15 Neural Tube Defects

15.1 Cranium

Beth M. Kline-Fath and Dorothy I. Bulas

Neural tube defects (NTDs) encompass a heterogeneous group of congenital brain and spine anomalies that result from the defective closure of the neural tube early in gestation.[1–4] The most common anomalies include myelomeningoceles, encephaloceles, and anencephaly. Anencephaly and spinal dysraphism are equal in prevalence, accounting for 95% of cases, whereas encephaloceles account for the remaining 5%.[8] After a review of epidemiology and embryology, these malformations will be discussed by their primary location, either cranial or spinal.

EPIDEMIOLOGY

NTDs are one of the most common fetal malformations, second only to cardiac anomalies. The lesions are present in 1 to 5 of 1,000 live births and occur due to failure of primary neurulation in the first 3 to 4 weeks postconception.[5] Causes are heterogeneous and include chromosomal or genetic abnormalities, teratogens, environmental, and maternal predisposing factors. Approximately 85% of NTDs have been related to a combined influence of environmental and genetic factors. The incidence varies with race, geography, and family history. NTD risk is highest among relatives of most severely affected patients. If one child is affected, the risk for subsequent siblings is around 3%, with two affected siblings 10%, and with three affected siblings 20%.[5a] There is marked geographical variation between countries, with the highest rates in the United Kingdom and the United States and the lowest in Japan.[6] Other significant factors include valproic acid, folic acid antagonists (methotrexate and aminopterin), vitamin A, maternal diabetes, maternal obesity, hyperthermia, and folate deficiency.[6] Despite these risk factors, 90% of children with NTDs are born to women with no identifiable risk factor.

In the past few decades, the number of births with NTDs worldwide has declined because of primary prevention with folic acid supplementation in pregnancy and early ultrasound (US) diagnosis followed by therapeutic termination.[7] Women are advised to consume food high in folate or take folate supplements at least 3 months prior to pregnancy.[7] There has been a 27% decline in NTDs in the United States with folic acid fortification in grains.[7]

EMBRYOLOGY

Dysraphism is the result of defective closure of the neural tube and is reserved for defects of primary neurulation, or dorsal induction, which involves tubulation of the neural plate and disjunction of superficial from neural ectoderm.[1–3]

The neural tube forms from infolding of the embryonic ectoderm—the neural plate. The fusion of the neural groove starts in the middorsal aspect, usually the cervical area, and proceeds anteriorly to the lamina terminalis, also known as the anterior neuropore (cranial), and posteriorly in the sacral area, also known as the posterior neuropore (spinal). The anterior neuropore closes at day 24, and posterior at day 26. The neural tube separates from the ectoderm, and the mesoderm proliferates laterally to form the axial skeleton and dura (Fig. 15.1-1). If this process is interrupted, a defect in the neural tube results. At times, the process is interrupted on both ends, resulting in cranial defects such as anencephaly with myelomeningoceles.

ACRANIA/EXENCEPHALY-ANENCEPHALY

Description: *Acrania* is a defect that occurs due to complete or partial absence in the development of the cranial vault above the orbits, with absence of parietal, squamousal, occipital, temporal, and frontal bones above the supraciliary ridge.[9] *Exencephaly* is acrania with protrusion of substantial brain into the amniotic cavity.[10–12] *Anencephaly* represents absence of forebrain, midbrain, and skull. The cerebral hemispheres are replaced with residual covering of hemorrhagic, fibrotic, degenerated neurons and glia with little definable structure (Fig. 15.1-2).

Incidence: The incidence of anencephaly is difficult to assess, but in the United States, frequency is estimated at 1 in 1,000 pregnancies.[13] A progressive decline is suspected with periconceptional folate fortification and termination.[14,15] Anencephaly has a higher rate in countries such as Egypt, Lebanon, Ireland, Scotland, and New Zealand. In the United States, fetuses of Caucasian and Hispanic ethnicity are more frequently affected than those of African descent.[16] Twin gestations also have a higher risk for anencephaly. There is a female preponderance of 3:1.[15,16] Ninety-five percent of infants born with anencephaly are in families with no prior history for a NTD.[15]

Pathogenesis: Exencephaly–anencephaly sequence is the most severe NTD and results from failed closure of the rostral end of the neural tube. The severity of the bone defect is variable and may result in absent brain or rudimentary disorganized brain. Exencephaly pathologically demonstrates a highly vascular layer of epithelium with two relatively equivalent disorganized, dysplastic cerebral hemispheres.[12,13,17] With progression to anencephaly, the cerebral hemispheres are replaced by a mass of connective and vascular tissue with scattered islands of brain tissue, so-called angiomatous stroma or area cerebrovasculosa.[17,18]

Acrania is a developmental anomaly that is characterized by partial or complete absence of the cranium with complete but abnormal development of the cerebral tissue. This disorder is hypothesized to occur at the beginning of the 4th week at the

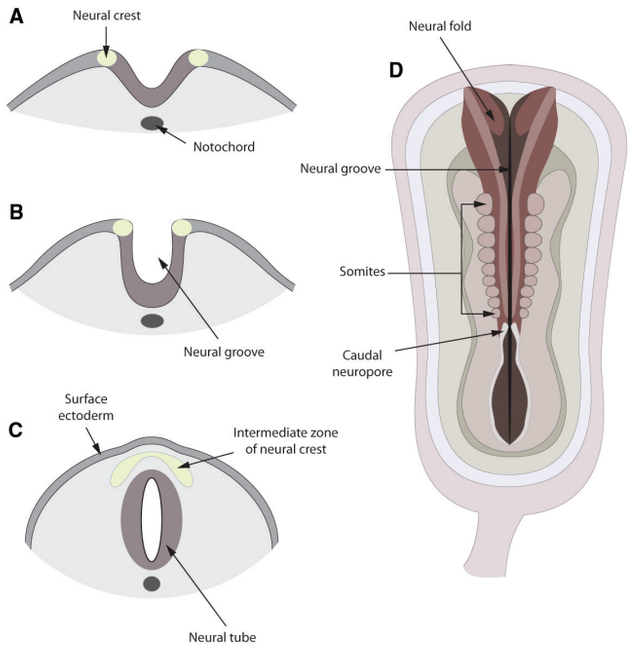

FIGURE 15.1-1: Embryology of primary neurulation in which neural plate develops **(A)** and then infolds to become a groove **(B)** and with closure a neural tube **(C)**. **D:** Diagram of the dorsal aspect of the developing craniospinal area in the embryo.

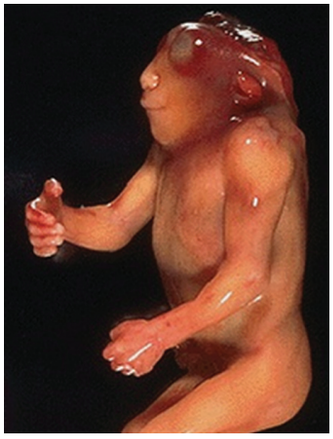

FIGURE 15.1-2: Postmortem of a fetus with anencephaly.

same time the anterior neuropore closes, but is related to failure of the mesenchyme to migrate under the ectoderm and superficial to the cerebral hemispheres.[8] The cerebral hemispheres are present but disorganized, and the brain is covered only by a thin membrane.

The major insult in acrania, exencephaly, and anencephy is due to lack of cranial development. The cerebral tissue is not protected by meninges, skull, and skin, and is progressively destroyed through exposure to amniotic fluid and mechanical trauma.[17] As a result, the brain disappears from 14 weeks onward.[19,20] Prior animal and US reports have demonstrated that there typically is progression of acrania-exencephaly to anencephaly (AEA).[7,17,21] In some cases, residual disorganized brain may persist late in gestation or even postnatal.

Etiology: AEA appears to be multifactorial in origin, being from both genetic and environmental causes.[9] Associated chromosomal syndromes have been reported in 5% to 10% of these cases and include trisomy, triploidy, mosaic trisomy 11 and 20, and a number of deletions and duplications or single gene disorders.[7] Hyperthermia, deficiency in zinc and copper, and occupation solvent exposure have been associated with a higher risk of anencephaly.[14,20] Most relevant is inadequate dietary consumption of folates prior to conception.[7,13,14]

Diagnosis: Preliminary screening for high maternal serum alpha-fetoprotein (AFP) at 10 to 15 weeks may disclose evidence of leakage from the fetal neural tube in 90% of cases.[22] The combination of elevated AFP and low estriol levels is highly predictive for anencephaly.[22,23] However, screening can be falsely positive and may require confirmation with amniocentesis or US.

Ultrasound: Sonography can identify almost 100% of anencephalic fetuses.[6,9,21,24] The disorder can be diagnosed transvaginally prior to 10 weeks' gestation by the presence of a widened cranial pole, altered brain echotexture, variable asymmetric or lobulated disorganized tissue, and decreased head-to-trunk ratio.[24,25] However, confirmation is usually obtained after 11 to 12 weeks' gestation when calvarial ossification defined as a hyperechogenic structure compared with the underlying soft tissues is noted to be absent.[6,21,24,25] Detection may also improve after 14 weeks when the brain has completely formed, although in AEA a moderate to large amount of disorganized cranial tissue may be present early in gestation as it has not yet been destroyed by amniotic fluid.[19] From 10 to 14 weeks, the "Mickey Mouse" sign can be seen on coronal images, as cerebral lobes floating in amniotic fluid above the orbits (Fig. 15.1-3).[26] AEA may result in a reduced crown rump length or chin length-to-crown rump length ratio, but in some cases the measurement is normal and can lead to a false negative study below 14 weeks.[19,26–28] Echogenic amniotic fluid, believed to represent particles of degenerated brain, has also been described in the first trimester.[20]

In the second trimester, the diagnosis is easier as less brain tissue is present. The typical "frog eyes" sign on coronal plane is due to prominent orbits in conjunction with the symmetric absence of a normally formed calvarium and brain (Fig. 15.1-4).[18] Exposed residual neural tissue may be echogenic, cystic, or normally formed with pseudosulcations.[12,18]

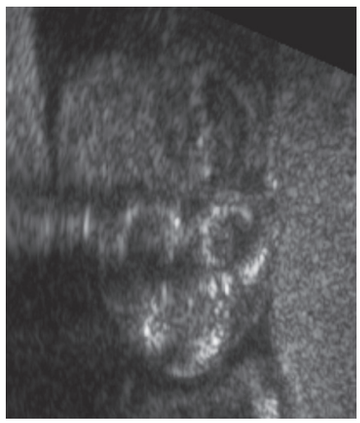

FIGURE 15.1-3: Coronal US of acrania/exencephaly with absent calvarium and protruding brain above orbits giving rise to Mickey Mouse appearance.

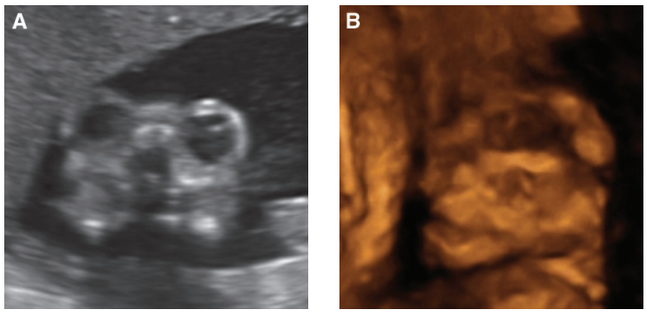

FIGURE 15.1-4: Anencephaly **A:** Coronal 2D image shows prominent "frog eye" appearance. **B:** 3D image demonstrating lack of skull above the orbits.

The cerebellar hemispheres may be absent, and spinal segmentation anomalies are common, especially in the cervical area. In the second or third trimester, as many as 30% to 50% of cases have associated polyhydramnios from impaired fetal swallowing, excess CSF across the meninges, or increased fetal urine output due to absent antidiuretic hormone.[18]

MRI: Fetal MRI is usually not required to confirm the diagnosis of anencephaly. MRI may be utilized when there is limitation in US imaging (obesity) or in the case of medical, legal, or ethical issues.[29] It can be helpful to exclude other pathologies mimicking AEA and useful in multiple gestations when it is necessary to confirm normal development of the co-twin.

The calvarium is absent, and there may be disorganized brain tissue in the area of the cerebral hemispheres in the presence of acrania or exencephaly (Fig. 15.1-5). With anencephaly, the orbits are prominent, no brain tissue is seen, and a cervical spine defect with absence of brainstem and spinal cord can be identified (Fig. 15.1-6).

Associated Anomalies: Associated spinal lesions can be found in up to 50% of cases. Other common anomalies include cleft lip/palate, cardiac, gastrointestinal, clubfoot, and omphalocele.[8,9,30]

Differential Diagnosis: Differential includes large cephaloceles, osteogenesis imperfecta (OI), and hypophosphatasia. In both OI and hypophosphatasia, the bones are present but poorly mineralized, and other fractures, bone shortening, and/or bowing are typically present.

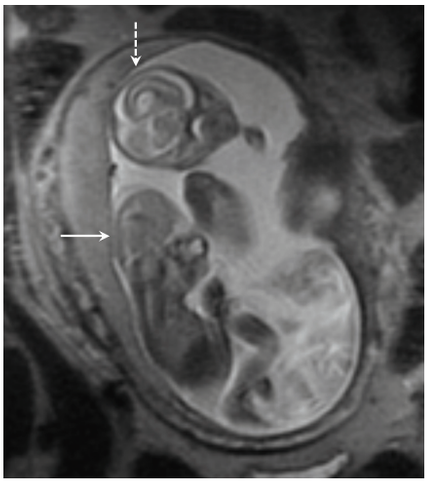

FIGURE 15.1-5: SSFSE T2 fetal MR showing lack of calvarium and dysmorphic brain in acrania/exencephaly *(solid arrow)* and normal brain and calvarium in co-twin *(dashed arrow)*.

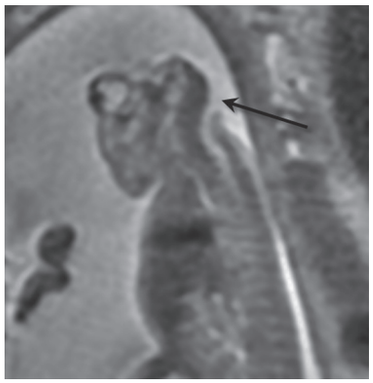

FIGURE 15.1-6: SSFSE T2 sagittal image of fetus with anencephaly demonstrating cervical spine defect and absent brainstem and cervical cord *(arrow)*.

This disorder should be distinguished from amniotic band syndrome, in which there is an asymmetric brain defect, multiple limb or digit amputations, asymmetric ventral wall defects, and unusual craniofacial or spinal defects.[11] Amniotic band is often associated with oligohydramnios, which is rare in anencephaly.[18]

Prognosis: Approximately 65% of pregnancies with anencephaly die in utero.[20] Affected fetuses born alive have a rudimentary brainstem. The brainstem can support reflex actions such as breathing and sometimes responses to sound and touch. Children with AEA are not viable and have only short-term survival.[13]

Management: Elective termination is often considered. In the United States, prenatal diagnosis and pregnancy termination have decreased the prevalence of anencephaly at birth by 60% to 70%. In Europe, America, and Asia, the overall frequency for termination of anencephaly pregnancy is 83%, ranging from 59% to 100%.[30,31]

Labor and delivery are commonly associated with unstable fetal lie, dysfunctional labor, shoulder dystocia, and postpartum hemorrhage.[32] Up to 35% of anencephalic infants will die during labor. For the 45% that are born alive, supportive care is typically provided for minutes to days.[32] The potential for neonatal organ donation has raised both legal and ethical issues.

Recurrence Risk: There is a 2% to 5% recurrence risk.[9,15] Increased risk also exists for those with relatives affected by anencephaly or those with genetic predisposition.

CEPHALOCELES

Description: A cephalocele is a defect in the skull and dura with extracalvarial extension of intracranial structures enclosed by overlying skin.

There are four major types.[33,34] *Meningoencephaloceles,* the most common, are herniations of cerebrospinal fluid (CSF), brain, and meninges through a calvarial defect. If an encephalocele includes part of a ventricle and choroid plexus, it is termed *meningoencephalocystocele*. *Meningoceles* are herniations of only meninges and CSF. An *atretic cephalocele* is typically parieto-occipital and consists of a tract and small defect of dura, fibrous tissue, and degenerated brain. *Glioceles* are glial-lined CSF defects.

Incidence: Cephaloceles account for 10% to 20% of craniospinal dysraphisms. Estimated prevalence is 0.8 to 4 per 10,000 live births.[39] The actual incidence may be higher as many of these malformations result in termination, in utero demise, and stillbirth.[40] There is a difference in incidence geographically. The Western hemisphere reports 1 to 3 per 10,000 births, whereas Southeast Asia reports 1 in 5,000 births.[28] In the West, occipital encephaloceles are most common (80%), while midline frontal and parietal are evenly divided between the remaining 20%.[41] Females are affected twice as commonly as males in the occipital location.[39,42] In Southeast Asia and Russia, frontal cephaloceles are most prevalent.[43]

Pathogenesis: Cephaloceles occur early in embryogenesis, at between 24 and 60 days.[40,44] Several theories have been suggested. Many believe that a cephalocele occurs because of a failure of neural tube closure.[44,45] Occipital and parietal cephaloceles, sometimes associated with other craniospinal defects, are more likely to develop from this pathophysiology.[34,39] However, the presence of skin over the defect raises the question of a mesodermal insufficiency, with herniation of brain and meninges due to a primary defect in the bone and dura.[35,36,43,46,47] Anterior cephaloceles may be mesodermal in origin as they are not commonly associated with other NTDs.[36] A third theory emphasizes the guidance of genes, stating that variation in the pattern of cranial neural tube closure is a genetically determined factor.[48]

Etiology: Cephaloceles have been associated with both genetic and environmental teratogens. The defect can develop owing to exposure to trypan blue, irradiation, excess vitamin A, folic acid antagonists, triamcinolone, warfarin exposure, hyperthermia,

Table 15.1-1 Syndromes/Association in Cephaloceles

Syndrome/Association	*Genetic Transmission*
Occipital	
Meckel–Gruber	Autosomal recessive
Knobloch	Autosomal recessive
Walker–Warburg (Chemke, HARD ± E)	Autosomal recessive
Cryptophthalmos	Autosomal recessive
Dyssegmental dwarfism	Autosomal recessive
Von Voss	Autosomal recessive
Joubert	Primary autosomal recessive
Klippel–Feil	Variable
Craniostenosis	Variable syndrome
Hemifacial microsomia (oculoauriculovertebral)	Sporadic
Ectrodactyly–ectodermal dysplasia	Sporadic and familial
Warfarin embryopathy	
Dandy–Walker	
Arnold–Chiari	
Iniencephaly	
Myelomeningocele	
Parietal	
Absent corpus callosum	
Atretic form	
Frontal	
Roberts syndrome	Autosomal recessive
Frontonasal dysplasia	Autosomal recessive
Cleft lip/palate	
Absent corpus callosum	
Basal/transphenoidal	
Cleft palate/lip	
Hypothalamic pituitary dysfunction	
Absent corpus callosum	

and malnutrition.[35,47] Cephaloceles are seen at a higher rate with increased maternal age, maternal diabetes mellitus, rubella, and consanguineous marriages.[47] Geographic differences in the distribution of encephaloceles suggest racial and other environmental effects.[39] Although most cephaloceles are sporadic, some are part of recognized genetic and nongenetic syndromes (Table 15.1-1).[43,49]

Diagnosis: An elevated antenatal AFP can be present if the lesion is incompletely covered.[50] However, many cephaloceles are covered with normal or dysplastic skin and show no elevation in AFP.[39,47] Because of inconsistency, prenatal diagnosis is typically dependent on US. Most cephalocele defects are found midline or paramidline and named for their location. The most common types are occipital, frontoethmoidal, parietal, and basal.

- *Occipital:* The defect is between the lambda and the foramen magnum, can include the infratentorial and supratentorial brain, and may demonstrate venous sinus extension into the lesion[33,35] (Fig. 15.1-7).
- *Frontoethmoidal:* The defect is at the foramen cecum, anterior to the crista galli where the frontal and ethmoidal bones meet. Failure of involution can lead to a nasal dermal sinus, nasal glioma, or encephalocele.[35–37] A nasal dermal sinus occurs when there is incomplete separation of the dura from the skin, resulting in dermal inclusion cysts anywhere along the tract, including intracranial. Nasal gliomas are heterotopic glial tissue without intracranial connection that can be found in the nose or, more commonly, above the nose (glabella) (Fig. 15.1-8). The cephalocele defect can be at the foramen cecum or through other sites along the midline frontal bone (Fig. 15.1-9).[28] Hypertelorism is a common association.[39]
- *Parietal:* The defect is between the intersection of coronal sutures and the lambda. Atretic cephaloceles are commonly found in this location and have a good prognosis. The atretic lesion is typically identified in the presence of a vertical straight sinus (falcine sinus), minimal dysplastic extracranial

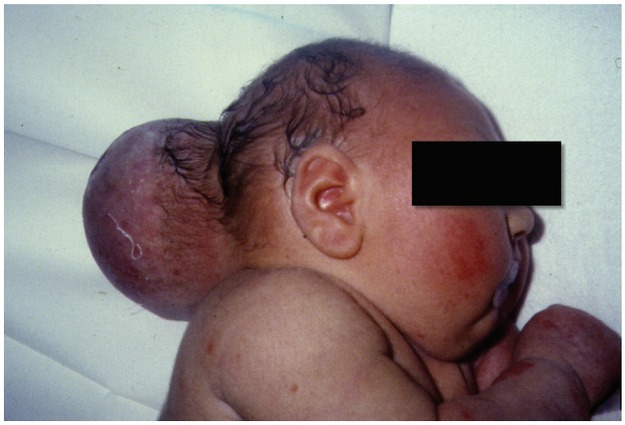

FIGURE 15.1-7: Postnatal image of a child with large occipital encephalocele.

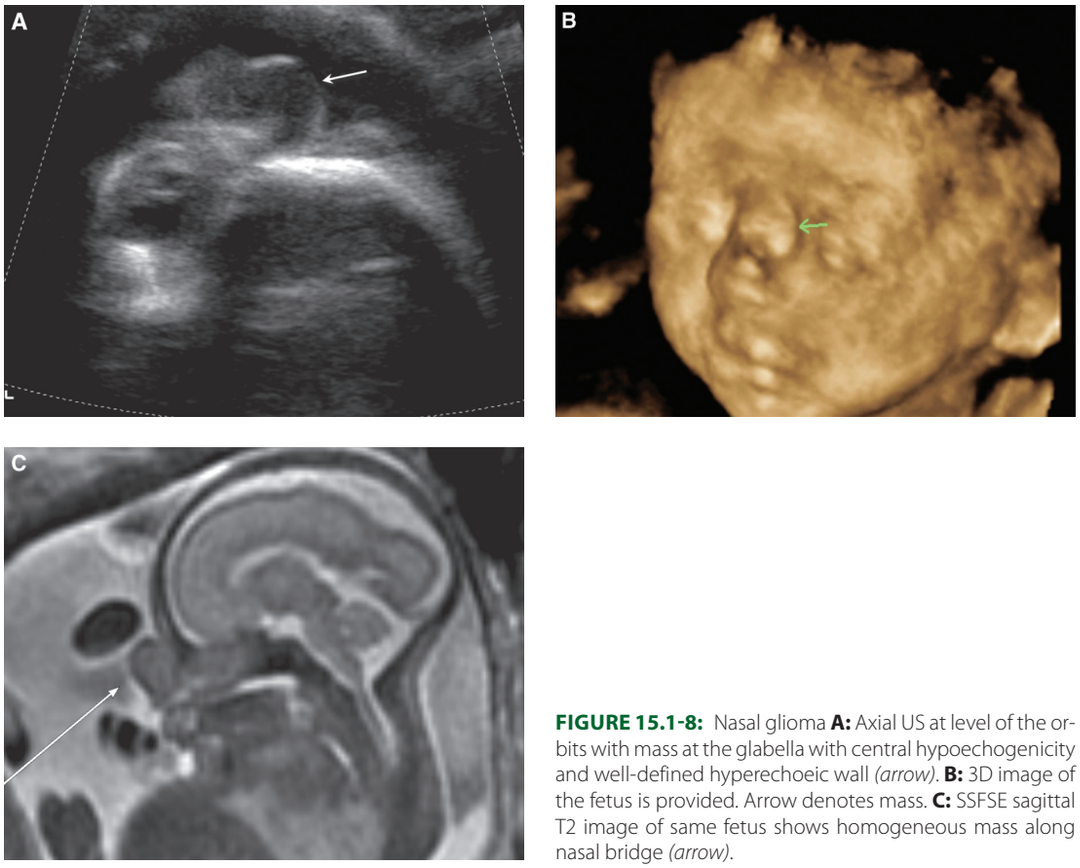

FIGURE 15.1-8: Nasal glioma **A:** Axial US at level of the orbits with mass at the glabella with central hypoechogenicity and well-defined hyperechoic wall *(arrow)*. **B:** 3D image of the fetus is provided. Arrow denotes mass. **C:** SSFSE sagittal T2 image of same fetus shows homogeneous mass along nasal bridge *(arrow)*.

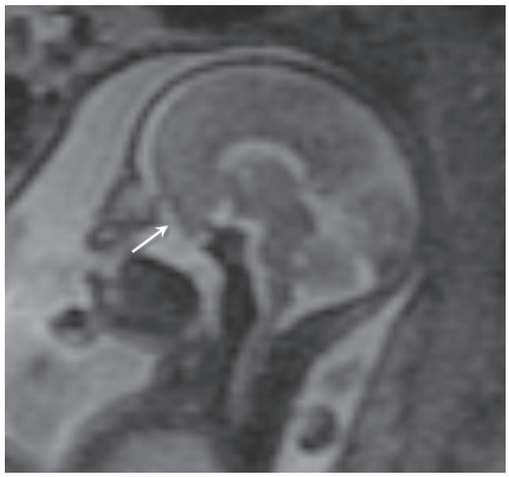

FIGURE 15.1-9: Sagittal SSFSE T2 MR image demonstrating large frontoethmoidal encephalocele with herniation of brain and CSF *(arrow)* through defect. The child was diagnosed with Roberts syndrome after birth.

tissue, and CSF cigar-shaped tract within the posterior interhemispheric fissure[38] (Fig. 15.1-10).

- *Basal:* This rare defect is in the skull base at the junction of the sphenoid and ethmoid, and may present as a mass in the mouth or posterior pharynx.[33]

Ultrasound: Prenatal US detects approximately 80% to 100% of cephaloceles.[51,52] The diagnosis can be confidently made during the second and often in the first trimester.[51] Transvaginal imaging can improve diagnosis and identify sac contents as early as 12 weeks.[50,53] The utilization of three-dimensional (3D) US can improve detection of small lesions and provide assistance in the first trimester.[51,54]

Cephaloceles are variable in size, shape, and echotexture and may enlarge or change over time.[34] To diagnose a cephalocele, a defect in the cranial vault and continuity between the defect contents and the intracranial structures must be demonstrated[50] (Fig. 15.1-11). However, care must be taken to ensure that the calvarial defect is not an artifact related to angle dropout or the normal posterior fontanel.[41,52] If the skull defect is small (up to 20% of cases), diagnosis can be difficult.[41]

Cephaloceles may be solid, cystic, or mixed[41] (Fig. 15.1-12). Detection of fetal brain with a gyral pattern within the sac is helpful, although the US appearance may change throughout gestation with solid tissue becoming more cystic with time[51,55] (Fig. 15.1-13). Thus, it can sometimes be difficult to discriminate a cranial meningocele from an encephalocele.[47] A cephalocele can be differentiated from an extracranial lesion by the acute angle with the surface of the fetal head.[47,50] Vascular flow into and around the lesion can indicate venous sinus extension and may be helpful in securing diagnosis of a cephalocele (Fig. 15.1-14). Factors on US that can help to predict a good outcome include: a sac containing only CSF or a nubbin of neural tissue, no associated anomalies, normal-sized brain, and absence of ventriculomegaly.[56] If more than 50% of the intracranial contents are exteriorized, survival and outcome are poor.[50]

Associated anomalies commonly identified on US include ventriculomegaly, microcephaly, loss of normal cerebral landmarks, lemon skull, Chiari II, obliteration of cisterna magna, and flattened basiocciput[43,50] (Fig. 15.1-15). Evaluation of extracranial structures should be performed with special attention to the kidneys and spine.[57] The presence of oligohydramnios, polycystic kidneys and occipital cephalocele should raise suspicion for Meckel–Gruber syndrome.[50] Although prenatal US can diagnose cephaloceles, assessment can be difficult because of low amniotic fluid, maternal obesity, or fetal head positioning.[41,50]

MRI: Given high soft tissue contrast and large field of view, MRI can diagnose 100% of cranial dysraphisms.[29] In the presence of a NTD, fetal MR has been shown to detect new findings that change US diagnosis in 15% of cases and discern new findings that were not defined on US in 42% of cases. MRI has the ability to influence management decisions such as continuation of pregnancy or mode of delivery in 21%.[29] Multiplanar imaging allows sharp delineation of the calvarial defect and can define the varying amounts of brain tissue, venous sinus

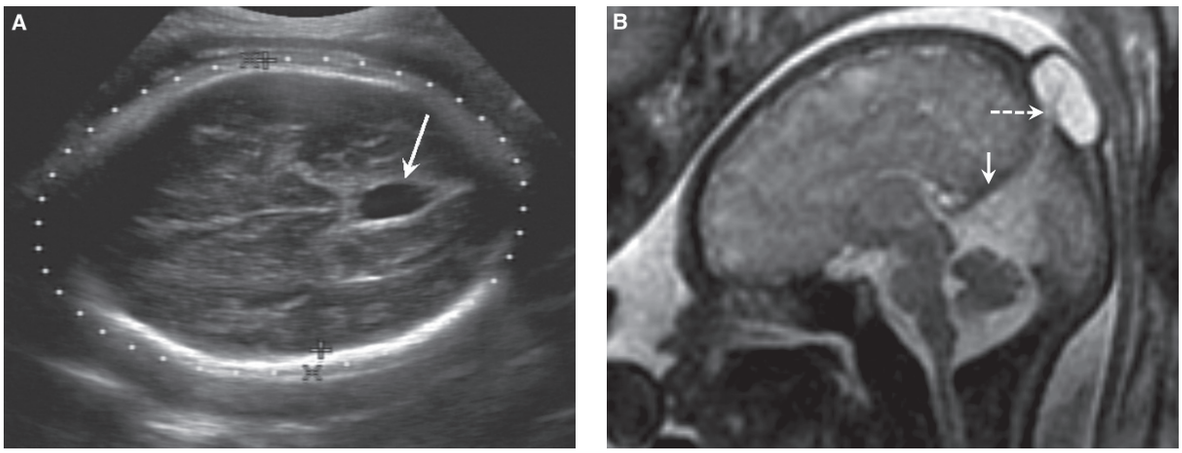

FIGURE 15.1-10: Atretic Parietal Cephalocele **A:** Axial US shows cigar-shaped interhemispheric CSF collection (*arrow*) in a fetus in third trimester. **B:** On sagittal SSFSE T2 image, the same fetus shows vertical straight sinus *(solid arrow)*, small parietal calvarial defect, and CSF extracranial *(dotted arrow)*.

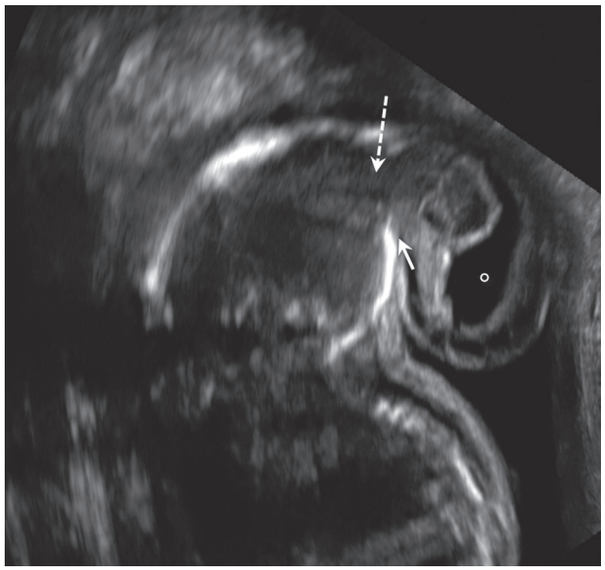

FIGURE 15.1-11: Sagittal ultrasound images in fetus with meningoencephalocystocele. There is a defect in the calvarium *(solid arrow)* and continuity of intracranial brain extending into sac *(dotted arrow)*. Cystic dilatation in extracranial tissue represents dilated ventricle *(circle)*.

extension, and CSF in the cephalocele sac, thus providing important information with regard to prognosis (Fig. 15.1-16).[29,58] SSFP imaging demonstrates good contrast between water and soft tissue and can be helpful at defining borders of the defect (Fig. 15.1-17). Diffusion imaging can exclude ischemia or lesions such as dermoids, which show restricted diffusion.

Fetal MR is also extremely useful in identifying additional CNS anomalies, such as hindbrain malformations, corpus callosum dsygenesis, and cerebral parenchymal abnormalities[29] (Fig. 15.1-18). Because of its ability to define other anomalies, fetal MR can aid in the diagnosis of syndromes.

Associated Anomalies: Both intracranial and extracranial anomalies have been cited in up to 50% of children with cephaloceles.[40] Associated extracranial anomalies include facial, cardiovascular, gastrointestinal, genitourinary, limb, heterotaxy, and other NTDs.[40,59]

Complications of intracranial malformation include hydrocephalus and microcephaly. Ventriculomegaly has been reported in 65% of occipital cephaloceles and 15% of frontal encephaloceles.[60] Spinal defects are noted in 7% to 15% of all cephaloceles.[60] Microcephaly has been observed in 20% of postnatal studies.

Differential Diagnosis: Demonstration of a calvarial bone defect confirms the diagnosis of cephalocele. However, if the fetus has an asymmetric cephalocele and constriction deformities, findings are more consistent with amniotic band syndrome. In the presence of a small skull defect, extracranial lesions can mimic cephaloceles. The differential diagnosis of a mass adjacent to the fetal skull includes teratoma, vascular malformation or hemangioma, branchial cleft cyst, and scalp edema.[61] A lesion arising from the skin surface should have an obtuse angle with the skull on US.[50] Rarely, fetal hair mimicking a thin membrane on US may be misinterpreted as a defect.[61] A frontal encephalocele should be differentiated from simple dermoid cyst and dacrocystotcele.[62] Basal encephaloceles must be differentiated from epignathus and congenital granular epulis tumors.[63]

Prognosis: Predictors of poor outcome include associated intracranial abnormalities, development of hydrocephalus, seizure disorder, microcephaly, and presence of brain tissue in the malformation.[42,64,65] Occipital lesions in some series do worse than anterior or parietal lesions.[39,42] In the presence of hydrocephalus, other intracranial abnormalities or genetic syndrome, the prognosis is poor.[56] The overall mortality rate is 5% to 29%.[40,64] The disability rate is approximately 52%.[61] Up to 20% will have seizures and 50% hydrocephalus.[31,65]

Management: In the presence of a cephalocele, karyotyping should be considered as 44% have a chromosomal abnormality.[41] If the encephalocele is large, with severe microcephaly and/or association with other anomalies, termination of the pregnancy may be considered.[51] A caesarean section is recommended to minimize trauma to the brain if the defect is

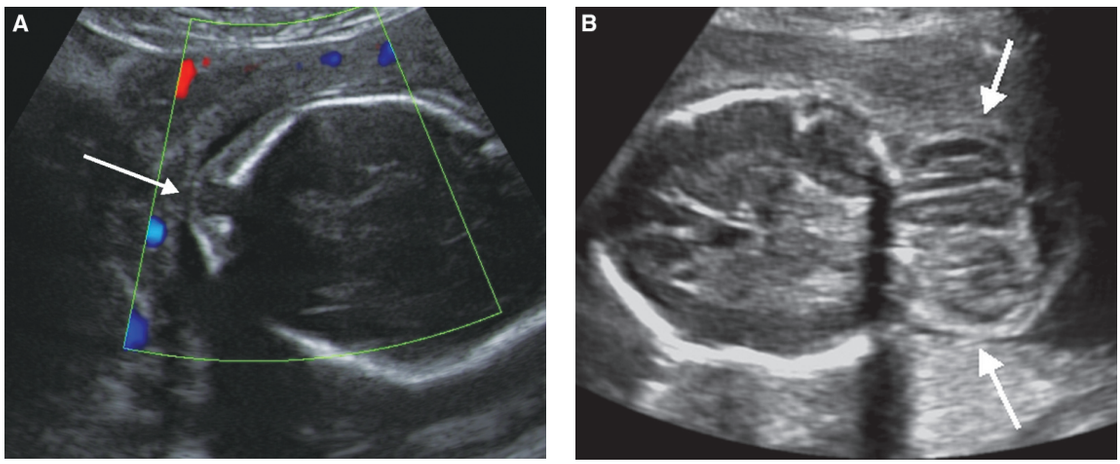

FIGURE 15.1-12: Variable appearance of cephaloceles **A:** Axial color US shows small defect in calvarium in association with cystic appearance of sac (*arrow*). **B:** Axial US shows sac containing mainly solid, brain parenchymal tissue (*arrows*).

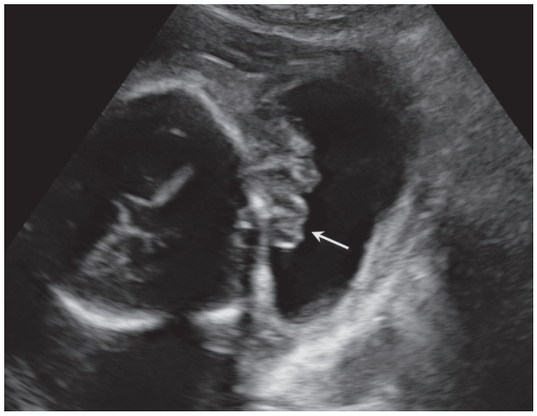

FIGURE 15.1-13: Axial US of meningoencephalocele showing pseudosulcation of herniated brain tissue *(arrow)*.

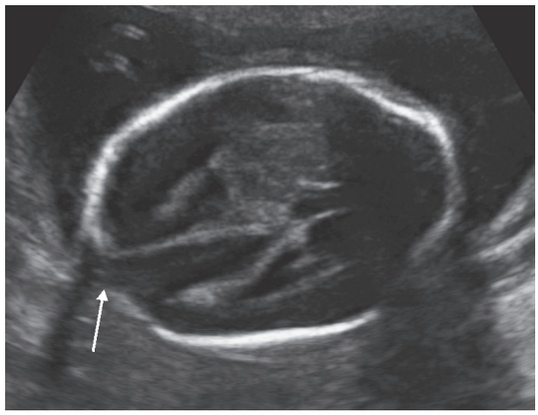

FIGURE 15.1-15: Axial US demonstrating lemon configuration and ventriculomegaly *(arrow)* in fetus with cephalocele.

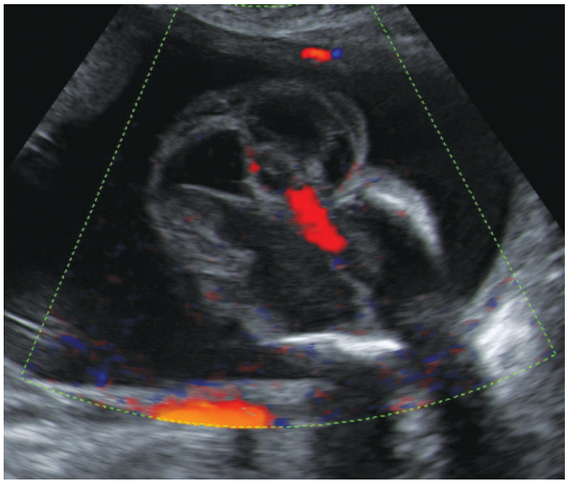

FIGURE 15.1-14: Axial color US with sagittal sinus extending into meningoencephalocele.

large.[51,61] If the cephalocele is small, vaginal delivery may be considered. Most cephaloceles are treated with surgery because of risk of injury to displaced brain, leakage of CSF, or facial maldevelopment.[55] As the lesion is covered with skin, timing of surgery is typically elective. A staged procedure may be indicated in complex cases.[33,42] Postoperatively, children with cephaloceles are at risk for hydrocephalus, CSF leak, infection, and lesion recurrence.

Recurrence: The sporadic cases do not have an increased risk of recurrence.[28] In the presence of a genetic syndrome, recurrence can be increased.

AMNIOTIC BAND SYNDROME

Synonyms: Adhesions, amniotic disruption complex, amniotic bands, constricting bands.

Description: Amniotic band syndrome is a collection of malformations thought to be secondary to fetal entanglement in

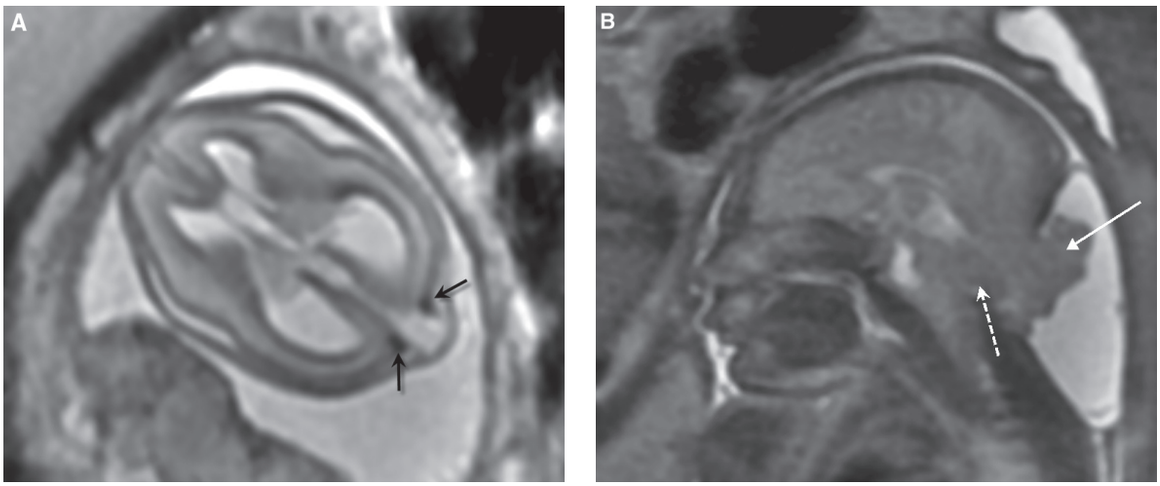

FIGURE 15.1-16: Cephalocele imaging on MRI **A:** Axial SSFSE T2 MRI showing meningocele containing CSF and venous sinuses as dark flow voids *(arrows)* along either side of the occipital skull defect, corresponding with US in Figure 15.1-12A. **B:** Sagittal SSFSE T2 image in occipital meningoencephalocele, corresponding to US in Figure 15.1-13, with sac containing supratentorial *(solid arrow)* and infratentorial *(dotted arrow)* brain.

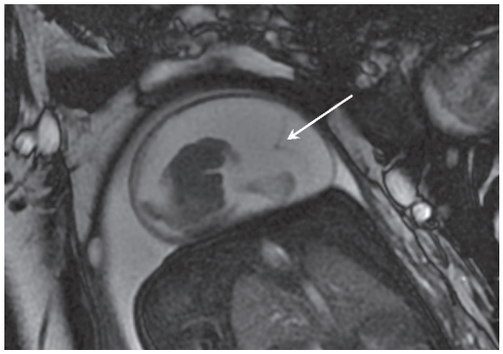

FIGURE 15.1-17: Coronal SSFP in same fetus as Figures 15.1-13 and 15.1-16B, showing membrane from herniated meninges *(arrow)*.

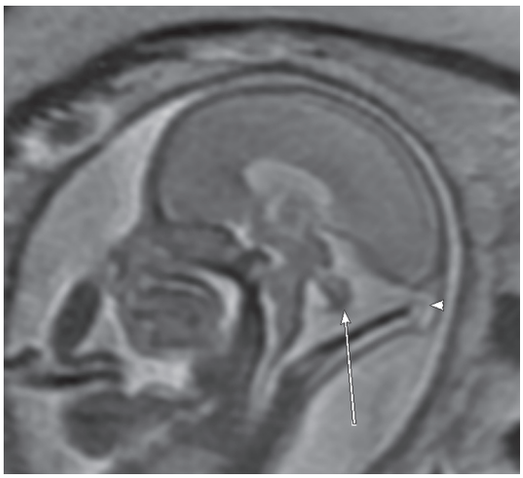

FIGURE 15.1-18: Sagittal SSFSE T2 image from fetus in Figure 15.1-12A, demonstrating occipital defect and sac *(arrowhead)* but also vermian hypogenesis *(arrow)*.

bands resulting in asymmetric defects that can involve the spine or the cranium.[66]

Incidence: 1 in 1,200 to 15,000 live births.[67]

Pathogenesis: Etiology is unknown. The exogenous theory suggests early amnion rupture leading to fibrous bands, which entrap the fetal body.[66] There is asymmetric amputation of fetal parts. If it occurs early, cranial or spinal defects may develop. The endogenous theory suggests lesions are secondary to vascular compromise. Neither mechanism explains all anomalies seen in this syndrome.

Diagnosis: Whenever unusual clefts are noted by US or MRI, such as asymmetric spine defects, cephaloceles, extremity amputation, or facial defects, the diagnosis should be considered. Clefts involving more than one region are also suggestive of the diagnosis.[67] Diagnosis has been made in the first trimester with nuchal translucency reported.[68]

Differential Diagnosis: Open NTD, anencephaly, encephalocele, limb body wall complex, and body stalk anomaly can look similar.

Associated Anomalies: Variable anomalies have been associated including major cranial, facial, thorax, abdomen, or spine anomalies. Limb constriction, clubfeet, scoliosis, and single digits are often noted.

Prognosis: Outcome depends on location size and number of defects.[69–72] Termination is considered if severe craniofacial and visceral abnormalities are present.

Recurrence: Most cases are sporadic.

INIENCEPHALY

Description: *Inion* is Greek for the nape of the neck. Iniencephaly involves the occiput and inion with rachischisis of the cervical and thoracic spine with fixed extension of the head. Iniencephaly apertus is associated with an encephalocele, while iniencephaly clausus has no encephalocele.[73–75]

Incidence: 0.1 to 10 in 10,000.

Etiology: Etiology is likely similar to other open NTD. Folic acid supplements may decrease the risk of iniencephaly. Antiepileptic drugs, diuretics, and sulfa drugs have all been associated with increased risk for NTD.[75,76]

Pathogenesis: Onset is likely a few days later than anencephaly. Features include deficit of the occipital bone with enlarged foramen magnum and partial or total absence of cervical and thoracic vertebra with lack of segmentation and irregular vertebral archfusion. Shortening of the spinal column with hyperextension of the cervical thoracic spine is present. The face is upturned with the mandibular skin continuous with the chest because of the short neck.

Diagnosis: AFP is typically elevated.[77]

Ultrasound: Fixed dorsal flexion of the head "star gazing," short cervical and thoracic spine, and irregular vertebrae can be noted by US. A common cavity between the spinal cord and the brain is present owing to the neural arch defects. The skin of the chest directly connects to the face, while the scalp is directly connected to the back[78–80] (Fig. 15.1-19). Polyhydramnios is often noted. Cephaloceles are present in the open form. Associated anomalies such as arthrogryposis can be identified. Three-dimensional sonography has been used to further assess this complex anomaly.[81]

MRI: MRI is a useful adjunct in confirming the diagnosis and is superior in the delineation of the complex brain and spinal cord anomalies.[74,76]

Associated Anomalies: Associated anomalies include cleft palate, anencephaly, cephaloceles, omphalocele, gastroschisis, congenital diaphragmatic hernia, cardiac malformations, renal anomalies, arthrogryposis, and clubfoot. Polymicrogyria, heterotopias, holoprosencephaly, and vermian agenesis have been reported.[73,78]

Differential Diagnosis: Differential diagnosis includes Klippel–Feil syndrome, which also has a short neck because of fusion of

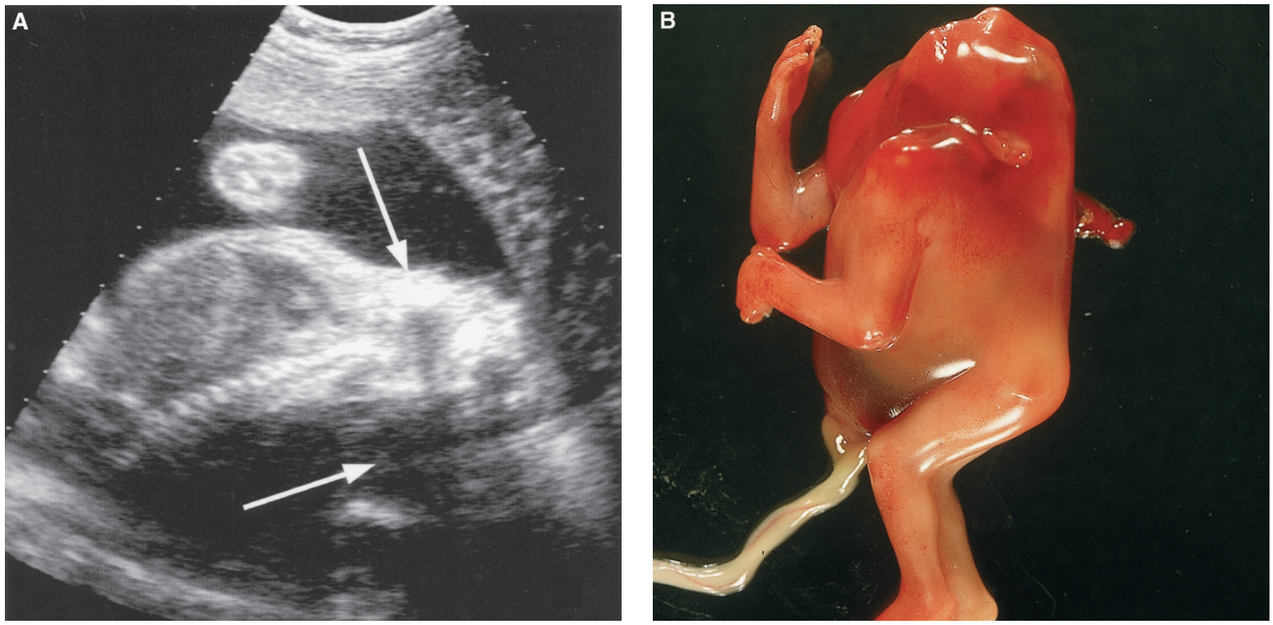

FIGURE 15.1-19: Iniencephaly. **A:** Sonogram shows the anterior neck *(top arrow)* is contiguous with the chest and the chin without the normal protrusion of the mandible. Note the retroflexion of the neck *(bottom arrow)*. **B:** Postnatal photograph of a similar case shows anencephaly with marked retroflexion of the neck. (From McGahan JP, Pilu G, Nyberg DA. Neural tube defects and the spine. In: Nyberg DA, McGahan DP, Pretorius DH, et al. *Diagnostic Imaging of Fetal Anomalies*. Philadelphia, PA: Lippincott Williams & Wilkins; 2003:291–334.)

cervical vertebrae and scapular anomalies. However, retroflexion of the head is typically not as severe, and AFP is normal. Anencephaly, cervical myelomeningocele, and encephaloceles should also be considered in the differential. In these cases, the cervical spine is typically normal.

Prognosis: Iniencephaly of both types are typically lethal. Cases of stillbirth or death within hours of delivery have been described.[79,82]

Management: Decisions regarding termination of pregnancy or providing supportive care at delivery should be discussed. Dystocia has been reported, and thus avoidance of a ceasarean section may require early induction.[82]

Recurrence Risk: The risk of recurrence increases to 1% to 5%.[76]

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