in 23/24 (96%), ventriculomegaly, in 6/26 (23%); microcephaly, in 12/24 (50%); beaked tectal plate, in 6/16 (38%); and flattened basiocciput, in 9/24 (38%). Of the 26 cases, 14 had normal amniotic fluid volume, five had oligohydramnios and seven had polyhydramnios. Fetuses with oligohydramnios had the highest incidence of concurrent fetal abnormalities; four of five fetuses (80%) with oligohydramnios had additional structural abnormalities. In the overall population, a very high incidence of other abnormalities was found; 17/26 (65%) cases showed additional abnormalities, some of which were not detected by ultrasound. Five fetuses had Meckel–Gruber syndrome and three had amniotic band syndrome. Only one of the 18 karyotypes obtained was abnormal (trisomy 18). Survival was very poor; only two of the eight who survived until birth are currently living.

INTRODUCTION

Ultrasound detection of fetal cephalocele has been reported since 1978¹. Since that time, sonographic features and clues to diagnosis continue to be described² as more is learned about this condition and as ultrasound equipment improves. Demographics and prognosis have been

derived largely from pediatric series^{3–5}, with prenatal management based predominantly on pediatric data. For better understanding of the natural history of fetal cephaloceles, it is imperative that they be studied *in utero*. However, fetal cephaloceles are quite rare, occurring approximately one-tenth as frequently as other open neural tube defects, such as spina bifida, associated with the Arnold Chiari II malformation. Thus, fewer data are available on the prenatal detection and management of fetal cephalocele than on many other fetal central nervous system abnormalities. Continued reporting of fetal series, especially large series such as the present one, will contribute to the overall understanding of cephalocele and its natural history *in utero*, thus improving prenatal management and patient counselling.

MATERIALS AND METHODS

Case records were reviewed at the University of California, San Diego and University of California, Davis from 1978 to 1991 for fetuses or newborns with the diagnosis of cephalocele. Twenty-six of 30 cases found had prenatal sonograms and could be included in the study. The four without prenatal sonograms were excluded.

All sonograms were performed with commercially available real-time equipment, including Acuson-128 and Acuson-128XP (Mountain View, California), Hitachi-410 (Tokyo, Japan), and Toshiba SSA 270A (Tustin, California), both sector and linear array transducers of 3.5 MHz and 5 MHz were utilized. All examinations were performed transabdominally. In two fetuses, additional endovaginal imaging was performed with a 7-MHz endovaginal probe for better evaluation of the fetus in cephalic presentation. All examinations were performed initially by registered sonographers and checked and elaborated upon subsequently by physicians. The sonograms were reviewed for cephalocele size, location and characteristics (presence of solid tissue, tissue with a

sulcal pattern or cystic areas), percentage of intracranial contents exteriorized (determined by comparing cephalocele size to cranial size), identification of a skull defect, flattened basiocciput², lemon sign², microcephaly (head size greater than two standard deviations below the mean), beaked tectum², hydrocephalus, ultrasound age at diagnosis, amniotic fluid volume and the presence of any other anomalies.

Medical records were reviewed for referral basis, maternal serum α -fetoprotein (MSAFP) level, method of delivery, gestational age at delivery, survival and karyotype. Pathology reports were reviewed for confirmation of the cephalocele and other anomalies detected on ultrasonography, as well as for identification of anomalies not detected by ultrasound.

RESULTS

Clinical

Twenty-six cases of cephalocele for which prenatal sonograms were available were identified from our case records. The greatest number of cases occurred in 1989 (six cases) and 1990 (seven cases). Eighteen terminations (12 dilatation and extractions (D&Es), six labor inductions) were performed. Six women had spontaneous vaginal deliveries (three preterm, three at term), and two had Cesarean sections (one for placental abruption at 35 weeks' menstrual age and one elective at 32 weeks' gestation to optimize infant survival). Eighteen of the 26 cephaloceles were confirmed by pathological study at autopsy or by physical examination or surgery after birth. Of the 12 D&E specimens, eight cephaloceles could not be confirmed due to disruption of the specimen and four could be confirmed.

Patients were referred for a variety of reasons, the most frequent being elevated MSAFP, which was seen in 12 patients. The values ranged from 2.65 to 14.00 multiples of the median (MoM) in these 12 women. One patient had a normal MSAFP level. Serum for determining MSAFP levels was drawn in 1986–91 in all cases. Eight patients were referred for anomalies detected on outside sonograms. Other reasons for referral included multiple gestation, family history of central nervous system (CNS) anomaly, size/dates discrepancy, insulin-dependent diabetes mellitus and premature rupture of membranes. Menstrual age at diagnosis ranged from 13 to 35 weeks.

Cephalocele characteristics

Seventeen cephaloceles (65%) were located in the occipital bone; four (15%) were frontal, three were superior and two were associated with a widely open cranial vault. Ultrasound detected 24 of 26 cephaloceles. Two of the occipital cephaloceles were not identified on prenatal sonograms. One of these was in a fetus with oligohydramnios, enlarged echogenic kidneys and probable polydactyly, leading to the diagnosis of Meckel–Gruber syndrome. At autopsy, only a small cranial defect was

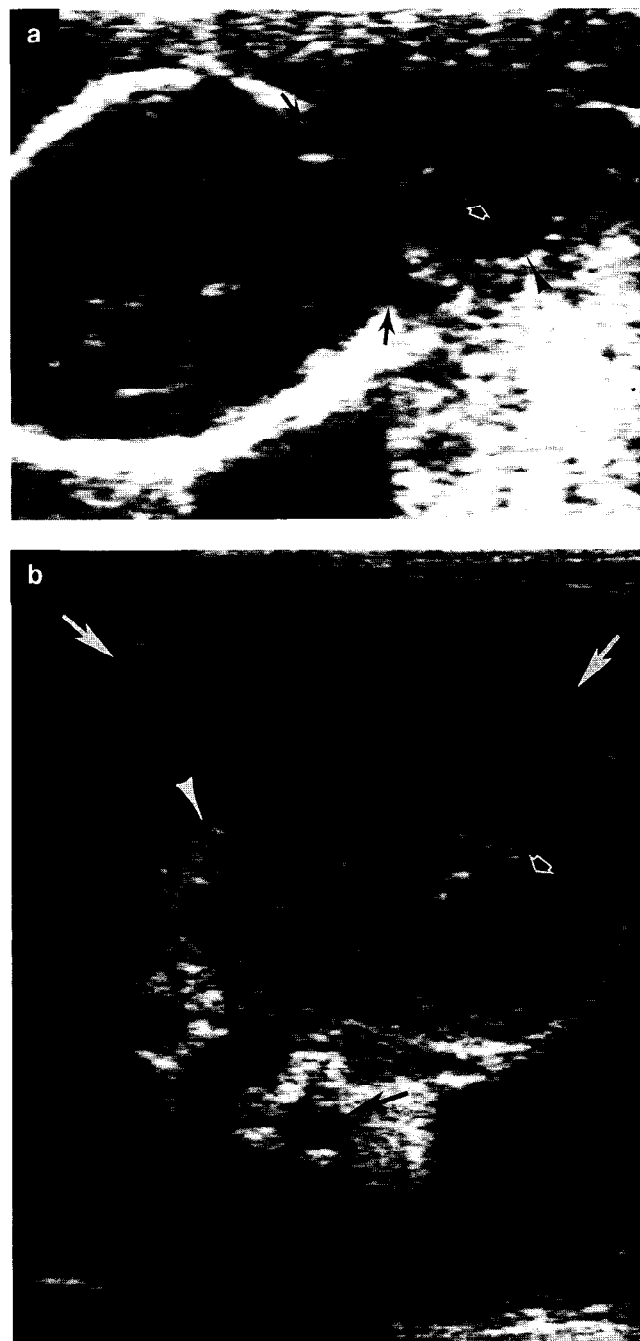


Figure 1 (a) Posterior skull defect (arrows) with occipital cephalocele (arrowheads) containing sulci (open arrow) at 20 weeks' gestational age; (b) large frontal cephalocele (white arrows) containing sulci (white arrowhead) as well as large cystic areas (open arrowhead) at 27 weeks' gestational age. Orbits marked by black arrows

identified without protruding brain or meninges. Whether this represented a small cephalocele which retracted during fetal extraction or a true cranium bifidum lesion is not certain. The other cephalocele not identified prenatally was in a 32-week fetus referred for suspected microcephaly. This fetus remained in a persistent cephalic presentation during two different sonograms. Microcephaly and a lemon configuration of the frontal bones were identified, as well as a flattened basiocciput and small cerebellum. Even with endovaginal

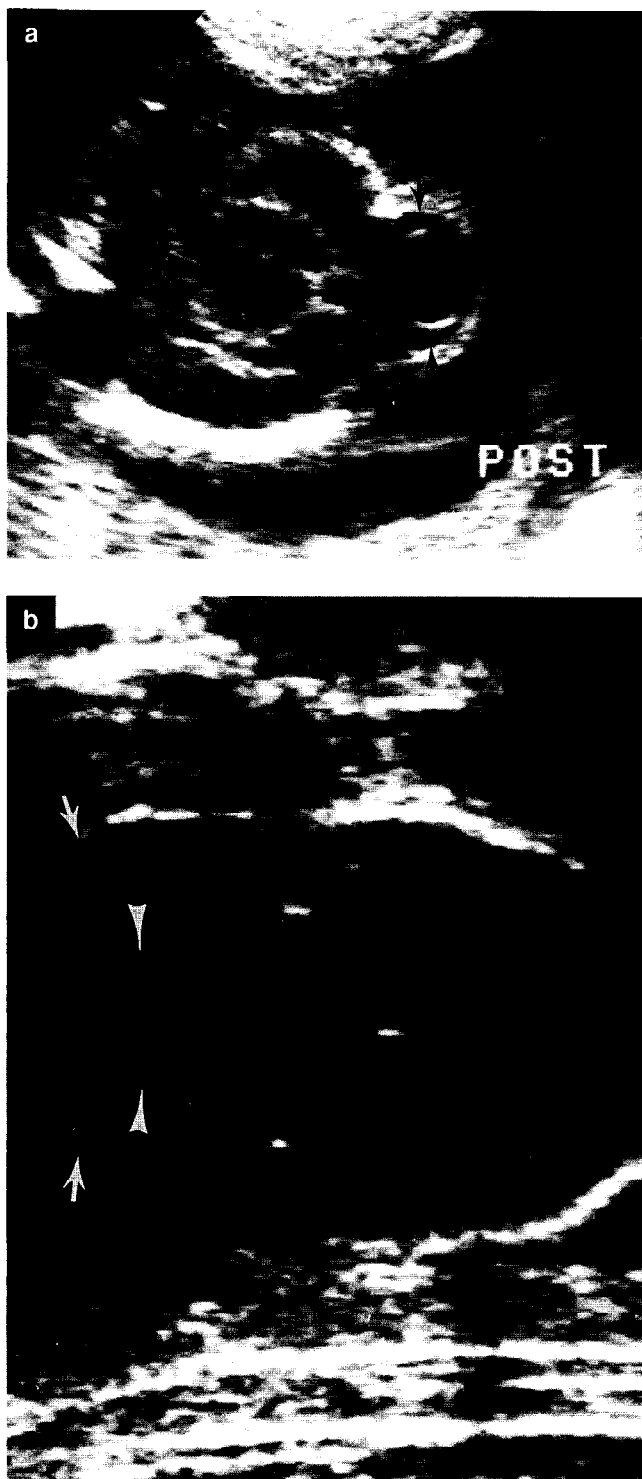


Figure 2 (a) Endovaginal image of posterior cephalocele which is cystic with rim of brain mantle but without a sulcal pattern (arrows), at 16 weeks' gestational age; (b) cystic posterior cephalocele (arrows) with a small central solid area (arrowheads) at 19 weeks' gestational age

imaging, neither a skull defect nor a cephalocele could be identified.

Fifteen cephaloceles detected prenatally had a sulcal pattern (identified between 16 and 36 weeks' gestation), and seven of these also had cystic areas (Figure 1). Three lesions were predominantly cystic; two of these had a peripheral rim of brain mantle without a sulcal pattern and one had a small central solid area, arising from the

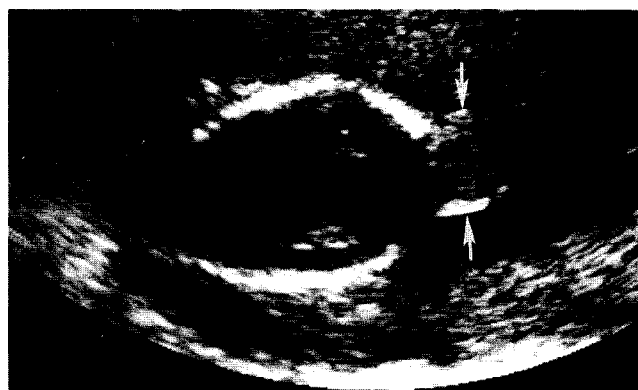


Figure 3 A solid posterior cephalocele (arrows) without sulcal pattern at 21 weeks' gestational age

skull defect (Figure 2). Five cephaloceles, detected between 13 and 21 weeks, were solid masses without a sulcal pattern (Figure 3). One of these also contained significant cystic areas. One lesion appeared solid at 21 weeks, then became cystic with soft tissue strands at 26 and 30 weeks. This was found to be a simple meningocele on postnatal magnetic resonance imaging and on pathological examination after surgery (Figure 4). The size of this lesion increased minimally from 1.0×1.5 cm at 21 weeks *in utero* to 2.5×2.5 cm at 4 days after birth. It was the only simple meningocele in the series. Only one other patient had serial sonographic examinations. In this fetus, the solid mass remained unchanged in size, 1×1 cm, at both 13 and 18 weeks' menstrual age.

Cephalocele size

The smallest cephaloceles identified were 0.4×0.5 cm in size (frontal, at 20 weeks) (Figure 5) and 1.0×1.0 cm (occipital, at 13 weeks). Neither of these required endovaginal imaging for detection. The largest cephalocele identified was 10.0×9.0 cm (frontal, at 27 weeks). In 13 fetuses more than 50% of the intracranial contents were exteriorized, in four fetuses 25–50% were exteriorized and in seven less than 25% were exteriorized. Comparison of the MSAFP levels and cephalocele sizes demonstrated no correlation. Some very small lesions were associated with very high MSAFP levels (0.4×0.5 cm at 20 weeks' menstrual age, MSAFP 8.35 MoM), whereas some larger lesions were accompanied by relatively milder MSAFP elevations (4.8×5.5 cm at 20 weeks' menstrual age, MSAFP 2.65 MoM). The type of cephalocele covering was specifically mentioned in the pathology report, surgical report or at physical examination in 11 of the cases: seven were incompletely skin-covered or membrane-covered and four were completely skin-covered.

Other cranial findings

We reviewed the sonograms for other cranial findings that might be related to cephalocele². A skull defect was identified in 23 of 24 fetuses (96%) in whom images permitted evaluation of this finding. Ventriculomegaly was identified between 13 and 32 weeks in six of the 26



Figure 4 (a) Small solid posterior cephalocele (arrows) at 26 weeks' gestational age, appearing partly cystic (arrowheads) and partly solid (open arrow). This mass initially appeared completely solid at 21 weeks; (b) T1-weighted image of the same lesion 2 days after birth, demonstrating a simple meningocele (arrows)

cephalocele cases (23%). The lemon sign was identified between 19 and 33 weeks in six of the 26 cases (23%). Only one case in our series had both ventriculomegaly and the lemon sign at diagnosis (21 weeks). Microcephaly was seen in 12 of 24 fetuses (50%). A beaked or displaced tectum (Figure 6) was seen in four of six fetuses (67%). A flattened configuration to the basiocciput (Figure 7) was seen in nine of 24 fetuses (38%); six of these cephaloceles were occipital, one was ethmoidal and two were superior in location.

Amniotic fluid

Amniotic fluid volume was normal in 14 patients; five had oligohydramnios and seven had polyhydramnios. The patients with normal amniotic fluid volume presented between 13 and 35 weeks' menstrual age; those

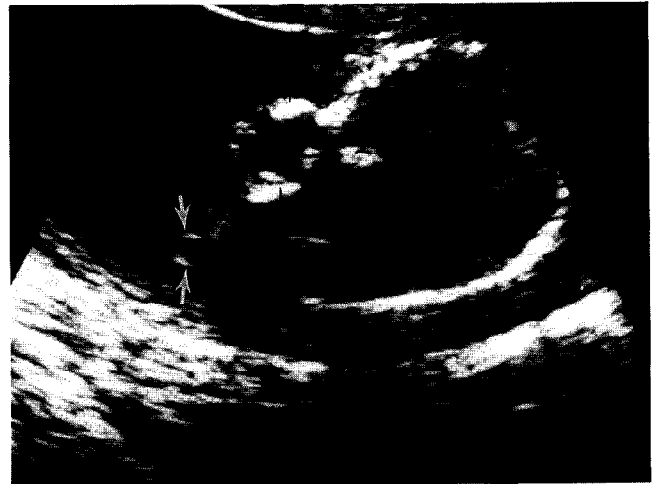


Figure 5 Small cephalocele (white arrows), which is frontal and measures 0.4×0.5 cm in size at 20 weeks' gestational age. Orbit marked by black arrowheads

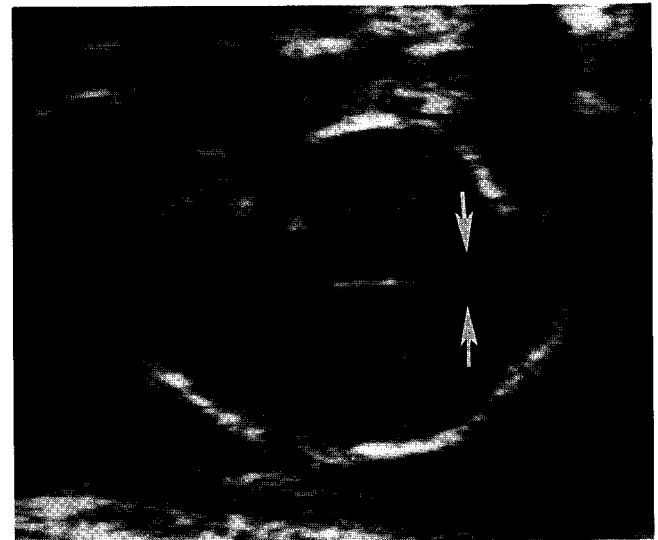


Figure 6 Beaked tectal plate (arrows) at 18 weeks' gestational age



Figure 7 Flattened basiocciput (arrows) with posterior cephalocele (arrowheads) at 24 weeks' gestational age

with oligohydramnios presented between 16 and 30 weeks and those with polyhydramnios presented between 16 and 33 weeks. Eleven of 14 fetuses with normal amniotic fluid volume had abnormalities at sonography in addition to the cephalocele. Three of six fetuses with polyhydramnios and four of five with oligohydramnios had other abnormalities at sonography.

Karyotype

Karyotyping was performed in 18 of the 26 fetuses with cephalocele in our population. Thirteen were males; five were females. Seventeen were normal and the single abnormal karyotype was a trisomy 18.

Other fetal abnormalities

Various other fetal anomalies were identified on prenatal sonogram (Table 1). In the central nervous system, cerebellar hypoplasia (two fetuses), vermian anomalies (Dandy–Walker malformation or variant in two fetuses), and spina bifida (three fetuses) were identified. Two of the patients with spina bifida had iniencephaly and in the remaining fetus the defect was in the thoracic region. Facial anomalies were identified in seven fetuses. Hypertelorism, as defined by Mayden and associates⁶, was identified in four patients; two had frontal cephaloceles, one had an occipital lesion and one had an asymmetric anterior lesion.

Table 1 Other anomalies identified on prenatal sonography. Number of cases shown in parentheses

<i>Central nervous system</i>	
Cerebellar hypoplasia	(2)
Dandy–Walker malformation/variant	(2)
Spina bifida	(1)
<i>Face and neck</i>	
Cleft lip/palate	(1)
Absent facial features	(2)
Hypertelorism	(3)
Cystic hygroma	(1)
<i>Limb</i>	
Polydactyly (suggested in)	(1)
Clubbing	(3)
Reduction defects	(2)
<i>Renal/urinary tract</i>	
Polycystic kidneys	(4)
Non-visualization of urinary bladder	(2)
Renal agenesis	(1)
Pyelectasis	(1)
<i>Chest</i>	
Ectopia cordis	(1)
Dextrocardia	(1)
Protruding pericardium	(1)
<i>Abdomen</i>	
Omphalocele	(2)
Echogenic bowel	(1)
<i>Other</i>	
Kyphoscoliosis	(2)
Two-vessel cord	(1)

Pathological or physical examination after delivery revealed other abnormalities that were not identified on prenatal sonograms (Table 2).

Syndromes

Pathological specimens (both fetuses and placentas) were evaluated carefully for abnormalities. Meckel–Gruber syndrome was identified by the presence of the classic triad of cystic renal dysplasia, occipital cephalocele and polydactyly⁷. Amniotic band syndrome was identified by non-artifactual absence of amnion over most of the placental surface with persistence of amniotic strands near the placental cord insertion site. Some fetuses with amniotic band syndrome had constriction defects of the extremities or strands of amnion adherent at the sites of various defects. Three fetuses in our population had

Table 2 Abnormalities found at autopsy not identified on prenatal sonograms. Number of cases shown in parentheses

<i>Central nervous system</i>	
Brainstem hypoplasia	(1)
Agenesis of corpus callosum	(1)
Forked ventricles	(1)
Aqueductal stenosis	(1)
Polymicrogyria	(1)
Cerebellar hypoplasia	(3)
Spina bifida	(1)
<i>Face and neck</i>	
Hypertelorism	(3)
Microphthalmia	(3)
Protruding tongue	(1)
Cleft lip/palate	(2)
Frontonasal absence	(2)
<i>Limb</i>	
Hypoplastic nails	(3)
Claw deformities	(1)
Reduction defects	(4)
Rocker bottom feet	(1)
Polydactyly	(4)
Clubbing	(1)
<i>Renal/urinary tract</i>	
Hydronephrosis	(2)
Hydroureter	(1)
Diminutive urinary bladder	(1)
<i>Chest</i>	
Pulmonary stenosis	(1)
Esophagogastric atresia	(1)
Atrial septal defect	(1)
Ventricular septal defect	(1)
Subpulmonic hypertrophy	(1)
Absent ductus arteriosus	(1)
Pulmonary hypoplasia	(4)
<i>Abdomen</i>	
Diaphragmatic hernia	(1)
Imperforate anus	(1)
<i>Other</i>	
Hypoplastic right pelvis	(1)
Hypoplastic ribs	(2)
Vertebral fusion anomalies	(2)
Scoliosis	(1)
Thoracic lordosis	(1)
Abdomen/chest wall defect	(1)

Table 3 Survival of infants with cephalocele who were delivered after 28 weeks' gestation

Case	Menstrual age at birth (weeks)	Cephalocele size (cm)	Percentage of intracranial contents exteriorized	Survival
1	36	unavailable	0–25%	9 months, then died
2	37	1.0 × 1.5	0–25%	2.5 years, still living
3	39	6.0 × 6.0	not seen*	2 years, still living
4	36	7.0 × 7.5	> 50%	immediate death
5	35	8.0 × 9.5	> 50%	immediate death
6	32	5.0 × 6.0	> 50%	immediate death
7	33	6.9 × 9.9	> 50%	2 months, then lost
8	28	9.0 × 10.0	> 50%	immediate death
9	31	7.0 × 9.0	> 50%	8 months, then died

*6 × 6 cm after birth

amniotic band syndrome. Five fetuses had Meckel–Gruber syndrome, and nine fetuses had multiple major anomalies but without an identifiable syndrome. Four cephaloceles were isolated lesions without other abnormalities. The remaining five were D&E specimens which were too disrupted to determine whether a syndrome was present. (Note: cephaloceles could not be confirmed in eight of 12 D&E specimens; however, in three of these, other features of a syndrome were present, leaving five specimens in which it could not be determined whether a syndrome was present.) All specimens were examined by pathologists experienced in fetal and placental examination, and, in the relatively intact fetuses and placentas, it is unlikely that amniotic bands or other indicators of a syndrome were missed.

Survival

Nine women in our population had normal spontaneous vaginal deliveries or Cesarean sections after 28 weeks' menstrual age. These cases are described in Table 3. The absolute sizes of the cephaloceles are included in the table; however, the relative sizes may be more informative in determination of significance of size upon survival. In two of the nine fetuses, 0–25% of the intracranial contents were exteriorized, and in six fetuses, more than 50% was exteriorized. The ninth fetal cephalocele was not detected antenatally. Four patients died within 2 h of birth (cases 4, 5, 6 and 8); in all of these infants, more than 50% of the intracranial contents were exteriorized on the prenatal sonogram. Five patients survived beyond 2 h of age. In two of these, less than 25% of the intracranial contents were exteriorized. One of these infants died of infection at 9 months of age (case 1); the other (case 2), who had a simple meningocele, is at present 2.5 years old and is developing normally. In two other infants who survived longer than 2 h, more than 50% of the intracranial contents were exteriorized; one of these infants (case 9) died at 8 months of age of respiratory failure and the other (case 7) was lost to follow-up after 2 months of age. The child (case 3) whose cephalocele was not detected prenatally (6 × 6 cm at birth) is now 2.5 years old and has numerous developmental problems; at the 2-year evaluation, the child exhibited motor skills equivalent to those of an 8-month-old child and speech skills equivalent to those

of a 1-year-old child. From these data, we see that at least five of six fetuses with more than 50% of the intracranial contents exteriorized have died. Only two of the nine liveborn infants are still living, one with normal developmental milestones and the other with significant developmental delay.

DISCUSSION

The differential diagnosis of a mass adjacent to the fetal cranium includes cephalocele, teratoma, cystic hygroma, hemangioma, branchial cleft cyst and cloverleaf skull^{8–11}. In most cases brain tissue is incorporated within the mass (23 of 24 (96%) detected prenatally in our population) and only a minority are purely cystic (one of 24 (4%) detected prenatally). While the primary sulci are reported to develop between 23 and 25 weeks' gestational age, sulcal patterns could be identified within the cephaloceles in the present population between 16 and 36 weeks of gestation. Those with a sulcal pattern prior to 23 weeks may have been due to abnormal development in the cephalocele tissue. The presence of a sulcal pattern in the mass (15/24 cases (63%)) leaves no question as to the diagnosis. However, a cystic mass or a mass that is solid but without a sulcal pattern may present a diagnostic dilemma, especially in the very young fetus. Several sonographic features are helpful in distinguishing fetal cephaloceles from other juxtacranial abnormalities. Cervical teratoma and hemangioma of the neck are usually complex masses. Although calcification in these masses would offer a distinct diagnostic clue, this has not been reported *in utero*⁹. A cystic hygroma usually has septa¹¹, but an occipital meningocele may also have strands of neural tissue that mimic septa. As noted by Goldstein and co-workers², a cystic hygroma will have an obtuse angle with respect to the fetal head surface, presumably because it arises diffusely beneath the surface of the skin. A cephalocele forms an acute angle with the surface of the fetal head as it protrudes through a skull defect. Identification of a skull defect is perhaps the most reliable aid in making the diagnosis of a cephalocele, but in rare instances such a defect may not be apparent, as in three of our 26 cases, owing to small size, cephalic presentation, or oligohydramnios. Teratoma, cystic hygroma, hemangioma and branchial cleft cysts are not associated

with the intracranial abnormalities traditionally found with cephalocele (ventriculomegaly, microcephaly and skull defect), nor with those cranial findings recently described by Goldstein and colleagues² in association with cephalocele (lemon configuration, beaked tectal plate and flattened basiocciput). Since in some instances the contents of the cephalocele may change, initially appearing solid and subsequently becoming cystic, it may be difficult to distinguish simple meningoceles from encephaloceles if the lesion is small. Finally, if the cranial vault cannot be seen or is imperfect, the differential diagnosis expands to include acrania, exencephaly or cranioschisis. Definitive diagnosis may not be possible until after birth.

Ordinarily, the diagnosis of a cephalocele is not difficult. In the Western world, the most frequent location is in the occipital bone, as was seen in 17 fetuses in the present population. Excluding the fetuses with widely open cranial vaults, occipital cephaloceles represent 71% of our cases, which approximates the incidence reported previously^{4,12}. Correct identification of 24 of 26 cephaloceles was accomplished in the present population. In a pregnancy at high risk for a neural tube defect, even tiny cephaloceles can be identified, as in the smallest lesion in this series (0.4×0.5 cm in size). However, certain circumstances, such as oligohydramnios, will prevent visualization of the cephalocele. In these cases, other abnormalities may lead to the correct diagnosis. Therein lies the value of identifying enlarged echogenic kidneys and polydactyly characteristic of Meckel-Gruber syndrome, amniotic bands or deformities related to the amniotic band syndrome, or abnormalities which may be directly related to the cephalocele, such as ventriculomegaly, skull defect, microcephaly, lemon configuration of the skull (as part of the Arnold Chiari III malformation), flattening of the basiocciput, or a beaked appearance of the tectum in the brainstem. The incidences of the cranial and intracranial findings in our series varied slightly from those in Goldstein's population². The most marked differences were ventriculomegaly and flattened basiocciput. Ventriculomegaly was found in a lower percentage of fetuses in our population (23%) than in Goldstein's population (54%)². Flattened basiocciput was seen in only 38% of our population, vs. 62–69% in Goldstein's population. Both of these features could be evaluated in most of our population. The reason for these differences is unknown. Interestingly, flattened basiocciput was seen not only with occipital lesions, but also in one ethmoidal and two superior lesions. The mechanism for flattening of the basiocciput is unknown, but appears unrelated to cephalocele location.

In a fetus in persistent cephalic presentation, particularly with maternal obesity, endovaginal imaging may be helpful in making a diagnosis. In the present series, the diagnosis was secured in one of two cases in which endovaginal imaging was utilized. In the first case, a 1×1 -cm mass protruding from the occiput was identified with endovaginal imaging in a fetus with oligohydramnios. This was predominantly cystic with a peripheral rim of brain mantle, and a 1-cm skull defect was identified

in the occipital bone. In the other case, endovaginal imaging did not identify a skull defect or the 6×6 -cm cephalocele found after birth, presumably because of advanced skull calcification (fetus first presented at 32 weeks) and compression of the cephalocele in the maternal pelvis. Bronshtein and Zimmer¹³ reported successful identification of a fetal cephalocele at 13 weeks' menstrual age using endovaginal imaging.

Amniotic fluid volume has traditionally been thought to be independent of fetal urine production¹⁴ prior to 20 weeks' gestation. However, oligohydramnios has been reported in younger fetuses with certain renal anomalies, such as urethral obstruction, polycystic kidneys, renal agenesis and Meckel-Gruber syndrome^{15,16}. Currently, it is generally accepted that the fetal kidneys become a major source of urine production between 14 and 16 weeks' gestation. In the present series, four of five cases with oligohydramnios had polycystic kidneys; these presented between 16 and 21 weeks. One of five fetuses with Meckel-Gruber syndrome had normal amniotic fluid volume. This fetus was diagnosed at 13 weeks' gestation, a time when amniotic fluid amount is not thought to be dependent upon renal output¹⁴. In contrast, only one of six cases with polyhydramnios presented prior to 21 weeks. While four of five fetuses with oligohydramnios had other sonographic abnormalities, only three of six fetuses with polyhydramnios and 11 of 14 fetuses with normal fluid volume did. Although polyhydramnios is an important clue to a large number of fetal anomalies¹⁷, the findings of the present study indicate that oligohydramnios, especially in the young fetus, may be a particularly helpful clue in the diagnosis of cephalocele, especially in the Meckel-Gruber syndrome, although it may obscure some sonographic findings, even the cephalocele.

When fetal cephalocele is identified, a conscientious effort should be made to identify any associated syndromes prenatally. Many of these pregnancies are terminated by D&E. Although some have demonstrated that D&E can reliably confirm the prenatal diagnosis¹⁸, this series is not in agreement, as the cephalocele could not be identified in eight of the 12 D&E specimens. Identification of a known syndrome will give the family the most accurate prognosis for future pregnancies. While many syndromes may be associated with cephaloceles¹⁹, most attention has gone to the amniotic band syndrome (12% of the present series)²⁰ and Meckel-Gruber syndrome (19% of the present series)²¹. If occipital cephaloceles are considered alone, five of 17 cases, or 29% of the present population, represented Meckel-Gruber syndrome, an even higher percentage than the 21% found by Nyberg and associates⁷.

Abnormal karyotypes have been found in up to 44% of fetuses with cephalocele². In the present study, only one of 18 fetuses (6%) who had undergone karyotyping had a chromosomal abnormality. This seems unusually low, and karyotype analysis in the additional eight cases would have been very helpful. However, in these cases, the families chose to decline amniocentesis and karyotype analysis. The single fetus with trisomy 18 had an

omphalocele and polyhydramnios but no other anomalies at sonography. While multiple fetal anomalies ordinarily alert the examiner to the possibility of abnormal chromosomes, the variety of other abnormalities present in this population (Tables 1 and 2) with mostly normal chromosomes suggests that a thorough examination of the fetus for other malformations is at least as important as karyotype analysis in assessing prognosis for the fetus with a cephalocele.

Knowledge of the natural history of fetal cephaloceles is limited; most of these which are diagnosed prenatally are terminated (17 of 26 in the present series). In the two fetuses in our series with multiple examinations, the cephalocele showed little change in size after initial diagnosis. Survival is quoted as 50–56% in pediatric series^{4,5}. However, if diagnosed *in utero*, survival is much poorer: in Goldstein's series, 21% survived² and in our population, 22% (Table 3). Most survivors with cephaloceles have significant developmental delay and neurological impairment, as in case 3 (Table 3). In pediatric series, cranial meningocele carries a better prognosis than true encephalocele^{4,5}. Fetal series have demonstrated that the prenatal appearances of cranial meningocele and cephalocele are similar enough that reliable distinction cannot be made sonographically². The present series cannot address this issue, since there was only one simple meningocele (case 2, Table 3), and this lesion appeared solid at 21 weeks, before appearing cystic at 26 and 30 weeks. However, this infant did have normal developmental milestones, which is in agreement with the better prognosis traditionally assigned to a simple meningocele. In the present population, the percentage of intracranial contents exteriorized was an important prognostic indicator: if more than 50% of the intracranial contents were exteriorized, survival was poor. This is in agreement with pediatric series, which demonstrate a poorer prognosis for large lesions⁴.

An elevated MSAFP level was the most frequent reason for referral in this series. Elevated MSAFP was found in all but one of the 13 in whom levels has been determined. The MSAFP level did not vary directly with the size of the cephalocele and thus cannot be correlated with prognosis. While cephaloceles are typically thought of as skin-covered, such that α -fetoprotein should not leak into the amniotic fluid², the skin is often thinned and parchment-like and may have focal defects²², all of which may permit protein leakage. In the present series, seven of 11 fetuses (64%) in which the covering was specifically mentioned in the pathology report had incomplete skin coverings or were membrane-covered. Thus the association of fetal cephalocele with elevated MSAFP is probably not spurious. However, MSAFP levels should not be considered a reliable screen for fetal cephalocele, since absence of an elevated MSAFP level does not exclude a skin-covered defect.

Prenatal diagnosis of a fetal cephalocele warrants careful examination of the remainder of the fetus for other anomalies, which are often present. These are important in identification of a syndrome, which may have a prognosis different from that of isolated cephalo-

cele. While a large variety of anomalies was associated with our cephalocele population (Tables 1 and 2), certain of these should alert the examiner of the possible existence of a fetal cephalocele. Multicystic kidneys and oligohydramnios are important in identification of the Meckel–Gruber syndrome, and asymmetric cephalocele and constriction deformities are consistent with amniotic band syndrome. Cranial findings may be present that specifically suggest a cephalocele (flattened basiocciput, skull defect) or which suggest the presence of a neural tube defect, even though a spinal abnormality cannot be identified (ventriculomegaly, microcephaly, beaked tectal plate, lemon sign). While only one of 18 karyotypes obtained in the present study was abnormal, karyotype analysis is warranted, as other large series report an abnormal karyotype in up to 44% of fetuses with cephalocele. Diagnosis of a fetal cephalocele has an even poorer prognosis than in pediatric series, with only 22% of our population surviving. Probably, this is due to population selection occurring in the pediatric studies, as many fetuses with cephaloceles do not survive long enough to be a part of a pediatric series. Family counselling should reflect this difference, and the neurosurgeon should become involved prenatally. Exteriorized brain tissue generally is abnormal and not salvaged if the cephalocele is resected; most survivors have significant mental impairment and developmental delay.

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