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RESEARCH LETTER

Prenatal diagnosis of frontonasal dysplasia using 3D ultrasound

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CASE REPORT

The presented case involves healthy non-consanguineous parents of caucasian origin, with no significant past medical history. This was the mother's first pregnancy at the age of 31 and followed spontaneous conception; pregnancy was uneventful until the mid-trimester routine anomaly ultrasound scan was performed at the patient's district hospital. The findings from this were of a normally grown female foetus with normal head shape, brain, spine, heart, kidneys, bladder, abdomen, thorax and limbs. The foetal profile was however abnormal, and showed an unusually flat profile with an absent or abnormal nasal bone. As a result of this ultrasound scan, the mother was referred to her local foetal medicine centre where a follow-up scan confirmed the abnormal facial profile finding (Figure 1(a)) in conjunction with borderline hypertelorism (intra-ocular diameter 15 mm, extra-ocular diameter 40 mm). The remaining foetal anatomy, including foetal lip measurements was normal though there appeared to be mild micrognathia. The foetus was normally sized for gestation. To gain more information and aid potential morphological genetic diagnosis, a 3D ultrasound examination as well as an MRI were carried out at 28 weeks' gestation. 3D ultrasound confirmed the abnormal facial finding and suggested an abnormally wide and flat nose that was skewed to one side (Figure 1(b)). MRI confirmed normal foetal brain appearance, but was unhelpful in further examination of the foetal face. The patient was counselled that differential diagnosis for the findings was Trisomy 21 (due to the absent nasal bone), Wolf-Hirschhorn syndrome, fronto-facial-nasal dysplasia or frontonasal dysplasia (FND; OMIM 136 760). Karyotyping was offered and performed by chorionic villus biopsy, revealing a normal female pattern (46,XX) with no $4p^-$ deletion. With apparently normal karyotype, the appearances were strongly suggestive of FND. The parents were informed of this likely diagnosis and its implications and after counselling, chose to continue the pregnancy, the remainder of which was uneventful. Serial ultrasound assessments showed normal growth and the child was born after spontaneous labour at term. Post-natal examination of the female child revealed all the features suggested by the prenatal investigation with the addition of the classical 'widow's peak' seen with FND (Figure 1(b)). No other additional features of FND were detected and the child's eyes were normal, thus excluding the other differential diagnosis of Fronto-facial-nasal dysplasia. Neuro-developmentally, the child appears to be normal at 1 year of age.

To our knowledge, this is the first description of a prenatally diagnosed FND using 3D ultrasound. FND is a heterogeneous syndrome affecting midline facial development with marked hypertelorism and a broad nasal tip which is cleft in most cases. Other features include a 'widow's peak' hairline, anterior encephalocele, anterior cranium bifidum, pre-auricular tags and low-set ears, agenesis of the corpus callosum and notching of the alae nasi. Micrognathia which was present in this case is not commonly found in FND and probably represents a constitutional variant in this case. Central nervous system involvement is uncommon and importantly, post-natal mental development is usually normal, although mental retardation and abnormalities of the corpus callosum have been described in previous cases (Pascual-Castroviejo *et al*., 1985). Eye abnormalities including strabismus, nystagmus, ptosis, optic nerve hypoplasia and colobomata, cataracts and corneal dermoids have also been described (Roarty *et al*., 1994), but these are more often found in the more severe fronto-facial-nasal dysplasia syndrome which is associated with the more severe facial hypoplasia. Most reported cases of FND are sporadic, but there have been reports of autosomal recessive inheritance in consanguineous families. The availability of 3D ultrasound is increasing, but its clinical usefulness has not yet been validated in many conditions. One exception to this is facial abnormality where 3D ultrasound examination has been shown

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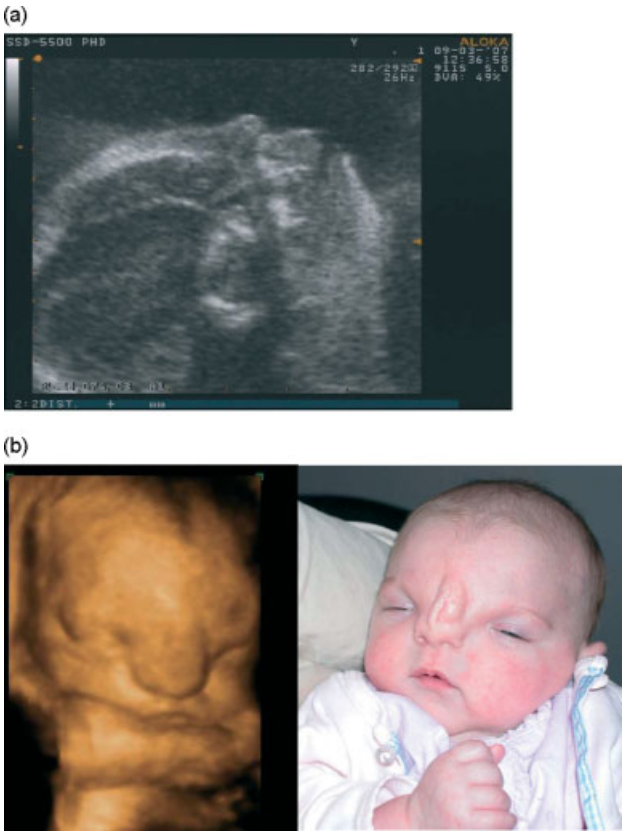

Figure 1—(a) Profile of foetus using 2D ultrasound at 20 weeks' gestation. (b) Foetal face image using 3D ultrasound and comparison of post-natal image of the infant

to improve accurate and successful diagnosis (Kurjak *et al*., 2007). In the present case, although 2D ultrasound examination suggested an abnormal facial profile, and MRI provided reassuring foetal brain imaging, it was not until 3D ultrasound images were obtained that comparison with post-natal infants with FND was possible. As with cleft lip therefore, the use of 3D ultrasound to provide clinical geneticists a potential facial appearance produced a likely diagnosis. Currently, there is no known gene for FND, and therefore while the 3D images were suggestive of the syndrome, it was not possible to provide a definitive diagnosis prenatally; however, we were able to reassure the parents of this child of the likely outcome if the diagnosis proved correct. Following delivery, the facial findings of the child were strikingly similar to those obtained *in utero*, and after assessment the clinical diagnosis of FND was confirmed. The case presented demonstrates the increasing usefulness of 3D ultrasound technology in prenatal diagnosis, particularly in conditions involving the soft tissue of the face. This may allow dysmorphological diagnosis to be made in conditions with no cytogenetic or molecular abnormality, thus providing parents with more information than is currently available with 2D ultrasound.

PATIENT CONSENT

Full written consent was obtained from the parents of the subject for use of images and description.

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