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Case Report

A rare case of VACTERL association with a genito-urinary anomaly

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ABSTRACT

VACTERL association is a cipher used to describe a cluster of conditions wherein there is a seemingly unexplainable non-random association of specific birth defects of multiple organ systems. It includes vertebral anomalies (V), anal anomalies (A), cardiac anomalies (C), tracheoesophageal fistula (TEF), renal anomalies (R) or radial bone anomalies (R), and limb defects (L). At least three of these seven malformations need to be present to constitute the VACTERL association. Other congenital anomalies of different systems may additionally be present with this association but are classified separately and the rarity of this occurrence is greater than even the VACTERL association. We report a neonate with congenital abnormalities of the cardiac system atrial septal defect and ventricular septal defect, tracheoesophageal fistula H type, and a multicystic dysplastic kidney. Additionally, the baby was also found to have a micropenis, a genito-urinary anomaly. With optimal surgical correction in the post-natal period and vigilant periodic follow-up, the prognosis may be relatively positive. Medical management can be used as therapy for treating long-term sequelae of the anomalies if any. Therefore, morbidity and mortality can be prevented to a great extent with early diagnosis and immediate intervention.

Keywords: VACTERL, Newborn, TEF

INTRODUCTION

Epidemiological studies in the USA and Europe have given a prevalence of 1 in 10,000 to 40,000 live-born newborns.[1] VACTERL is believed to result from an early embryonic insult, more specifically of blastogenic origin occurring during the first 4 weeks of embryogenesis.[2] From the limited research done about the origin of this association, this early embryonic event is understood to lead to various defects in different body systems. First identified in 1973 as VATER association alone, cardiac and limb anomalies were added in later years to complete the spectrum.[3,4] The first component to be identified in our case was the Tracheoesophageal fistula (TEF). H type of TEF accounts for about 5% of all fistulas and is a life-threatening anomaly.[5] The presenting features are usually recurrent respiratory symptoms, aspirations, and episodes of cyanosis during feeding.[6] Maternal diabetes, usage of oral contraceptives, teratogenic drugs, and physical stress in the early stages of pregnancy have been implicated as possible causes but with no strong evidence.[7]

CASE REPORT

A late preterm, 36-weeks, of birth weight 2200 grams, male baby presented to our NICU on day 9 of life with complaints of respiratory distress present since initiating first feed after birth, cyanosis, and episodes of choking during every feed since birth. Antenatal history was unremarkable and did not contribute to our final diagnosis. The baby had a smooth transition to extra-uterine life and did not require any resuscitation. It was not a consanguineous marriage and there was no history of congenital anomalies in the family. Initially kept nil per oral, the baby was started on oxygen supplementation via nasal prongs at 1 L/ minute, maintenance IV fluids, and investigated for sepsis. The positive findings included leukocytosis with raised WBC counts of 27,000/mm^3 and a raised CRP level of 24 mg/l. Chest X-

ray showed right lower lobe infiltrates and was suggestive of aspiration pneumonia. Intravenous antibiotics were administered, and the rest of the supportive treatment continued. Upon resolution of respiratory distress, the baby was subsequently started on OG tube feeds which were well tolerated. It was only when oral feeds were initiated that the baby experienced episodes of choking followed by regurgitation. Upper GI contrast studies with serial radiographs were undertaken and the diagnosis of an H-type of TEF was made. Due to the presence of micropenis (baby's stretched penile length measured 0.7 inches i.e., less than 2.5 SD below the mean), the suspicion of a syndromic association arose, and the baby was further evaluated with a 2D-Echo and an ultrasound abdomen. The cardiac findings were that of an ASD-5 mm and VSD-1 mm. Abdominal findings revealed a multicystic dysplastic left kidney with a normal right kidney. With the cluster of cardiac, tracheoesophageal, and renal anomalies present thereby satisfying the criteria of involvement of at least 3 systems, a diagnosis of VACTERL association with a genito-urinary anomaly was confirmed.

The baby was taken up for surgery on the 25th day of life after resolution of respiratory distress and completion of the antibiotic course for screen-positive sepsis. Surgical management was preferred over the endoscopic and a cervical approach done to ligate the fistula. The baby made a complete recovery and did not experience any post-operative complications. A serial 2D Echo was planned to monitor the heart defects and regular follow-up was arranged. At one year, on follow-up, both the ASD and VSD had closed spontaneously, baby's renal function was satisfactory keeping in mind only one kidney was taking up the entire renal load and was symptom-free. The child measured more than 50th percentile on growth charts and did not suffer from any nutritional deficiencies on follow-up at 1 year of age.

DISCUSSION

VACTERL association with the full range of anomalies has been reported in only 1% of cases.[8] The 70% of patients will have vertebral anomalies and it is the most common presenting core component of the association. These may be of several types and include hypoplastic, fusion, butterfly, supernumerary, hemi-vertebrae, or Absent type.[9]

Amongst the cardiac defects, ventricular septal defects are the most common (30%) while patent ductus arteriosus (26%) and atrial septal defects (20%) are the other common CHDs noted. Other heart defects like TGA and TOF are rarer still with an incidence of less than 10%.[10]

TEF and/or Esophageal atresia account for 55-70% of VACTERL patients. The H type of TEF has an incidence of one in 100,000 live births. Despite its rarity, due to modern surgical treatments and advanced postoperative care, the mortality rate for H-TEF has significantly decreased and patients often make a complete recovery.[11] Both surgical and endoscopic management of the condition is possible. Endoscopic management has lower morbidity and mortality compared to the surgical approach but is associated with a high recurrence rate therefore surgical treatment remains the mainstay. The various approaches for surgical correction include Anterior cervical, lateral cervical, and transthoracic approaches.[12]

Renal abnormalities include unilateral agenesis, ectopic, horseshoe kidney, cystic, and or dysplastic kidneys in decreasing frequency of occurrence and are occasionally accompanied by ureteral and genito-urinary abnormalities.[13] In our case, we found micropenis as a rarely associated finding.

Limb deformities comprise abnormalities such as polydactyly, syndactyly, radial aplasia/hypoplasia, humeral hypoplasia, and abnormal thumbs. These have been reported in 40% of VACTERL patients.[14]

Almost every organ system has been reported in association with VACTERL albeit with lower incidence rates, some of these are lung lobation defects, intestinal malrotation, hemifacial microsomia, external ear malformations, and genital anomalies like micropenis and hypospadias.[15]

The reason this condition is known as an association rather than a syndrome is that while all the birth defects are linked, it is unknown which genes engage in its etiology. Even though chromosomal abnormalities like 5p syndrome and trisomy 13 and 18 have presented in VACTERL patients, it is rarely seen more than once in a single family.[16]

Although the prime pathogenic mechanism behind this condition remains unknown, the most recent research has implicated defective sonic hedgehog pathway (SHH) signaling during embryogenesis.[17] Hedgehog (Hh) signaling is vital for the patterning and organogenesis of almost every system of the body. The specificity of these developmental processes is achieved through tight spatiotemporal regulation of Hh signaling. When evaluated in mice, defective Hh signaling exhibited a wide spectrum of anomalies strikingly resembling the defects of VACTERL association in humans.[17] Diagnosis remains largely clinical and based on suspicion; supportive investigations are conducted to find the individual components of the association.

The most interesting point of note is that despite several morbid anomalies and considerable medical challenges, the central nervous system is classically spared, and these patients do not display any form of neurological impairment. Treatment is directed towards the presenting and most critical symptom of the child. Various modalities of treatment exist for each condition and are

decided on a case-to-case basis. Surgical treatment is almost always required for at least 1 anomaly while supportive, medical management may be offered for mild conditions. A multidisciplinary team comprising of pediatricians and pediatric surgeons, cardiologists, urologists, and orthopedic surgeons is usually required while input from a child psychiatrist and physiotherapist may also be of help in the long-term management of the child. The severity of the anomalies dictates the prognosis but with great advancements in surgical correction of these anomalies, the baby can be expected to have a reasonable life expectancy with good growth and development in newborns who survive the infancy period.[18]

CONCLUSION

A high degree of suspicion and forming a connection among the presenting anomalies helps clinch the diagnosis of the VACTERL association. Its occurrence is sporadic, and pathogenesis remains a mystery. The focus of future research needs to be on the identification of this condition prenatally through an echocardiogram or MRI. Genetic workup and early identification may also play a crucial role in the future to provide an option for termination if detected before viability. VACTERL patients grow on to live a normal life provided early diagnosis and management of surgical and medical conditions is done owing largely to the intact neurocognitive ability.

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