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Case Report

Hysteroscopic fetoscopy: A role as virtuopsy for parents who refuse full autopsy? A case of facial clefting, proboscis, and limb deformities

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ABSTRACT

Objective: To describe the value of hysteroscopic fetoscopy (*virtuopsy*) at the time of uterine suction in a case of early diagnosis of congenital anomalies in parents refusing conventional full autopsy examination.
Case report: First trimester ultrasound diagnosis of proboscis, median cleft lip and palate and limb deformities. Chorionic villus sampling demonstrated normal karyotype. Parents refused medical induction of termination of pregnancy with subsequent conventional autopsy. At this stage, hysteroscopic fetoscopy was consented and carried out under local anesthesia prior to uterine evacuation.
Conclusion: Hysteroscopic fetoscopy (*virtuopsy*) proved to be a valuable complementary diagnostic investigation and enhanced the parental bonding process concerning the fetal phenotype. Notwithstanding, the woman declared an acceptable compliance during the procedure. In selected cases, *virtuopsy* may be a valid option in confirming early prenatal ultrasound diagnosis in parents refusing conventional autopsy or when full postmortem examination may not be clinically indicated or warranted.

Introduction

Proboscis may be attributed to a lesion occurring at embryological stage 13, which in the Carnegie staging system corresponds to an embryo with maximum length of 4–6 mm at approximately 32 days postfertilization. Convergence of the nasal disks indicates a head with a narrow median region, a nasal septum that fails to develop, and a single nasal cavity with a single nostril [1].

The lip usually closes by Week 4 of gestation and the palate by Week 12; specifically, the primary palate fuses between 4 weeks of gestation and 6 weeks of gestation, whereas the secondary palate fuses between Weeks 8 and 12. The unilateral cleft lip results from the failure of the maxillary process to close with the medial nasal prominence, and the clefting of the secondary palate is due to the failure of the palatine process to elevate or grow. Cleft palate always starts at the uvula (*uvula bifida* as the mildest form) and proceeds anteriorly along the midline to affect either the soft palate only or both the soft and hard palates, whereas cleft lip and palate always starts at the lip and proceeds dorsally (alveolus, hard palate, and soft palate) [2].

Case Report

A 28-year-old primigravida with a body mass index (BMI) of 40 kg/m^2 underwent first-trimester screening for Down syndrome at 12 weeks and 1 day of gestation. The ultrasound examination was performed using a Voluson E8 ultrasound apparatus (GE, Healthcare Medical System, Milwaukee, WI, USA) with a 4–8-MHz RAB4D multifrequency probe. Two-dimensional (2D) transabdominal ultrasound performed on the sagittal and coronal planes of the fetal face revealed an abnormal profile. This was followed by three-dimensional (3D) ultrasound in the multiplanar mode with volume rendering and tomographic ultrasound imaging (TUI), which was more effective than 2D ultrasound and led to a diagnosis of orofacial clefting (cleft lip *plus* cleft palate) associated with proboscis (Figure 1).

TUI was performed using thin (1-mm) slices with an interval of −3 mm to 3 mm. The facial cleft was displayed on reference line 0 (green reference dot), and the proboscis was shown on lines +2

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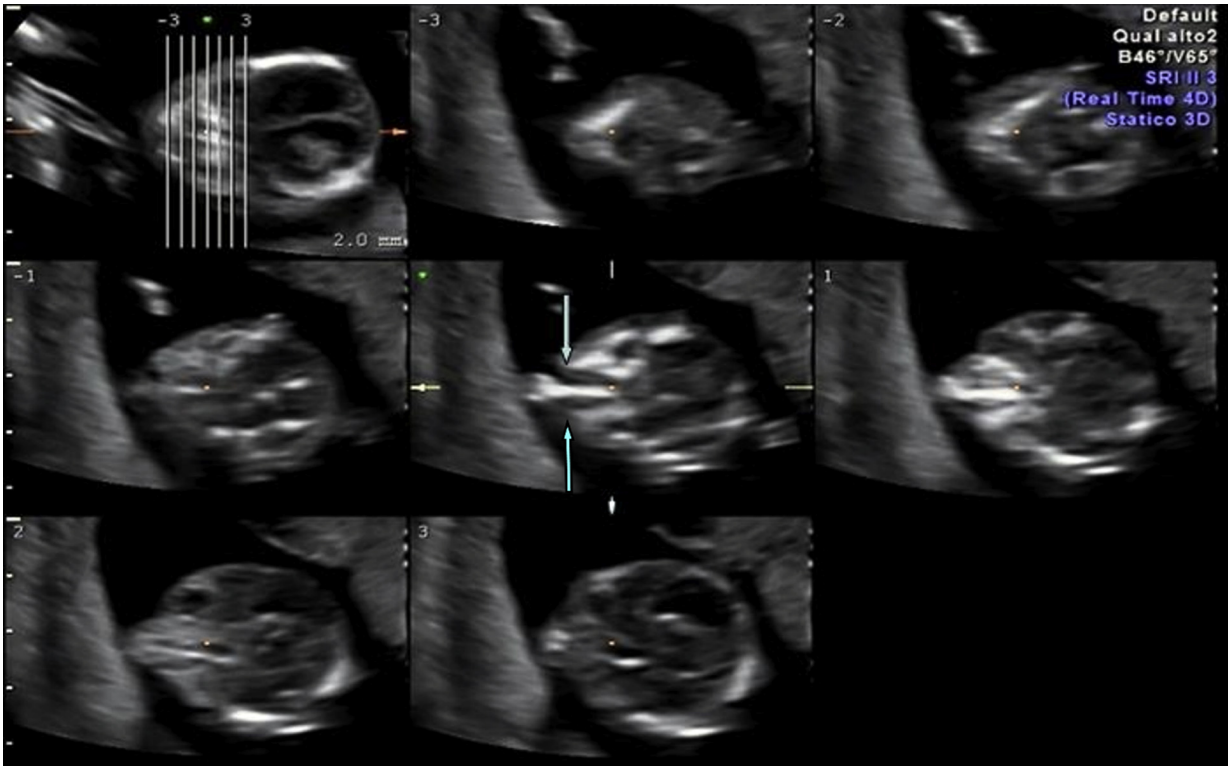

Figure 1. Tomographic ultrasound imaging of the fetal face (comprising the portion from the fetal orbits to the fetal chin), performed using thin (1-mm) slices, revealed median clefting (cleft lip *plus* cleft palate; marked by arrows).

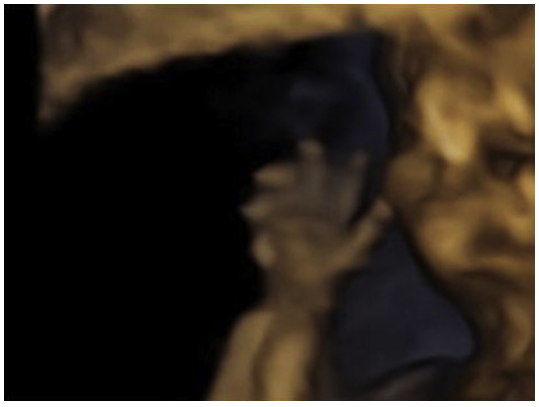

Figure 2. Three-dimensional ultrasound with surface rendering mode showing the proboscis and polydactyly of the right hand.

and +3. Limb deformities involving the upper limbs were detected; however, due to the high maternal BMI of 40 kg/m^2, precise resolution of this area was not possible. Polydactyly of the right hand and syndactyly of the left hand were identified on ultrasound (Figure 2).

Genetic counseling was offered, and chorionic villus sampling performed at 12 weeks and 2 days of gestation revealed a 46,XY fetus. Because of the major fetal congenital abnormalities, the parents requested termination of pregnancy, but refused administration of vaginal prostaglandin E and subsequent full necropsy examination; however, the mother consented to undergo hysteroscopic embryoscopy (*virtuopsy*) under local anesthesia prior to uterine evacuation.

The woman was placed in the dorsal lithotomy position, and the cervix and the vagina were cleansed with Betadine. One ampoule of lidocaine was injected laterally into the cervix. After dilation of the cervical canal until Hegar 5 mm, a rigid BETTOCCHI hysteroscope (Karl Storz, Germany) with a 12° angle view and both biopsy and irrigation channels was inserted transcervically into the uterine cavity. Continuous normal saline flow was maintained throughout the procedure (40–160 mmHg pressure) to help distend and clean the uterine cavity. The chorion and the amnion were opened using microscissors to obtain a detailed view of the embryo [3]. All procedures were displayed on a television monitor to enhance the mother's understanding (Figures 3A, B, and 4) and were recorded for offline viewing and analysis.

Surgical termination of pregnancy was accomplished by vacuum curettage of the uterus under general anesthesia.

Discussion

Although 3D ultrasound with volume rendering and TUI-enhanced 2D ultrasound detected lesions involving either the soft tissue (cleft lip and proboscis) or the hard palate (cleft palate), hysteroscopic fetoscopy (*virtuopsy*) provided a direct, extremely clear view of fetal abnormalities and allowed digital recording for subsequent offline analysis.

Considering that the parents refused a conventional full autopsy, *virtuopsy* had a dramatic clinical impact in guiding and aiding postprocedure genetic counseling.

In a previous study by Yin et al [4], which included 12 pregnant women scheduled for legal termination of pregnancy at 6–12 weeks' gestation, successful embryofetoscopies with clear visualization of the embryo or fetus were achieved in 50% of cases. Philipp and Kalousek [5] reported general embryonic maldevelopment in 31% of the cases by transcervical embryoscopy performed prior to evacuation in 154 cases of missed abortion. In that study, chromosomal abnormalities were found

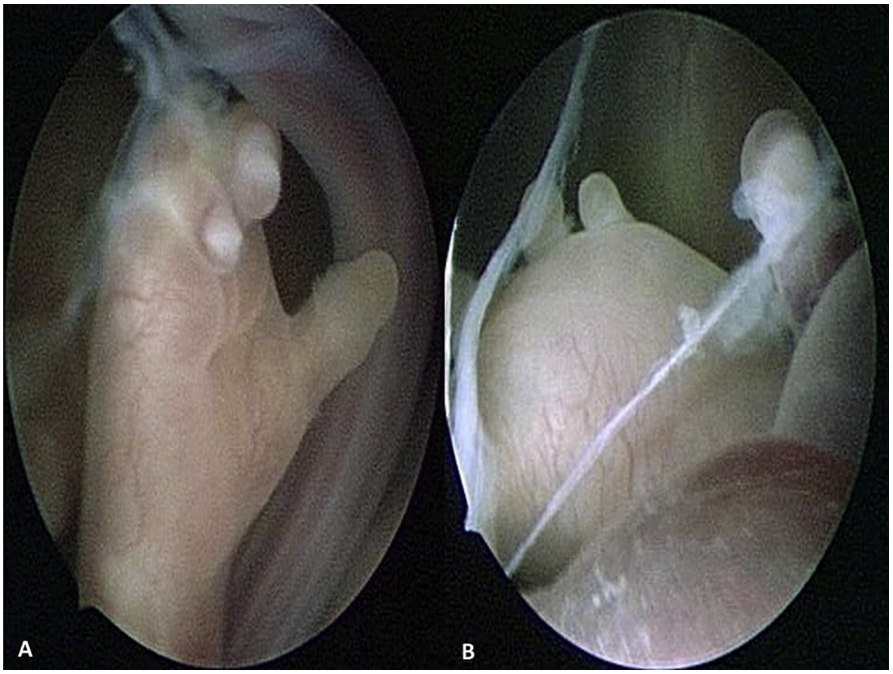

Figure 3. Saline fetoscopy using BETTOCCHI hysteroscope: details showing an amniotic band syndrome involving the fetal digits in coronal view (A) and in sagittal view (B).

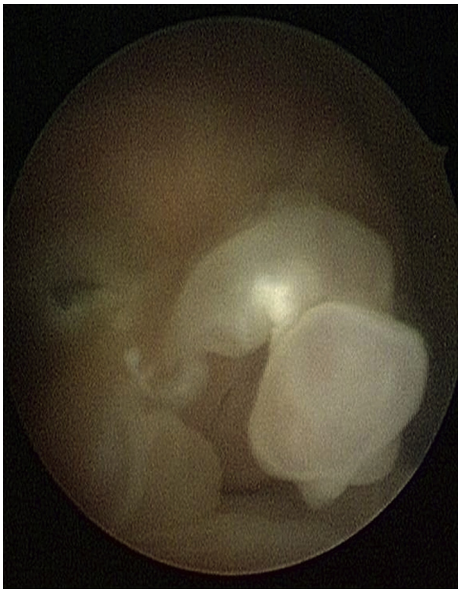

Figure 4. Saline fetoscopy using BETTOCCHI hysteroscope: the proboscis and the median cleft are clearly visualized.

in 70% of abortion cases with trisomies, which constituted 92% of cases. Philipp et al [6] demonstrated that aneuploidy is the major factor affecting normal embryonic development in missed abortions after *in vitro* fertilization (IVF). In their study, 21 of 23 IVF embryos showed structural defects (mostly chromosomal abnormalities) on embryoscopic examination performed before curettage. In addition, subsequent to embryoscopic and cytogenetic analysis of 233 cases of missed abortion, Philipp et al [7] reported 33 cases with normal external features, 71 cases with disorganized growth, and 129 cases with either isolated or multiple defects that included holoprosencephaly, anencephaly, encephalocele, spina bifida, microcephaly, facial dysplasia, limb reduction defect, cleft hand, syndactyly, pseudosyndactyly, polydactyly, various forms of cleft lip, and an amniotic adhesion. The 165 cases with an abnormal karyotype included 46 grossly disorganized embryos, 98 multiple defects, six single defects, and 15 morphologically normal cases. Of the 56 cases with a normal karyotype, there were 20 grossly disorganized embryos, 16 multiple defects, four single defects, and 16 morphologically normal cases.

Chan et al [8] have shown that transcervical hysterofetoscopy is a practicable tool for confirming external fetal structural abnormalities before surgical termination of pregnancy. They also demonstrated that the procedure can be performed under either general anesthesia or conscious sedation, and that umbilical cord blood collection can facilitate confirmation of genetic diseases and enable isolation of fetal mesenchymal stem cells in the first trimester of pregnancy.

Parental objection is the leading cause of failure to perform conventional autopsy. According to a UK survey, parental consent rates for fetal autopsy have declined from 55% to 45%, and rates for neonatal autopsy have declined from 28% to 21% [9], despite increases of >90% and 80% in the number of parents who are offered autopsy, respectively.

When a prenatal diagnosis of congenital anomalies is made, and the parents refuse full autopsy (for religious or ethical reasons), or in cases where a full autopsy may not be warranted, virtual autopsy by postmortem computerized tomography scan and/or magnetic resonance imaging (MRI) with laparoscopy and/or needle biopsy should be performed to confirm the diagnosis. MRI is more acceptable to parents than conventional autopsy [10,11] and has been shown to offer diagnostic accuracy that is similar to that of conventional full autopsy for detecting the cause of death or major pathological abnormality after death in fetuses, newborns, and infants [12].

From this standpoint, hysteroscopic fetoscopy or *virtuopsy* performed under local anesthesia immediately prior to uterine suction may be a useful ancillary investigative tool in cases where prenatal ultrasound may be inconclusive or the parents have refused full conventional autopsy. In such specific cases, *virtuopsy* may aid in parental understanding by directly displaying the anatomical features of the congenital malformation, and may also facilitate

genetic counseling and calculation of recurrent risk in couples wishing to conceive.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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