

## Quiz

### **Prenatal Diagnosis of Crouzon Syndrome by 2D Ultrasound Chawla et al. 2D USG to diagnose Crouzon Syndrome prenatally**

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#### **What is your Diagnosis?**

A 33year old, gravida three with previous 2 living issues was referred to our institute at 31 weeks period of gestation [POG] with an ultrasound finding of polyhydramnios. The patient belonged to a remote hilly area of the state and she did not seek any antenatal care in the first or second trimesters. On account of polyhydramnios, we performed a detailed anatomical survey of the fetus by 2 dimensional (2D) ultrasonography, and we were confounded by following subtle abnormalities: brachycephaly [Figure 1] with borderline increased cephalic index (85.3%), prominent and easy visualization of the eye balls and eyelids suggestive of orbital proptosis [Figure 2 and 3], mildly depressed nasal bridge with a beaked nose. [Figure 4]. Binocular and interocular distances were normal. All four limbs were normal. No other structural defect could be identified in the fetus. Maximum vertical amniotic fluid pocket was only 6 cm [1].

The husband reached the hospital only a day later. We were astonished to find that the father had similar dysmorphic facial features as well. Father revealed that the couple's two older children (a boy and a girl) looked like him too. He had a broad head with exophthalmos, widely separated and deviated eye balls, beaked nose and mid facial hypoplasia. His intelligence was normal and there was no associated structural defect in any other body part.

## Answer

Patient underwent a spontaneous normal vaginal delivery at 38 weeks and delivered a male baby of 3.1 kilograms. Baby [Figure 5] was born with all previously mentioned subtle dysmorphic features. Baby and father were evaluated by the geneticist at the institute. The phenotypic features of father, two previous children, this baby and the suggestive inheritance pattern all pointed towards a diagnosis of Crouzon syndrome. The family did not opt for genetic analysis due to financial constraints.

Crouzon syndrome is a rare disorder with an incidence of 15-16 cases per million live births.[2] It is an autosomal dominant disorder although sporadic cases have been reported too. It occurs due to mutations in fibroblast growth factor receptor 2 (FGFR2) gene located on chromosome 10.

Facial dysmorphism and related abnormalities in craniosynostosis depend upon which and how many of the cranial sutures fuse prematurely. Even after premature fusion of the sutures (may be in utero or after birth) the brain still continues to grow along the plane of remaining open sutures and the pressure gives an abnormal appearance and shape to the skull.[3,4,5] Crouzon syndrome is most commonly associated with bi-coronal synostosis that gives the typical brachycephaly. Other cranial sutures may fuse as well. Abnormal premature fusion of various sutures of base of skull and face is associated with midface hypoplasia and beaked nose (psitticorhinia). Retrusion of lateral and inferior orbital margins results in shallow orbits leading to proptosis and exotropia.[6] Structural abnormalities of the ear, narrowing and stenosis of the ear canal may lead to hearing loss. Arnold Chiari malformation is seen to be common in patients of Crouzon syndrome. Affected babies need to be followed up for development of ventriculomegaly and increased intracranial pressure. Choanal atresia and abnormalities of upper airway may lead to life threatening respiratory distress at birth. Since it is an autosomal dominant disorder with variable expression, the phenotype may be variable, even in members of the same family, with certain members having more prominent features and others having subtle dysmorphism as was in our case. The baby born in our case had most of the typical characteristic features (brachycephaly, proptosis, exophthalmos and beaked nose) however there was no hypertelorism or midface hypoplasia. Even the exophthalmos was very subtle.

Prenatal diagnosis of cranio-synostotic syndromes has been deemed difficult especially when gross abnormalities of fetal head are not present.[7] Even though Crouzon syndrome is the commonest of the cranio-synostotic syndromes, its prenatal diagnosis is extremely challenging and has rarely been reported in literature as the skull abnormalities may be very mild and there is lack of associated limb abnormalities.[7] To our knowledge there are very few reports of prenatal diagnosis of Crouzon syndrome by ultrasonography in literature till date. Prenatal diagnosis of Crouzon syndrome was first made in 1989 by Menashe et al in a 35 weeks period of gestation fetus where exophthalmos was the only facial abnormality detected on ultrasound.[8] Leo et al diagnosed Crouzon syndrome in a 16 weeks POG fetus with increased binocular and interocular diameters.[9] In 1993, Gollin et al identified a fetus with Crouzon syndrome at 23 weeks with cloverleaf skull, exophthalmos, hypertelorism with mild ventriculomegaly.[10] The same year, Escobar et al reported prenatal diagnosis of another fetus with Crouzon syndrome at 20 weeks period of gestation and with a positive family history.[11] In 2002, Miller et al published a retrospective study where they reported prenatal diagnosis of two cases, at 20 and 22 weeks by

noting brachycephaly and hypertelorism.[12] Norgaard et al in 2011 reported prenatal diagnosis of Crouzon syndrome in a 35 week fetus using both 2D and 3D ultrasonography.[13]

It is be important to identify cranio-synostotic syndromes prenatally for the following reasons: If diagnosis made is within the legal limit, parents may be offered an option of a medical termination of pregnancy; parents should be prepared for the birth of the child with special needs; to facilitate in-utero transfer/referral of mother to a tertiary care center equipped with facilities for a multidisciplinary (neonatology, geneticist, neurosurgeon, oro-maxillofacial surgeons) management of such syndromic babies; also a team should be ready for immediate management of anticipated respiratory compromise at birth of such affected babies.

**Informed Consent:** Informed consent from parents of baby was taken for purpose of publication The authors declare no conflicts of interest

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**Figure 1.** Ultrasound image (2D) of fetal head showing brachycephaly with cephalic index more than 85% [Biparietal Diameter (BPD)= 8.11 cm, Occipito – Frontal Diameter (OFD) = 9.5 cm , Cephalic index (BPD/OFD) = 85.4%]



**Figure 2.** Ultrasound image (2D) of coronal view of fetal face demonstrating easily visible eyeballs and palpebrae suggestive of orbital proptosis



**Figure 3.** Ultrasound image (2D) of transverse section of fetal face demonstrating bulging eyeballs suggestive of orbital proptosis



**Figure 4.** Ultrasound image (2D) of fetal facial profile showing mildly depressed nasal bridge with a beaked nose



**Figure 5.** Subtle dysmorphic features of the neonate including a broad head, orbital proptosis, depressed nasal bridge, beaked nose consistent with typical phenotype of Crouzon syndrome