17 3D Virtual Model Reconstruction by 3D Ultrasound Volume Data Sets in a Case of Prenatally Diagnosed Agnathia/Otocephaly Complex Associated with Multiple Congenital Anomalies

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17.1 Introduction

Agnathia/otocephaly complex (OMIM 202650) is a rare congenital malformation characterized by multiple malformations involving anatomic structures originating from the first pharyngeal arch as a consequence of failed mesenchymal migration of the maxillary prominence and atrophy of the development of the mandibular prominences [1]. Features of agnathia/otocephaly complex are absence or hypoplasia of the mandible, microstomia, hypoglossia/aglossia, and variable anterior midline fusion of the ears (melotia, synotia) [2]. An incidence of less than 1 in 70,000 births has been estimated [3]. The complex has been linked with a heterozygous mutation of the PRRX1 gene on chromosome 1q24. Genotype/phenotype heterogeneity is possible, and the disease may be inherited in either autosomal recessive or autosomal dominant patterns. In addition, association with environmental teratogens have been described [2, 4]. Recently, it has been demonstrated that perturbations in the PRRX1 and OTX2 genes may alter DNA signaling pathways, suggesting a role in palatal development [2, 5, 6].

17.2 Case Description

A 39-year-old nulliparous woman was referred for level II ultrasound examination for an unspecified complex facial anomaly detected on a routine third-trimester scan. The ultrasound examination was performed using transabdominal and transvaginal two-dimensional (2D) and three- and four-dimensional (3D/4D) volumetric probes. Digital 2D ultrasound imaging and 3D/4D volume datasets were stored onto an optical disk for offline analysis. Ultrasound

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examination showed findings consistent with congenital agenesis of the mandible (agnathia), proboscis, and hypotelorism (Fig. 17.1). Multiple skeletal anomalies were visualized, consisting of the absence of the right ulna and right fibula associated with shortening of the contralateral long bones, syndactyly of 5th finger of right hand, and bilateral clubfoot. A multicystic right dysplastic kidney, single umbilical artery, and polyhydramnios were additionally seen. 3D ultrasound volume datasets were transmitted to an expert at remote site (HW) and a physical model reconstruction on photopolymerized resin was constructed using postprocessing software. Specifically, Mimics v. 12, Materialise (Leuven, Belgium), was used for 3D virtual model reconstruction, and the model was exported into a standard triangular language (STL) format and converted into an "OBJ" extension for adjustment using 3D modeling polygonal software (Autodesk Mudbox, San Francisco, CA, USA).

A presumptive diagnosis of agnathia/otocephaly complex associated with multiple congenital anomalies was entertained (Fig. 17.2). Although prognosis of the disease was poor and the parents declined fetal magnetic resonance imaging (MRI) investigation, the 3D virtual model improved the parents' understanding of the fetal anomalies and aided counseling. Termination of pregnancy was not performed due to legal limitations. Intrauterine fetal demise occurred shortly after ultrasound examination and gross pathology confirmed the antenatal diagnosis (Fig. 17.3). Interestingly, the anatomic details of the 3D virtual model substantially overlapped with the characteristic features of the agnathia/otocephaly complex.

17.3 Discussion

Agnathia/otocephaly complex may be isolated [7] or associated with other anomalies. Anencephaly and meningomyelocele [8], skeletal, genitourinary, and cardiovascular anomalies, and situs inversus have been reported [3]. However, the most common associated congenital anomaly is holoprosencephaly [9, 10].

The antenatal diagnosis of agnathia/otocephaly complex is challenging. Although it has most commonly been detected in the third trimester [4, 11, 12], detection at 12 weeks has also been reported [13]. 3D ultrasound ultrasound may aid the prenatal diagnosis of agnathia/otocephaly complex [4, 10–13] and a systematic look at the "CHIN" is advocated ("CHIN": *c*hin, *h*eadbone outline, *i*nner head, *n*uchal translucency) [13]. 3D ultrasound has also proven to be of clinical value in the characterization of the disease and in planning neonatal treatment by the multispecialty team [14], although outcome is generally poor and newborns requires ventilatory support [1].

In addition to 3D virtual modeling of the anomaly that improves parents' understanding and enhances prenatal counseling, 3D computed tomography (CT) scan has been used postmortem in a case of agnathia/otocephaly complex associated with organomegaly to obtain detailed anatomic information about this lethal disease [15].

This work was based on a previously published report [4].

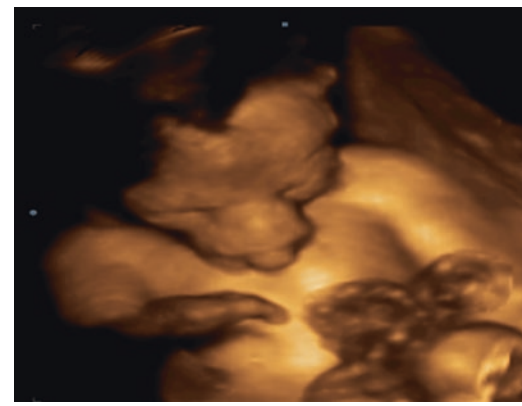

Fig. 17.1 Three-dimensional ultrasound in surface-rendering mode showing proboscis and severe hypotelorism

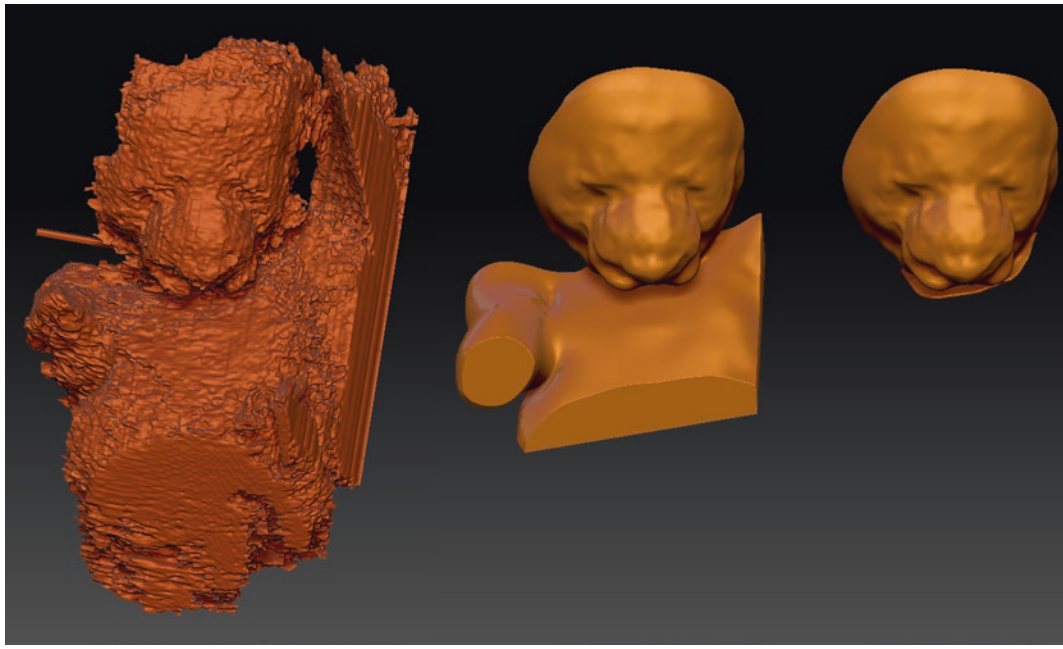

Fig. 17.2 3D virtual physical model showing the typical features of the congenital malformation

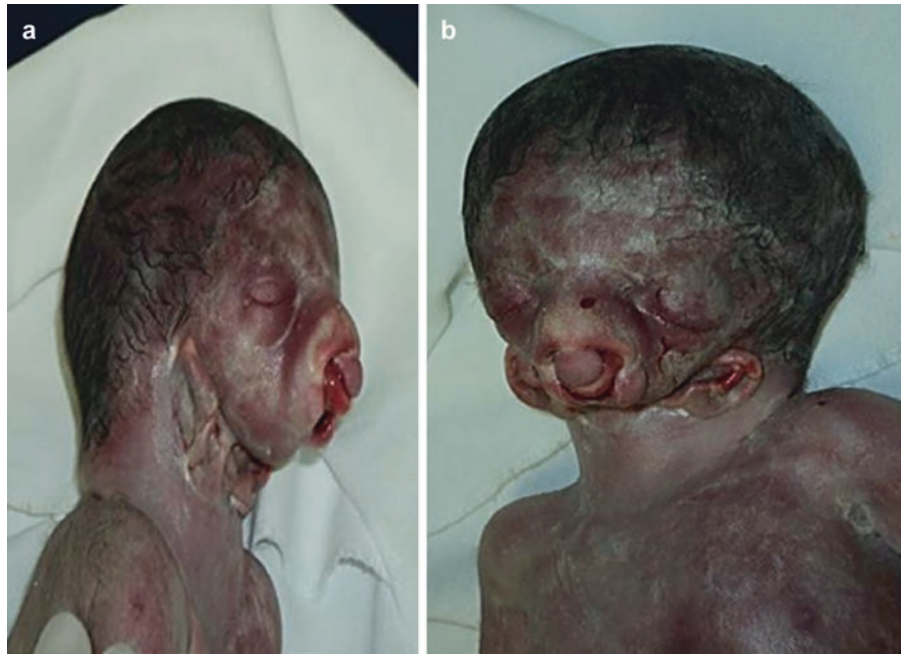

Fig. 17.3 Postmortem photographs showing the agnathia/otocephaly complex in lateral (**a**) and frontal (**b**) views confirming the accuracy of the prenatal ultrasound diagnosis

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