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HISTORY

G3P1 female at 11.3 weeks gestational age

- First pregnancy – Infant alive and well
- Second pregnancy – Fetus with "encephalocele" terminated. The patient was informed that recurrence was unlikely, but nonetheless was prophylactically started on high-dose folate before the current pregnancy. Review of the images from that case revealed virtually identical findings.
- Current Pregnancy – At 11.3 weeks gestational age the following images were obtained. After counselling the patient opted for termination.

FIGURES

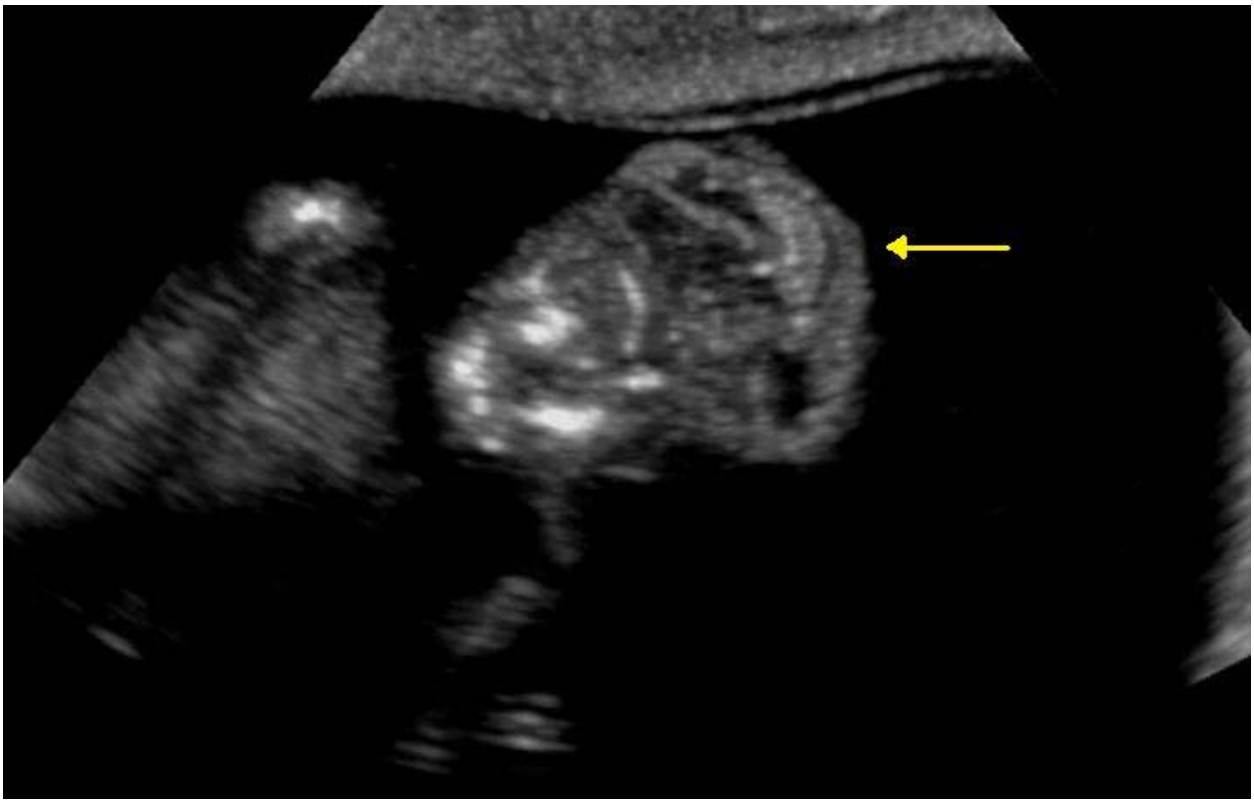

Figure 1A.

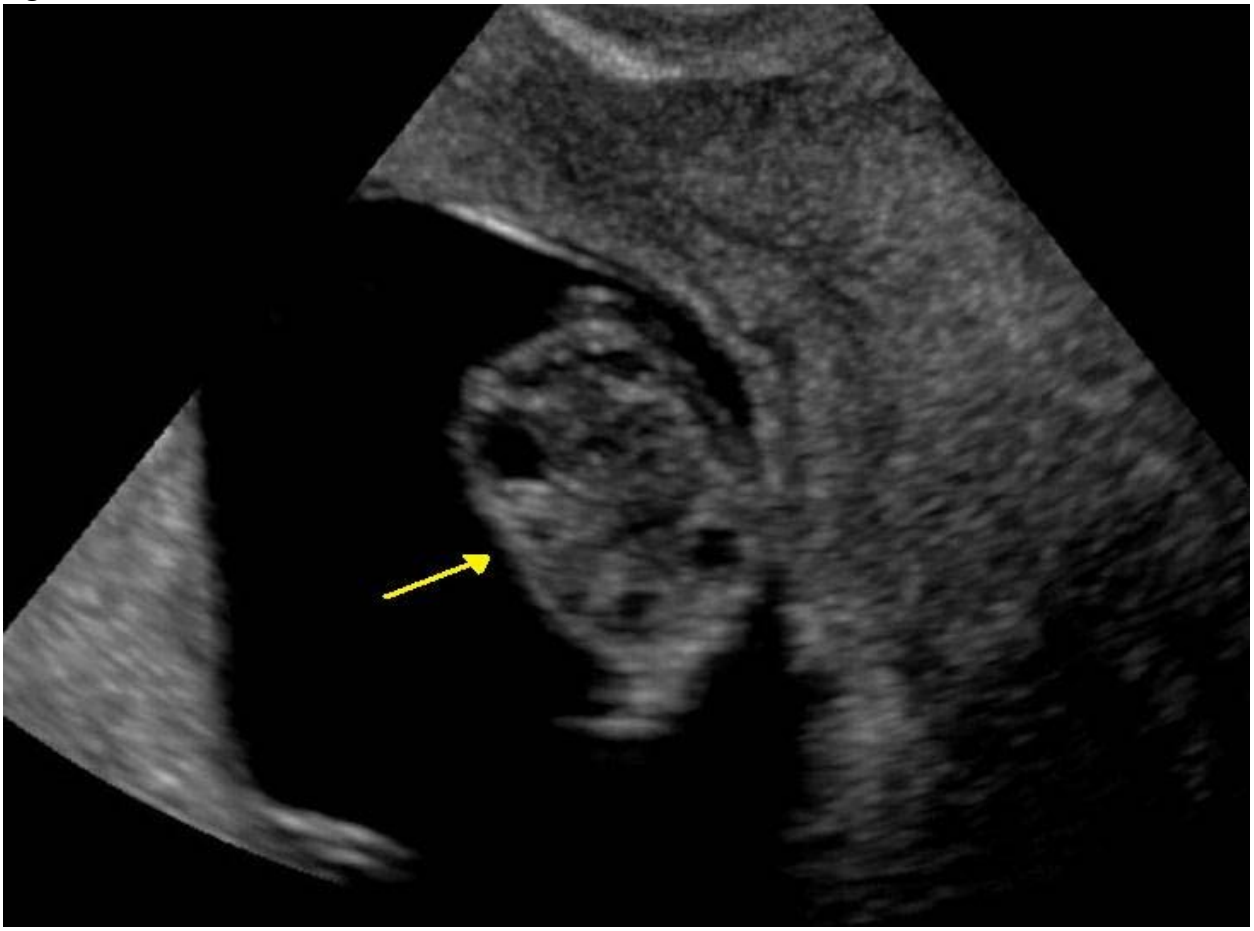

Figure 1B.

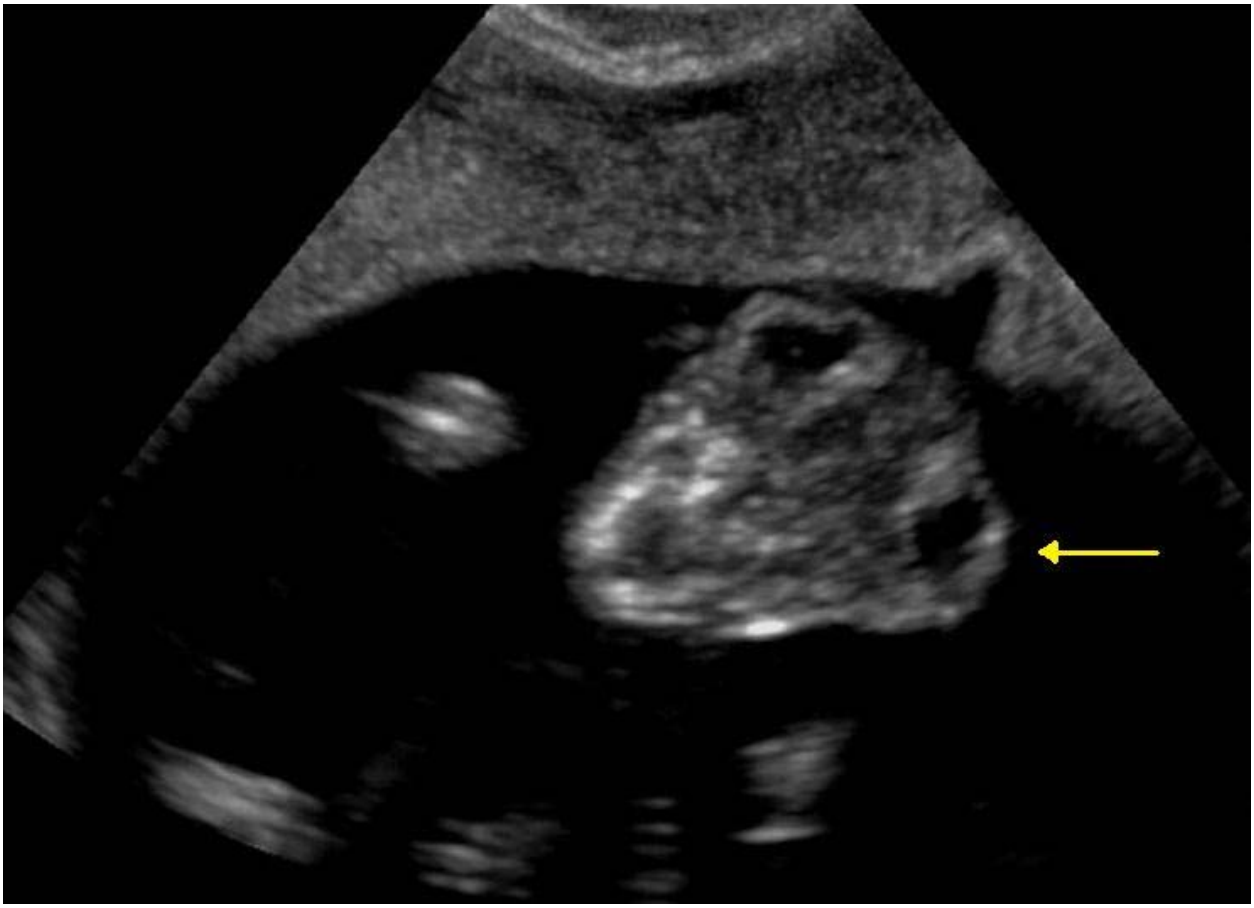

Figure 1C.

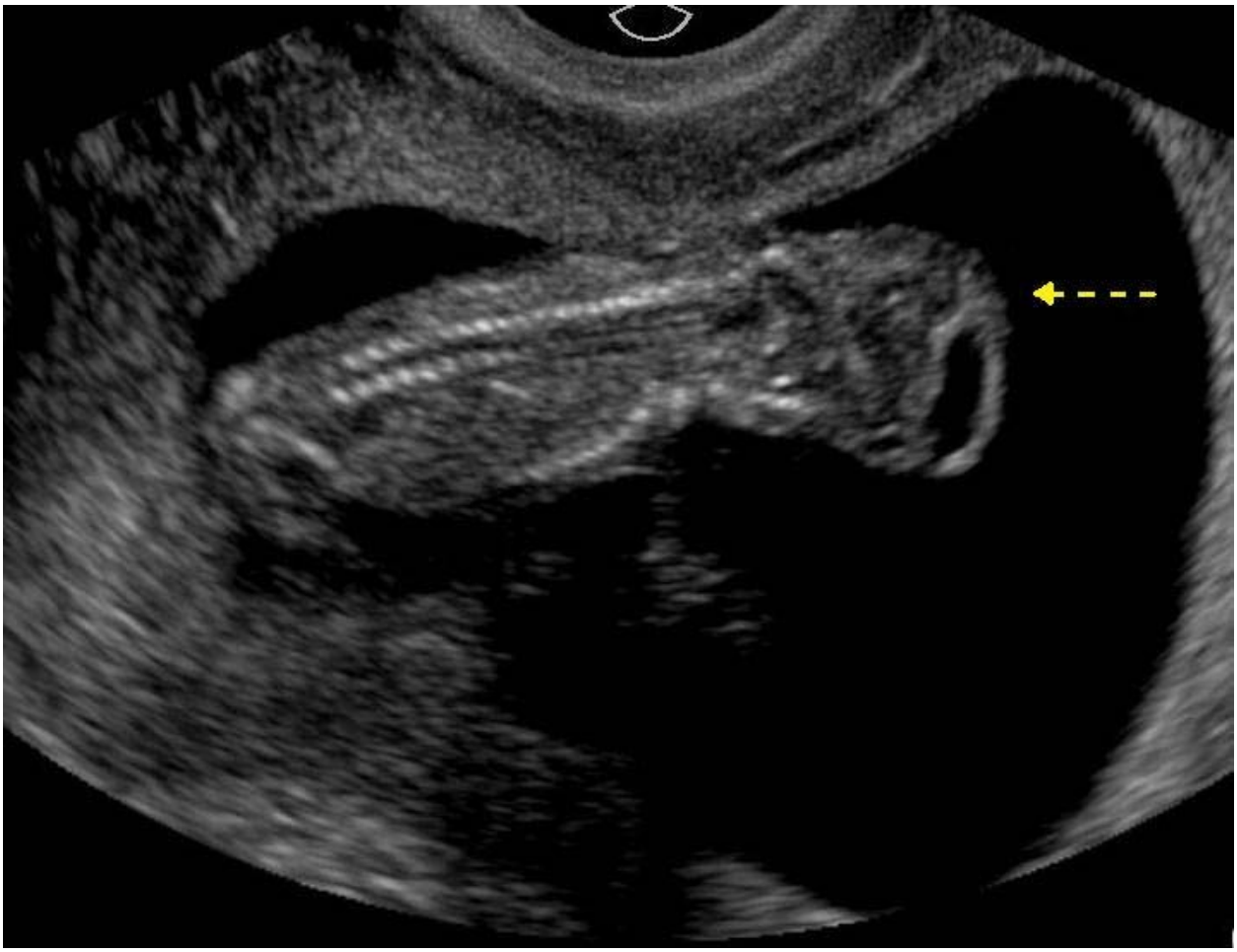

Figure 1D.

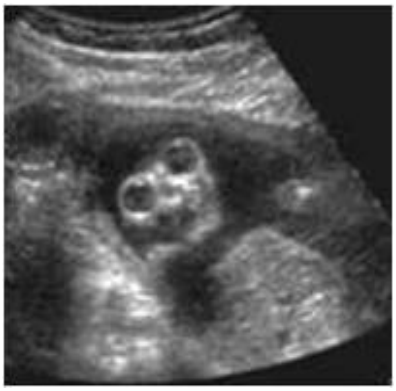

Figure 2.

FIGURE LEGEND

Figure 1:

Transvaginal ultrasound at 11.3 weeks gestational age. Note the large mass of dysmorphic brain tissue (arrows) and absent cranial vault ossification (perforated arrow). No normal brain tissue was identified.
A: Coronal Image, supraorbital mass of dysmorphic brain tissue (arrow).
B: Axial Image, dysmorphic brain tissue (arrow).
C: Coronal image, note "Mickey Mouse" appearance of dysmorphic brain.
D: Sagittal image, note absent calvarial ossification.

Figure 2:
Coronal image obtained in 3rd trimester demonstrates the classic "frog-eyed" appearance of anencephaly. No supraorbital brain tissue or calvarium is identified. The orbits appear to bulge contributing to the "frog eyed" appearance.

DIAGNOSIS: Exencephaly.

DISCUSSION

Definition: Exencephaly is a congenital lethal malformation where the brain tissue is dysmorphic and of variable volume, covered only by a thin membrane.

Significance: With the advent of the 11-14 weeks nuchal translucency examinations more cases are presenting early in pregnancy, thus familiarity with the sonographic signs of exencephaly is critical.

Background: Neural tube defects are the second most prevalent congenital anomaly in the United States, second only to cardiac malformations. Anencephaly is the most common neural tube defect, occurring in 1/1000 births. It carries an invariably lethal prognosis [1]. Exencephaly is hypothesized to represent the early appearance of foetuses that will go on to develop anencephaly. Acrania, exencephaly and anencephaly are characterized by an absent bony calvarium (variable degrees of absence). Acrania may occur in isolation; however, anencephaly and exencephaly are always accompanied by a degree of acrania. The majority of cases, > 90%, occur as a first time event. The incidence of anencephaly is increased in diabetes and among patients on anticonvulsants such as valproate and carbamazepine. There is no current treatment for an affected pregnancy; however, periconceptional folic acid supplementation is preventative. The concentrations of serum and red blood cell folate are lower in women carrying a fetus with a NTD. The recurrence risk for NTDs is approximately 2-4% with one affected sibling; the risk increases with each subsequent affected fetus. These high risk populations are recommended higher dose folate regimens than low risk populations.

Embryology: From an embryological perspective neural organogenesis occurs sequentially after 3-4 weeks gestational age. At 3-4 weeks, the neural tube closes. At 5-6 weeks, segmentation followed by diverticulation allows development of the forebrain and subsequently the cerebral hemispheres, thalami, optic and olfactory tracts, and the pituitary and pineal glands. So, at the time of an early obstetrical ultrasound at 10-11 weeks, normal findings include a relatively thin

brain parenchyma comprising hemispheres, thalami, and midbrain, surrounding relatively prominent ventricles and echogenic choroid plexus. Ossification of the frontal and parietal bones normally has taken place by this time [3]. If the neural tube fails to close, the neural parenchyma does not develop normally and the exencephaly – anencephaly sequence eventually results. Lack of normal development becomes progressively more obvious with increasing gestational age and anencephaly is usually diagnosed in the late second and the third trimester [4]. However, anencephaly is now favoured to be the end stage of a neural developmental anomaly spectrum, the earlier stages of which can be identified in the first trimester as exencephaly [5]. Thus first trimester diagnosis is predicated on the absence of normal brain development in association with absent frontal bone ossification at 10-11 weeks.

Ultrasound Findings: The ultrasound features of exencephaly in late first trimester include a mass of dysmorphic brain tissue in association with absent ossification of the flat skull bones above the orbits. Typically the volume of brain tissue is normal or even generous but is malformed (Figure 1). The appearance of an abnormally shaped head may be the initial clue to the diagnosis. The first trimester appearance of a broad bilobed brain in coronal imaging has been referred to as the "Mickey Mouse" sign (figure 1C) [6]. It is speculated that continued exposure to the injurious amniotic environment and ongoing mechanical trauma cause progressive degeneration of the exposed brain tissue ultimately resulting in the classic appearance of anencephaly where there is minimal remaining flattened brain tissue. This results in a "frog eyed" appearance of anencephaly where the orbits appear to be bulging and there is no supraorbital brain (Figure 2). An early indirect sign of the exencephaly/anencephaly sequence is a significant amount of low echogenic particulate matter within the amniotic fluid presumably due to the degradation of the exposed neural tissue. In later pregnancy polyhydramnios is commonly, secondary to absent or ineffective fetal swallowing [7].

Reliable sonographic diagnosis is usually possible by 10 -14 weeks gestational age, with virtually 100% sensitivity by the end of 14 weeks. A potential pitfall is an inexperienced operator who may confuse the rudimentary brain tissue with a normal fetal calvarium. Strict adherence to a policy of routinely identifying the normal brain anatomy and pattern of calvarial ossification in first trimester will minimize this pitfall.

Differential Diagnosis: The differential diagnosis will include conditions where there is decreased mineralization of the calvarium such as osteogenesis imperfecta type 2A or hypophosphatasia congenita; however, these conditions will have normal developmental brain anatomy. Large encephaloceles or sequelae of amniotic band syndrome may be confused with exencephaly. The former will have a similar prognosis and the latter will typically have other findings of amniotic band syndrome.

Management: The prognosis is dismal, with 75% fetuses stillborn and the remainder surviving for only short periods of time. Termination is considered an ethical option at any gestational age. Organ donation from anencephalic pregnancies have been suggested by some, but remain an ethically contentious practice. Counseling for future pregnancies should include a periconceptional high dose folate regimen. This regimen will prevent approximately 70% of

recurrence, although recurrence remains a possibility as in the case presented. Thus early screening with maternal serum alpha feto-protein and transvaginal ultrasound is recommended for subsequent pregnancies.

Conclusion: The diagnosis of exencephaly/anencephaly sequence can be reliably achieved by the end of the first trimester.

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