

VACTERL association in a newborn as a product of a twin pregnancy by egg donation

Asociación VACTERL en una recién nacida producto de embarazo gemelar por donación de óvulos

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Abstract

VACTERL association is a rare entity in newborns, with high mortality in the first year of life. We present a case of a female newborn, product of a twin pregnancy assisted by egg donation. During reanimation, absence of anal orifice and impossibility to pass the orogastric tube were evidenced, so she was admitted to the neonatal intensive care unit for study and treatment, where we found anal atresia, esophageal atresia type III, tetralogy of Fallot and duodenal atresia. There are no reports of this association in twin pregnancies by egg donation with an affected twin.

Keywords: VACTERL association. Congenital malformations. Twin pregnancy.

Resumen

La asociación VACTERL es infrecuente en los recién nacidos, con una alta mortalidad dentro del primer año de vida. Presentamos el caso de una recién nacida producto de un embarazo gemelar asistido por donación de óvulos. Durante la reanimación se evidenció falta de orificio anal e imposibilidad al paso de la sonda orogástrica, por lo que fue ingresada en la unidad de cuidados intensivos neonatales para su estudio y tratamiento, donde se encontró atresia anal, atresia esofágica tipo III, tetralogía de Fallot y atresia duodenal. No existen reportes de esta asociación en embarazos gemelares por donación de óvulos con un gemelo afectado.

Palabras clave: Asociación VACTERL. Malformaciones congénitas. Embarazo gemelar.

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Introduction

In 1972, Quan and Smith reported, for the first time, the VATER association, and currently the term VACTERL is widely accepted. This association is a set of congenital alterations that include vertebral anomalies (V), anal atresia (A), cardiac malformations (C), esophageal atresia with or without tracheoesophageal fistula (TE), renal alterations (R), and limb alterations (L). At least three of these criteria are required for diagnosis¹.

VACTERL association is of uncertain etiology, presumably multifactorial, with a relative infrequency in newborns (1:10,000 to 1:40,000) and predilection for the male sex (2.6:1) according to what has been reported in different publications^{2,3}.

The frequency of presentation of the anomalies does not have an established pattern, and different combinations can be found⁴. The general prevalence of congenital malformations is 2% in spontaneous pregnancies, with ultrasound being the test of choice for prenatal diagnosis^{5,6}. In the detection of this association, ultrasound presents a sensitivity of 84% and a specificity of 99.9%. The prognosis of these patients is poor, as 50-85% die in the first year of life⁷.

Case report

A 6-day-old newborn, product of a diamniotic-dichorionic twin pregnancy (according to the last ultrasonographic report) by egg donation. Mother aged 40 years, blood type O+ G1 P0 C1 A0, with UTIs in an unspecified trimester, treated with unspecified medications, without comorbidity or diseases during pregnancy, prenatal control from the beginning of gestation, intake of folic acid, iron, and vitamins, as well as normal quarterly control ultrasounds.

Father aged 40 years, blood type O+, with apparently healthy children from his previous partner.

Scheduled for cesarean section at 36 weeks of gestation, and a course of pulmonary maturation scheme was applied. Two products were obtained, with our patient being twin 1.

During resuscitation, APGAR scores of 8/9, SA 1, and a Capurro score of 36 weeks of gestation were given. Weight 1975 g, head circumference 31 cm, abdominal circumference 25 cm, thoracic circumference 27 cm, height 42 cm, heart rate 150 bpm, and respiratory rate 29 bpm. With good muscle tone, breathing and crying vigorously. Twin 2, apparently healthy.



Figure 1. Photograph showing the absence of the anal opening (arrow).

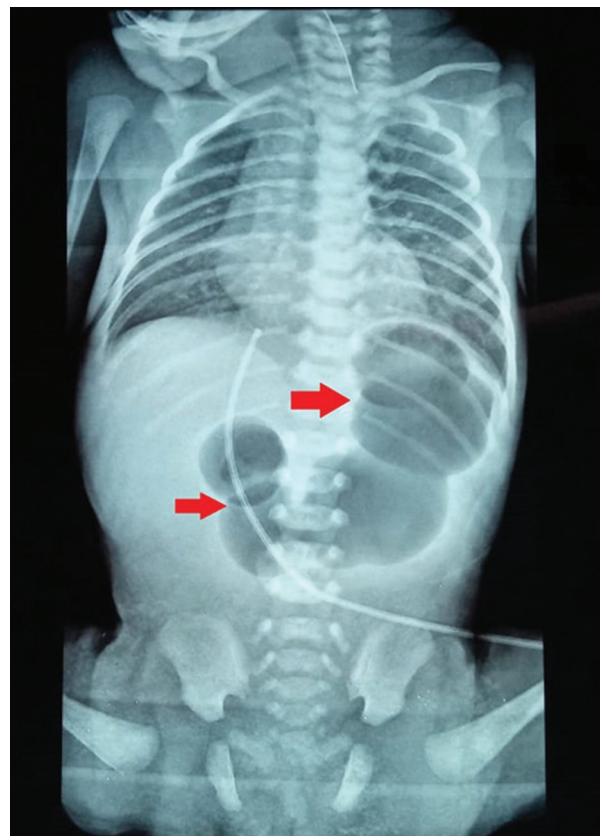


Figure 2. Thoracoabdominal radiograph showing a quadruple bubble image (arrows).

Placed in a radiant warmer at 37 °C with free oxygen at 2 L/min. On examination, choanal patency was found, primitive reflexes present, thorax and abdomen without compromise, stable hip, capillary refill of 3 seconds, anterior fontanelle approximately 1 cm and posterior partially closed; no anal fossa was found (Fig. 1) and there was an impediment to the passage

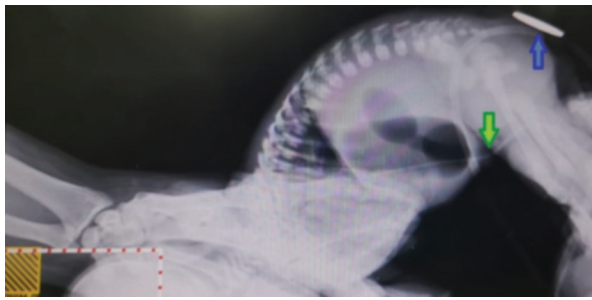


Figure 3. Invertogram showing the proximal height of the air column (green arrow) and the anatomical site of the anal opening (blue arrow).

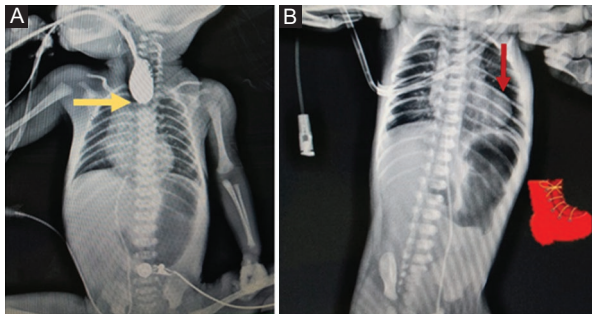


Figure 4. A: barium esophagogram showing a blind pouch at the level of the T2 vertebra (arrow). B: thoracoabdominal radiograph with characteristic "boot-shaped" image (arrow).

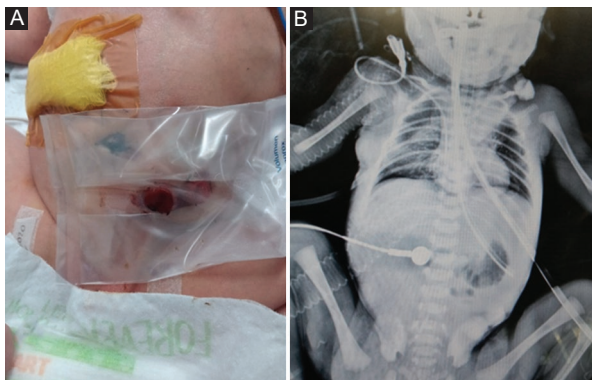


Figure 5. A: diverting colostomy. B: control thoracoabdominal radiograph.

of the orogastric tube. An anteroposterior thoracoabdominal radiograph was performed, which evidenced a characteristic quadruple bubble image and absence of distal air, suggesting intestinal atresia (Fig. 2). In light of these alterations, it was decided to transfer the patient to our public center.

The newborn was admitted to the neonatal intensive care unit at 20 hours of extrauterine life, where a

grade III/IV murmur and a split second heart sound were auscultated leading to the decision for comprehensive multidisciplinary management.

An invertogram was requested to determine the height of the colonic stump; however, the probable presence of duodenal or jejunal atresia did not allow for a correct assessment (Fig. 3). The search for meconial cells in urine was negative.

Upon performing a barium esophagogram due to suspected esophageal atresia, a blind pouch was observed at the T2 level (Fig. 4), likely a type III atresia, which was confirmed during surgery.

Due to the radiological characteristics of the heart, consistent with the "boot-shaped" image (Fig. 4), the auscultated murmur, and skin tone, a cardiology pediatric service consultation was requested. An echocardiogram was performed, confirming Tetralogy of Fallot with the following characteristics:

- Enlarged and hypertrophic right ventricle.
- Ventricular septal defect of 5.6 mm x 5.5 mm, with bidirectional shunt predominantly right-to-left.
- Aortic overriding of 50%, with presence of mitral-aortic continuity.
- Moderate mixed pulmonary stenosis, infundibular, valvular, and supra-valvular, with valvular hypoplasia and pulmonary artery trunk with a maximum velocity of 3.9 m/s, maximum gradient of 60 mmHg, and mean of 34 mmHg.

A 3.4 mm patent foramen ovale with bidirectional shunt was evidenced, and biventricular systolic and diastolic functions were preserved. The anatomy was unfavorable.

Surgery was planned and performed by a pediatric surgeon, correcting the esophageal atresia by anastomosis of the proximal and distal ends via a right posterior thoracic approach, as well as closure of the tracheoesophageal fistula, leaving a pleural seal. The intestinal atresia was corrected, being a type 1 duodenal atresia, and rectal atresia was found, so a diverting colostomy was performed during the same surgical procedure, at 4 days of extrauterine life (Fig. 5).

The patient was intubated before starting the surgery and remained intubated in the neonatal intensive care unit to prevent anastomosis dehiscence. The surgery was concluded without complications or incidents, and a control radiograph was performed at 12 hours (Fig. 5).

A subclavian-pulmonary shunt was planned by cardiovascular surgery as soon as the vessels had the necessary diameter for the procedure.

In the following days, the patient remained under sedation and began to present episodes of hypoxia that resolved with magnesium sulfate, steroids, and beta-agonists, reaching saturations as low as 20%. She had a cardiorespiratory arrest on the 8th day of life, achieving a good response with cardiopulmonary resuscitation. She died at 6 days of life, from a second cardiorespiratory arrest. Although the cause of death remains uncertain, it was probably due to the cardiac alterations inherent to Tetralogy of Fallot, since lab test showed no data of infection or hydroelectrolytic imbalance, and the control radiograph showed no alarm pattern.

Discussion

A study of 25 patients with VACTERL association in our country reported that the risk factors found were gestational diabetes and consumption of statins, cocaine, or marijuana, among others⁸.

According to what has been reported by other authors, cardiac alterations are the most common in VACTERL association, followed by anal and vertebral anomalies⁴.

In a case study from *Hospital para el Niño Poblano*, it was reported that the most frequent combinations were the triad (35.7%), the tetrad (37.5%), the pentad (21.43%), and the hexad (7.14%), reporting only one case of Tetralogy of Fallot⁹.

Similarly, a different group of researchers from the University of California, Irvine Medical Center, Miller Children's Hospital Long Beach, and Children's Hospital of Orange County, reported a series of 36 patients, of whom 61.1% had anal atresia, 6 patients had duodenal atresia and 6 patients had Tetralogy of Fallot, and 69.44% of patients had some type of tracheoesophageal fistula and esophageal atresia¹⁰. The presence of duodenal atresia together with VACTERL association has been reported only in 5% of cases¹¹.

In a case study from the Joint Research Centre-European Surveillance of Congenital Anomalies published in 2019, 6% of cases were in patients with a history of twin pregnancy⁴. A retrospective study with 142 patients with this association reported that pregnancies with assisted reproductive therapy (ART), including egg donation, have a higher risk of presenting the VACTERL complex, with an odds ratio (OR) of 4.8¹²; this same study suggests that primiparity, overweight, obesity, and absence of folic acid intake are also risk factors.

The compendium of 28 registries from 15 countries of the European Network for the Surveillance of Congenital Anomalies (EUROCAT) showed that ARTs in general present an increase in this entity (OR: 2.3)¹³. Currently, about 2% of pregnancies are achieved with ARTs¹⁴. In both studies, twin pregnancy was not a risk factor^{13,14}.

The presence of duodenal atresia along with VACTERL association has been reported only in 5% of cases; *per se*, duodenal atresia has an overall mortality rate of 13%^{11,15}.

Per se, duodenal atresia has an overall mortality of 13%¹⁵. It is worth noting that the coexistence of esophageal atresia (with or without tracheoesophageal fistula) and any type of heart disease has a survival rate of around 25%, which further complicated our patient's life expectancy¹⁶.

The low survival in this type of patient may be due to the complications inherent to the association, such as renal failure, which is characteristic, the complications of malformations, or the sequelae of complications from multiple surgical interventions, such as tracheomalacia, recurrent tracheoesophageal fistula, dehiscence or leaks of esophageal or duodenal anastomoses (in cases accompanied by duodenal atresia), and sepsis. Sudden cardiac death secondary to the development of arrhythmias in heart diseases is a factor that must be taken into consideration. Neurocognitive development is intact, and therefore comprehensive and timely management is essential^{15,17-19}.

In this case, despite adequate prenatal control, no ultrasonographic signs were identified that would suggest this condition, perhaps because it was a twin pregnancy.

In Mexico, there are few reported series and cases of VACTERL association, and worldwide, twin cases with one affected newborn and the other healthy, associated with ART, are practically non-existent. Therefore, this report can be considered the first of its kind. In addition, the presence of Tetralogy of Fallot is unusual, as is the coexistence of duodenal atresia.

Conclusions

VACTERL association is a rare finding, and no specific etiology is known; however, advanced maternal and paternal ages, insufficient folic acid supplementation, psychoactive substance use, some drugs, and ARTs, among others, are factors that can contribute to its appearance. Prenatal control can prevent and

detect this association early. However, the low life expectancy can be linked to the multiple affections, since each one has an individual mortality risk, as well as to the possible complications derived from surgical procedures for the correction of malformations.

Despite not being a common finding, it is essential to disseminate the findings, since this and other types of diseases classified as rare can be suspected with just a physical examination.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of people and animals. The authors declare that the procedures followed conformed to the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Declaration of Helsinki. The procedures were authorized by the institution's Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed the confidentiality protocols of their institution, have obtained informed consent, and have the approval of the Ethics Committee. The recommendations of the SAGER guidelines have been followed, according to the nature of the study.

Statement on the use of artificial intelligence.

The authors declare that they did not use any type of generative artificial intelligence for the writing of this manuscript.

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