

Early prenatal diagnosis of oculoauriculofrontonasal syndrome by three-dimensional ultrasound

J. M. JOHNSON*, B. BENOIT§, J. PIERRE-LOUIS*†, S. KEATING‡ and D. CHITAYAT*†

*Division of Maternal–Fetal Medicine, †The Prenatal Diagnosis and Medical Genetics Program and ‡Department of Laboratory Medicine and Pathobiology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada and §Princess Grace Hospital, Principality of Monaco

KEYWORDS: 3D ultrasound; cleft lip/palate; diagnosis; facial cleft; first trimester; prenatal diagnosis

ABSTRACT

Oculoauriculofrontonasal syndrome is a rare developmental field defect that represents an abnormal morphogenesis of the frontonasal eminence. It consists of features of both oculoauriculovertebral spectrum and frontonasal malformation. A few cases in the literature have described this syndrome, but to the best of our knowledge the present case is the first early prenatal diagnosis of this severe condition using three-dimensional ultrasonography. Copyright © 2004 ISUOG. Published by John Wiley & Sons, Ltd.

CASE REPORT

The mother was a 42-year-old woman, gravida 2 para 1, who conceived through a donor sperm insemination. A transabdominal ultrasound examination for nuchal translucency screening at 11 + 5 weeks' gestation showed an abnormal profile. The nasal bone and maxilla could not be seen, and there was severe micrognathia. Transvaginal ultrasound also showed a facial cleft. No other fetal abnormalities were visualized. Chorionic villus sampling was performed and revealed a normal female karyotype (46,XX).

A three-dimensional (3D) ultrasound scan (GE Voluson 730, GE Medical Systems, Waukesha, WI, USA) was undertaken to better delineate the extent of the facial abnormality. This showed a very extensive craniofacial abnormality, including a hypoplastic mandible and a large facial cleft extending from the upper lip to the inner canthus of the right eye. There was severe hypertelorism, low-set ears and an abnormally shaped nose with a single nostril (Figures 1a and 2a). The images were reviewed with the parents, who felt that

the 3D images, compared to the two dimensional (2D) images, enabled them to better appreciate the extent of the abnormality. The differential diagnosis prenatally included Treacher Collins syndrome, agnathia otocephaly and amniotic band syndrome. After much consideration, including consultation with professionals in medical genetics, craniofacial surgery and medical imaging, the parents elected to terminate the pregnancy at 18 weeks' gestation.

The autopsy confirmed the large facial cleft, severe hypoplasia of the maxilla and mandible, bifid nose with absent left nostril, low-set ears with microtia and preauricular skin tag, no left orbit or eyelid, absent right eyelids, hypoplasia of the optic nerves and micrognathia (Figures 1b and 2b). The brain was normal and the corpus callosum was present. No other significant abnormalities were found. The findings were consistent with the oculoauriculofrontonasal syndrome (OAFNS).

DISCUSSION

The term OAFNS was first coined by Carey and Yong¹ in 1981, and consists of features of both frontonasal malformation (FNM) and Goldenhar syndrome (oculoauriculovertebral spectrum, OAVS). The first report of this combination of clinical manifestations was by Gupta *et al.*² in 1968, and 25 cases have been reported to date^{1–7}. These cases were isolated, apart from one recurrence.⁸

FNM is an etiologically heterogeneous developmental field defect caused by an abnormal development of the frontonasal eminence⁶. It consists of midfacial anomalies that involve the eyes, nose, forehead and occasionally the brain⁹. The common features are orbital hypertelorism and an abnormal nose (bifid or cleft), and occasionally

Correspondence to: Dr J. M. Johnson, Division of Maternal Fetal Medicine, 4th floor, North Tower, Foothills Medical Centre, 1403–29th Street N.W., Calgary, Alberta T2N 2T9, Canada (e-mail: jjohnson@mtsinai.on.ca)

Accepted: 6 July 2004

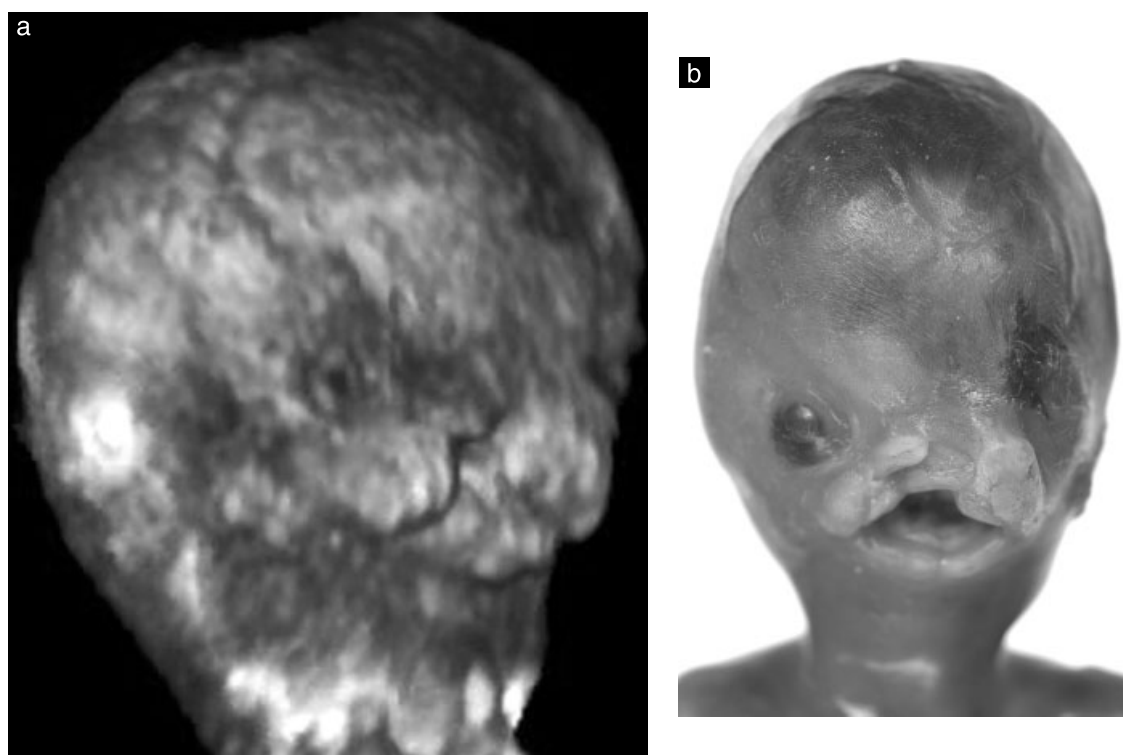


Figure 1 Three-dimensional ultrasound image showing hypertelorism and a large facial cleft (a). Frontal view of face at postmortem examination. The brow ridge and nasal bridge are absent and no left nostril is seen. The right eye is displaced laterally and the eyelids are absent (b).

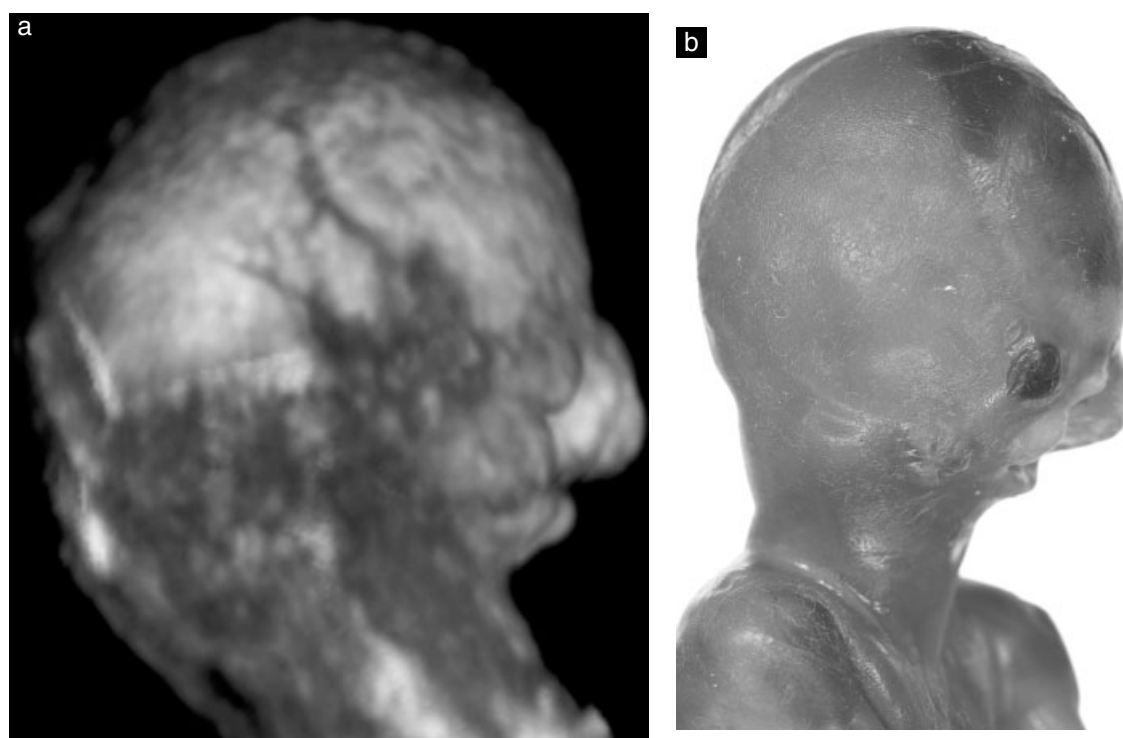


Figure 2 Three-dimensional image of the fetal profile (right side) showing large facial cleft and retrognathia (a). Right side of head at postmortem showing lateral displacement of right eye, lack of zygomatic arches, malformation of nose and mouth and pronounced micrognathia. The right ear is very low set and the pinna consists only of ridges of skin with no external auditory meatus (b).

Table 1 Abnormalities reported in frontonasal malformation (FNM), oculoauriculovertebral spectrum (OAVS) and oculoauriculofrontonasal syndrome (OAFNS) in comparison to the present case

Abnormalities	FNM	OAVS	OAFNS	Present case
Malar, mandibular, maxillary hypoplasia	–	+	11/20	+
Facial asymmetry	–	+	12/25	+
Cleft lip/palate	+	+	13/20	+
Epibulbar dermoid	–	+	17/25	–
Ear abnormalities, microtia/preauricular tags/pits	+	+	25/25	+
Notched/broad nasal tip	+	–	20/25	–
Vertebral abnormalities	–	+	3/18	–
Brain abnormalities	+	+	7/25	–

cleft lip. In severe cases, an anterior encephalocele may be present.

OAVS is a non-random association of abnormalities involving the first and second branchial arches. It encompasses a broader range of defects that include hemifacial microsomia and Goldenhar's syndrome⁷. The most common findings in this condition are epibulbar dermoids, cleft lip/palate, mandibular hypoplasia, facial asymmetry and occasionally midbrain lipoma, encephalocele and vertebral defects.

OAFNS has been described as a combination of both FNM and OAVS. However, the pattern of malformation primarily involves the craniofacies; the reported cases have no cardiac abnormalities or encephaloceles, and only occasional vertebral defects (two cases)⁸ (Table 1). The etiology of this condition is unknown and, apart from two siblings born to the same diabetic mother⁸, no recurrence has been reported. The findings in the present case are consistent with OAFNS (Table 1).

Although there have been several reports of postnatal diagnosis, prenatal diagnosis of this condition has not previously been reported. In the present case, the fetal position and maternal body habitus, especially at this

early gestation, did not allow us to establish views of the face by conventional 2D techniques. With the use of 3D ultrasound the surface rendering permitted us to appreciate the extent of the defect much more clearly than with 2D ultrasound, and provided critical information that enabled the couple to make an informed decision with respect to management of the pregnancy. The present case also illustrates the importance of evaluation of the fetal profile at the time of the 11–14-week scan and the benefits of early and accurate diagnosis.

REFERENCES

- Carey JC, Yong SL. Frontonasal dysplasia and Goldenhar syndrome: the oculo-auriculo-frontonasal syndrome. Paper presented at the Conference on Malformations and Morphogenesis (March of Dimes), Dartmouth College, Hanover, NH, USA, 1981.
- Gupta JS, Gupta SD, Prashar SK. Oculo-auricular-cranial dysplasia. *Br J Ophthalmol* 1968; 52: 346–347.
- Guion-Almeida ML, Richieri-Costa A, Saavedra D, Cohen MM J. Frontonasal dysplasia: analysis of 21 cases and literature review. *Int J Oral Maxillofac Surg* 1996; 25: 91–97.
- Cohen MM Jr, Sedano HO, Gorlin RJ, Jirasch JE. Frontonasal dysplasia (median cleft face syndrome): comments on etiology and pathogenesis. *Birth Defects Orig Artic Ser* 1971; 7: 117–119.
- Tenconi R, Hall BD. Hemifacial microsomia: phenotypic classification, clinical implications, and genetic aspects in treatment of hemifacial microsomia. In *Treatment of Hemifacial Microsomia*, Harvold EP, Vargervik K, Chierici G (eds). Alan R Liss: New York, NY, 1983; 33–39.
- Casey HD, Braddock SR, Haskins RC, Carey JC, Morales L. Frontonasal malformation and the oculoauriculovertebral spectrum: the oculoauriculofrontonasal syndrome. *Cleft Palate Craniofac J* 1996; 33: 519–523.
- Ishmael HA, Begleiter ML, Regier EJ, Butler MG. Oculoauriculofrontonasal syndrome (OAFNS) in a nine-month old male. *Am J Med Genet* 2002; 107: 169–173.
- Golabi M, Gonzalez MC, Edwards MS. A new syndrome of oculoauriculovertebral dysplasia and midline cranial facial defect; the oculoauriculofrontonasal dysplasia. Two new cases in sibs. *Birth Defects Orig Artic Ser* 1983; 19: 183–184.
- Fratterelli JL, Boley TH, Miller RA. Prenatal diagnosis of frontonasal dysplasia (median cleft syndrome). *J Ultrasound Med* 1996; 15: 81–83.