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Left Nostril Agenesis in a Fetus with VACTERL Association: A Case Report

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Abstract

VACTERL association represents a rare condition with a broad spectrum of coexisting congenital abnormalities. Although a multifactorial origin has been described, the etiology is still unclear. Prenatal diagnosis can be challenging, as specific characteristics may be difficult to be determined before birth. This case report describes the finding of multiple congenital abnormalities in a male fetus at 30 weeks of gestation. The most notable findings were the presence of duodenal stenosis, esophageal atresia with distal tracheoesophageal fistula (type 3), interatrial septal communication foramen ovale, and left nostril and choana agenesis. After birth and making a broad differential diagnosis, all these characteristics oriented the diagnosis towards the VACTERL association. To the best of our knowledge, no cases of VACTERL association and unilateral nostril and choana agenesis have been previously described.

Keywords

VACTERL Association, Nostril Agenesis, Fetal Ultrasound, Fetal MRI

1. Introduction

VACTERL association is a condition involving the presence of multiple congenital anomalies such as vertebral anomalies, anal atresia, cardiac anomalies, tracheoesophageal fistula or atresia, renal anomalies, and limb anomalies. At least three of the described defects should coexist to establish a diagnosis [1]. Nonetheless, cases diagnosed with VACTERL are heterogeneous. Indeed, associated dental and craniofacial anomalies have also been reported [2]. Here, we describe a case with VACTERL, in which not well-known morphological abnormalities were present.

2. Case Report

This case report describes a 45-year-old pregnant woman through *in vitro* fertilization (IVF) with egg donation, with a history of a miscarriage at 11 weeks. Neither the patient nor her partner had a relevant personal or familial medical history. In the current pregnancy, she was sent to the tertiary La Fe University and Polytechnic Hospital (Valencia, Spain) at 30 weeks gestation due to suspected fetal duodenal stenosis.

The first-trimester combined screening revealed a low risk of trisomy 21, 18, and 13. Polyhydramnios with mild ventriculomegaly were visualized in the morphological ultrasound at 20 weeks. The O'Sullivan test (administration of 50 g of oral glucose to rule out gestational diabetes) resulted in 116, within normal limits, and the serologies were negative.

Fetal ultrasound at 27 weeks gestation showed the double bubble sign at the level of the stomach and duodenum (Figure 1) associated with polyhydramnios. Thus, duodenal stenosis was suspected. The posterior horn of the lateral ventricles was within normal limits at this gestational age.

An advanced fetal ultrasound was performed at 30 weeks of gestation when the patient was referred to the tertiary hospital. A male fetus was seen with an estimated fetal weight according to the gestational age. The fetal color Doppler study revealed an abnormal cerebroplacental ratio (2nd percentile). An enlarged stomach with a double bubble sign associated with polyhydramnios (amniotic fluid index (AFI) of 39.8 cm and a maximum vertical pocket of amniotic fluid of 12.1 cm) suggested duodenal stenosis. Finally, the left choana and nostril atresia was also observed by 2-dimensional (2D) and 3-dimensional (3D) ultrasound, as shown in Figures 2-5. No signs of cleft lip or palate were observed.

The pregnant patient underwent a genetic amniocentesis. Moreover, fetal magnetic resonance imaging (MRI) was performed after an amniodrainage at 32 weeks gestation. Fetal MRI revealed findings that were in concordance with those visualized by fetal ultrasound. Additionally, agenesis of the first left cranial nerve and esophageal atresia with distal tracheoesophageal fistula (type 3) was described.

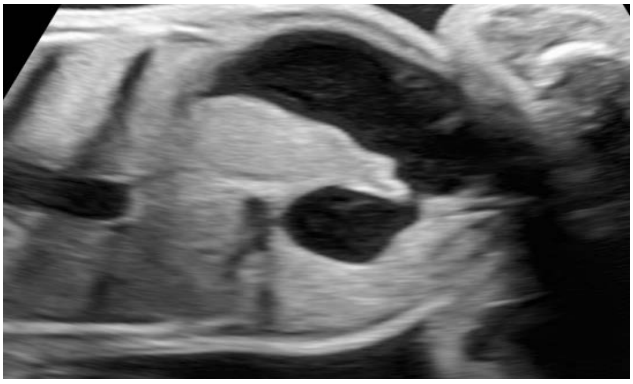


Figure 1. Double bubble sign detected by fetal ultrasound at 27 weeks of gestation. Coronal view of the fetal abdomen.

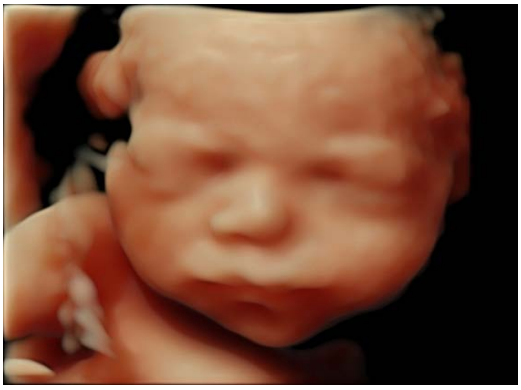


Figure 2. Left nostril agenesis showed by fetal 3D ultrasound.

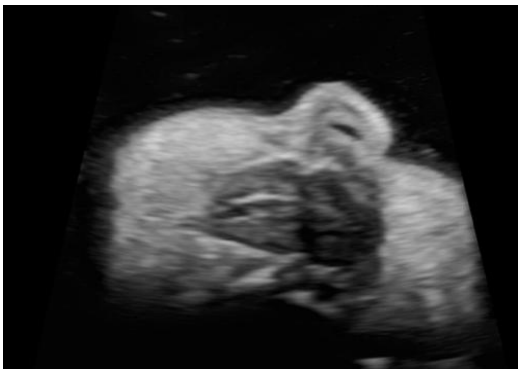


Figure 3. Coronal view of the single nostril by fetal ultrasound.

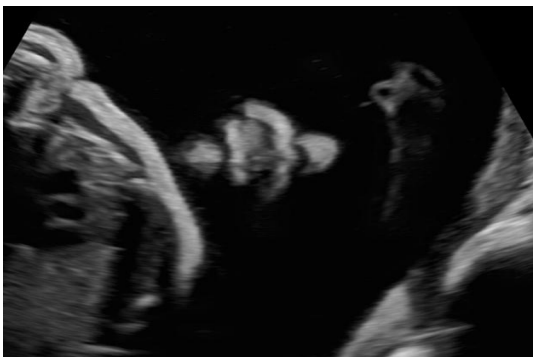


Figure 4. Facial coronal view by ultrasound of the fetal lips and right nostril.

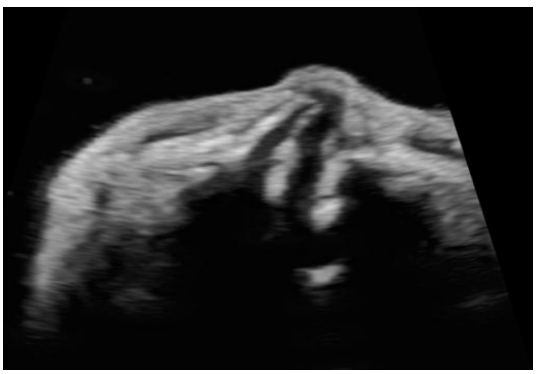


Figure 5. A fetal ultrasound, axial view shows the right choana and agenesis of the left.

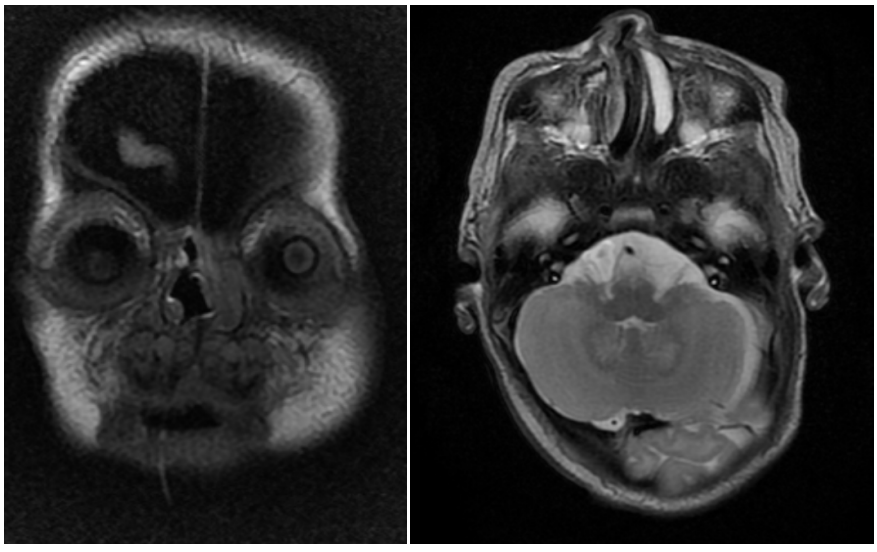
At 36^{+1} weeks of gestation, the patient was admitted to the Hospital due to preterm premature rupture of membranes. An emergency cesarean section was performed due to persistent fetal bradycardia. The weight of the male newborn was 2425 g, Apgar score 9/9, and artery pH 7.29. The newborn was transferred to the neonatal intensive care unit, and an emergent surgical intervention was performed hours after birth due to esophageal atresia.

After the cesarean delivery, the study of the polymalformative complex was enlarged. The congenital anomalies revealed by fetal ultrasound and fetal MRI were confirmed. Additionally, neonatologists reported left D2-D3 hemivertebra, left cervical rib, partial absence of coccyx, interatrial septal communication foramen ovale, and left dacryocystocele. Moreover, an MRI was performed on the newborn, clearly showing the described facial abnormalities (**Figure 6(a)** and **Figure 6(b)**).

Genetic tests were subsequently received within normal limits. Thus, the newborn was diagnosed with VACTERL association due to vertebral anomalies, tracheoesophageal fistula, and cardiac anomalies. The child has adequate neurodevelopment at six months and is still awaiting further diagnostic tests, including a 3D craniofacial computed tomography scan before facial reconstructive surgery.

3. Discussion

In the VACTERL association, prenatal diagnosis may be challenging because several defects are not easily detectable by fetal ultrasound. The incidence of the VACTERL association is approximately 1 in 10.000 to 1 in 40.000 live-born infants, and only 1% have all of the described characteristics [3]. Vertebral anomalies occur in up to 60% - 80% of cases, and anal atresia is found in almost 90% of cases [3] [4] [5]. Cardiac abnormalities appear in 40% - 80% of the affected



(a) (b)

Figure 6. MRI images of the newborn in coronal T2 FLAIR sequence and axial T2 FSE sequence, respectively, showing agenesis of the left choana.

fetuses, tracheoesophageal fistula affects up to 50% - 80% of cases [6], and limb defects usually occur in 50 % of cases [3].

There is no available objective laboratory test for the diagnosis of VACTERL association [4]. Thus, the diagnosis is based on the abovementioned morphological manifestations. VACTERL association is typically considered a diagnosis of exclusion [7]. The etiology of the VACTERL association is still unclear. Given that its phenotypes are too heterogeneous to be defined as a syndrome, and no major gene exists for this condition, it is still referred to as an "association". Future studies are needed to identify epigenetics and environmental causes for VACTERL syndrome [4].

In this case report, genetic tests were within normal limits. Thus, the newborn was diagnosed with VACTERL association due to vertebral anomalies, tracheoesophageal fistula, and cardiac anomalies. Co-occurrence with duodenal atresia occurs only in 5% of cases [8]. Noticeably, the newborn also manifested midline defects that had not been previously described in association with VACTERL. Interestingly, fetal ultrasound has rarely described left nostril agenesis and left choanal atresia [9]. Moreover, none are in association with VACTERL.

Although facial dysmorphisms are not frequently related to VACTERL, associations are heterogeneous and may involve other abnormalities arising from different developmental processes with midline effects [2]. Pariza *et al.* described a case report regarding a newborn with VACTERL association and micrognathia [1]. Carli *et al.* reviewed 25 cases of VACTERL association, and 3 of them presented facial asymmetries [10]. Due to its heterogeneity, many authors suggest broadening the diagnostic criteria to refine the knowledge of the phenotypic spectrum of the VACTERL association.

The prognosis of people affected by the VACTERL association is uncertain. It depends on the surgical correction of the defects in the postnatal period. It is essential to know that it is generally not associated with neurocognitive defects [11].

4. Conclusions

The VACTERL association is a rare health condition associated with heterogeneous physical abnormalities and highly variable prognoses. Thus, a multidisciplinary approach is essential, including the joint work of obstetricians, radiologists, pediatricians, and geneticists.

This case is unique within the published literature on the VACTERL association. No cases of VACTERL association and prenatal diagnosis of the unilateral nostril and choana agenesis have been described. More studies are still needed to assess the possible association of VACTERL with other congenital abnormalities not defined in the traditional association. It is also important to continue investigating the epigenetic and environmental causes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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