Prenatal sonographic features of fetal craniosynostosis

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Craniosynostosis is characterized as the early closure of the calvarial sutures.[1] The classification of skull malformations in craniosynostosis is based on the sutures involved.[1] Craniosynostosis involves approximately one infant in 2000 live births. More than 150 different types of craniosynostosis have been described and most isolated cases of craniosynostosis have multifactorial or sporadic inheritance,[2] although some families show autosomal dominant or autosomal recessive inheritance.[1,2] Cloverleaf and oxycephaly are complex forms that involve various combinations of closure of coronal, lambdoid, squamous and sagittal sutures.[1] Currently, craniosynostosis syndromes such as Crouzon's, Apert's and Pfeiffer's syndromes are mainly complex autosomal dominant appearances associated with other abnormalities.[1-4] Prenatal diagnosis of craniosynostosis depends mainly on the detection of associated anomalies and molecular analysis of fetal DNA, which is only possible in some syndromic forms in well-documented families.[1,2] It is not clear whether skull deformities arise as a straight result of premature closure of the suture.[2] The purpose of this report is to describe the prenatal sonographic findings in a fetus with craniosynostosis, and also to review the sonographic findings of all published cases of craniosynostosis that were specifically detected on sonography. This case is unusual due to the extremely prominent eyes at the time of diagnosis.

A 30-year-old Sudanese woman, gravida 2, para 1, was referred to the fetomaternal unit (FMU) of Hamad Medical Corporation, Doha, Qatar at 32 weeks of gestation after a third trimester sonogram performed in a private clinic revealed a skull deformity. Her prenatal course and family history were unremarkable. There was no relevant medical history, and she was taking no other medication. The first trimester and second trimester ultrasound were not performed. Before this time, the pregnancy had been completely uncomplicated, with excellent maternal health. The ultrasound examination at the FMU showed a singleton pregnancy with femur length and abdominal circumference consistent with a 32-week, 4-day gestation. The head circumference measurement, however, reflected a 29-week gestation. In the axial and coronal planes, the calvarium had brachycephaly and cloverleaf morphology. In addition, the eyes appeared extremely prominent (both orbits protrude 1.5 cm in front of the nasal plate in the axial plane), with the orbit diameters measuring 1.6 cm (both around the 50th centile) and the intra-orbital diameter 1.7 cm (around the 5th centile), suggesting the presence of hypotelorism. The abnormal fetal profile with frontal bossing and a low nasal bridge became more marked with gestation. However, no intracranial abnormality could be seen and the palate was intact, and the remainder of the ultrasound examination appeared normal. Fetal growth was normal and fetal echocardiography showed normal 4–chamber view and outflow tract. The placenta was located posteriorly, and the amniotic fluid volume was within normal limits. Obstetricians and pediatric neurosurgeons counseled the patient and her husband during the pregnancy that chromosome abnormalities were highly suspected and was offered genetic amniocentesis. She proceeded with fetal karyotype testing, and the result showed normal 46 XX chromosome. However, molecular testing for mutational analysis in the fibroblast growth factor receptors (FGFRs) from genomic DNA was not performed. Up until 39 weeks, the pregnancy had been uneventful. Based on the ultrasound findings, a presumptive diagnosis of Crouzon syndrome or Apert syndrome was made. After being informed about the possibility of a poor prognosis, the couple decided to continue the pregnancy. She was admitted for elective cesarean delivery at 39 weeks due to fetal abnormality. A baby girl was born with Apgar score of 6 and 9 at 1 and 5 minutes, and passed away on the second day. Examination of the neonate confirmed the ultrasound diagnosis (**Figures 1a & 1b**). The family declined autopsy.

Craniosynostosis is a congenital abnormality characterized by a premature fusion of one or more calvarial sutures and is classified into various syndromes or isolated craniosynostosis according to the clinical features.[1,2,5] The fusion can occur in any suture, either symmetrically or asymmetrically, and the profiles and skull shapes are different in each type of craniosynostosis.[1,2] For instance, synostosis of the coronal, sagittal and lambdoid sutures results in acrocephaly in Crouzon and Carpenter syndromes, and synostosis of coronal and sagittal sutures results in brachycephaly in Pfeiffer syndrome.[3,5] In Apert syndrome, brachycephaly results from synostosis of the coronal suture.[4,5] Cloverleaf skull deformity is the very striking consequence of intrauterine fusion of multiple cranial sutures. It may occur as an isolated occurrence or as part of a multiple malformation syndrome. In most cases, this condition is associated with poor prognosis. In the present case, the finding of prominent proptosis, brachycephaly, and

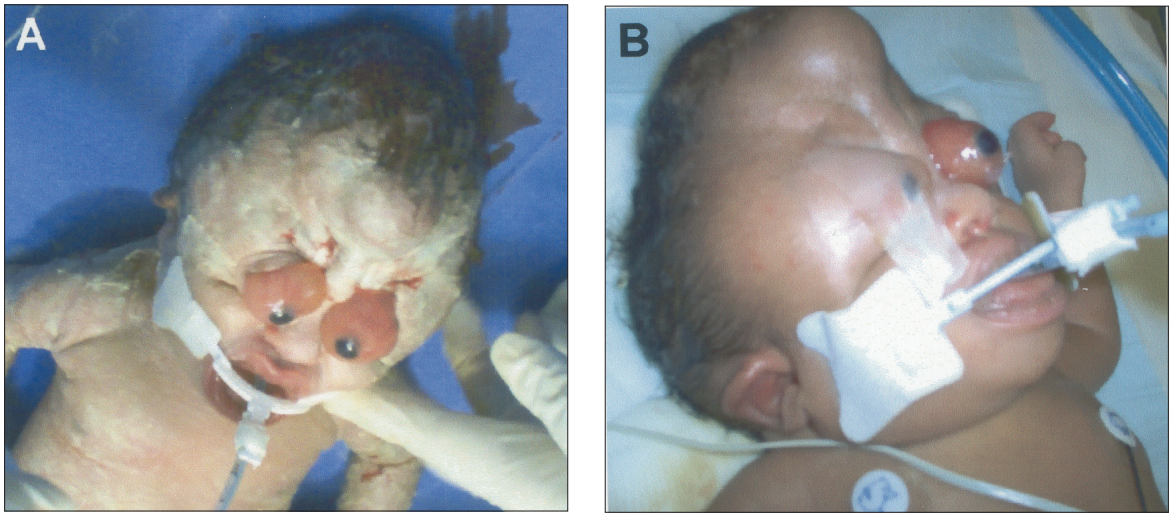

Figure 1 - Two-day-old neonate with suspected Crouzon syndrome showing **a)** high forehead and cranium, **b)** flattened nasal plate with prominent proptosis.

cloverleaf skull deformity during the third trimester led to a differential diagnosis of Crouzon syndrome. However, antenatal detection is difficult, as other specific ultrasound findings, including micrognathia, maxillary hypoplasia, and cardiac anomalies, which have been described in association with Crouzon syndrome were not found, and mutational analysis in the FGFRs gene was not performed.[1,2] Finger abnormalities such as polydactyly, or syndactyly, or both, are common in Carpenter, Apert and Pfeiffer syndromes.[4] Apert syndrome is characterized by craniosynostosis of the coronal suture, bilateral syndactyly of the fingers and toes, the presence of a broad distal thumb and big toes and mid-facial hypoplasia. It is consistent with autosomal dominant inheritance, although most cases arise by mutation.[4] Bernstein and colleagues described the prenatal diagnosis of Pfeiffer syndrome with a characteristic sonographic appearance of a clover-leaf skull.[3] In cases with the presence of one fused suture, such as in Apert syndrome, however, antenatal detection is difficult, because the deformity of the skull is not severe.[4] Pooh and colleagues[4] were the first to describe the details of the intracranial structure and morphological changes of the fetal profile in Apert syndrome. A significant number of patients with Apert syndrome are mentally retarded, but mental retardation is not so common in some of the craniosynostosis syndromes such as Pfeiffer and Antley-Bixler syndromes.[4] Coher and Kreiborg[6] suggested that malformations of the central nervous system may be responsible for most cases of mental retardation. Prenatal ultrasound findings may help us to recognize the fetal craniosynostosis during the intrauterine period. Every detail obtained from sonograms may act as secondary confirmation of suspected craniosynostosis. Hence, the prenatal diagnosis and counseling of parents in suspected cases is not easy and should be commenced cautiously.

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