Neonate with VACTERL Association and a Branchial Arch Anomaly without Hydrocephalus

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Abstract

VACTERL (vertebral anomalies, anal atresia, cardiac defect, tracheoesophageal fistula, renal anomaly, limb anomalies) is an association of anomalies with a wide spectrum of phenotypic expression. While the majority of cases are sporadic, there is evidence of an inherited component in a small number of patients as well as the potential influence of nongenetic risk factors (maternal diabetes mellitus). Presence of hydrocephalus has been reported in VACTERL patients (VACTERL-H) in the past, with some displaying branchial arch anomalies. We report the unique case of an infant of diabetic mother with VACTERL association and a branchial arch anomaly—in the absence of hydrocephalus.

Keywords
- VACTERL association
- neonate
- branchial arch anomaly
- infant of diabetic mother

Case Presentation

An African American male infant was born at 38 $^{6/7}$ weeks gestation via repeat, scheduled cesarean section to a 41-year-old gravida six, para three mother with maternal history of type-2 diabetes mellitus (DM2) and antenatal concern for possible tracheoesophageal (TE) fistula as part of VACTERL (vertebral defects, anal atresia, cardiac malformations, tracheo-esophageal fistula, renal anomalies, limb anomalies) association. In addition to the possible TE fistula, there were prenatal sonographic findings of pyelectasis, ventricular septal defect (VSD), hemivertebrae, and scoliosis. Gestational history was also significant for polyhydramnios and diabetes mellitus, which was well controlled in the later part of gestation. Due to the concern for TE fistula, preparations were made in advance for neonatal intensive care unit (NICU) admission.

On admission to the NICU, all parameters were appropriate for gestational age: weight was 3.8 kg, length was 48.0 cm, and head circumference was 35.0 cm. Physical examination was remarkable for a mildly flat nasal bridge, bilateral hypoplastic external ears with a fluctuant cystic structure posterior to the right ear (►**Fig. 1**), and mandibular hypoplasia; a systolic heart murmur was auscultated at the left sternal border. The infant was voiding adequately via normal appearing external male genitalia. The sacrum and anorectal area were well formed with a normal stooling pattern.

A sonogram of the postauricular cyst showed a fluid collection within the superficial soft tissues of the skin, measuring 1.5 cm × 0.9 cm × 0.7 cm. This was followed by a computed tomographic scan of the temporal bones which demonstrated deformed and hypoplastic bilateral pinna and the presence of the auditory canal with complete opacification of the tympanic cavity on the right side but well aerated on the left side. The cochlea was present bilaterally. Further work up to rule out other anomalies included chest and abdominal X-rays, a neurosonogram, an echocardiogram, and a renal sonogram. The X-rays revealed scoliosis, numerous vertebral segmentation anomalies in cervical, thoracic, and lumbar areas as well as multiple rib fusion anomalies (►**Fig. 2**). It also showed a stomach gas bubble with the orogastric tube tip, ending in the stomach and the presence of air in the rectum. The spinal sonogram showed an abnormally low position of the conus. A spinal magnetic resonance imaging confirmed the above findings and also suggested a tethered cord. A skeletal survey combined with

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Fig. 1 Right lateral facial view demonstrating branchial cyst posterior to the right hypoplastic ear.

Fig. 2 A single frontal supine radiograph of the chest and abdomen demonstrating scoliosis due to numerous vertebral body segmentation anomalies and bilateral rib fusion anomalies. The presence of air in the rectum and the enteric tube tip ending in the stomach is also noted.

the physical examination ruled out limb anomalies. The renal ultrasound revealed a congenital solitary right kidney. Head sonogram was unremarkable with the exception of a bilateral grade 1 intraventricular hemorrhage. The echocardiogram demonstrated a small-to-moderate membranous VSD with inlet extension, and a small secundum atrial septal defect (ASD). Ophthalmology consultation to rule out Goldenhar syndrome did not reveal any abnormal ocular findings.

Array comparative genomic hybridization was sent because of the patient's multiple congenital anomalies. No deletions or duplications were noted. Given his constellation of findings, the patient met a clinical diagnosis of VACTERL association. Diagnosis of the first branchial cleft cyst was established by the typical location posteriorly and inferiorly to the external auditory canal and by the imaging. The infant required gastrostomy tube placement due to poor nippling secondary to mandibular hypoplasia, and was subsequently discharged home with early intervention services and multidisciplinary follow-up in place.

Discussion

VACTERL association is a well described entity of congenital malformations that is diagnosed clinically. The incidence is between 1/10,000 and 1/40,000.[1,2] Its etiology remains unclear. Although there are no definitive clinical criteria, three of the following are usually required for diagnosis: vertebral defects, anal atresia, tracheoesophageal fistula, cardiac defects, renal anomalies, and limb anomalies. Importantly, another view stresses the importance and presence of one "core" feature: anorectal malformations or tracheoesophageal fistula/esophageal atresia in addition to two other ones.[3]

Our infant met the broader criteria for VACTERL association with his vertebral, renal and cardiac anomalies. In VACTERL, vertebral anomalies are the most frequently reported defect (60–80%). These defects, which are often accompanied by rib anomalies, include segmentation defects, hemivertebrae, "butterfly vertebrae," "wedge vertebrae," vertebral fusions, abnormal spinal curvature, and supernumerary or absent vertebrae.[4,5] Renal anomalies are reported in 50 to 80% of the cases with unilateral renal agenesis (solitary right kidney in our case), horseshoe kidney, and cystic and/or dysplastic kidneys being among the most often seen defects. ASD and VSD were recorded echocardiographic malformations with an estimated frequency of 40 to 80%. These cardiac defects can range from severe to minor structural defects. Notably absent in our patient were gastrointestinal/genitourinary malformations as well as limb anomalies.

The findings of costovertebral segmentation defects, congenital heart disease (ASD, VSD), and solitary kidney as well as ear malformations in our infant suggest the presence of maternal DM2 as a potential risk factor for VACTERL association. Traditionally, DM1 has been linked to diabetic embryopathy including cases of VACTERL related to maternal DM1.[6] However, with markedly increasing maternal age at conception (mother of the infant was 41 years old at the time of delivery), overlapping rates of major congenital

malformations in DM1 and DM2 are being reported.[7] Additionally, our patient's mother A_{1C} level early in gestation was elevated at 11%. After in-house hospitalization for glycemic control, she attained and maintained adequate control for the remainder of gestation. Uncontrolled diabetes mellitus early in pregnancy during the critical period of embryonic development places the fetus at risk for congenital anomalies.

Another interesting and unique observation is the presence of the first branchial arch anomaly (cyst) in VACTERL association in the absence of hydrocephalus.

VACTERL with hydrocephalus (VACTERL-H) is a rare condition with poor prognosis that has been reported to be inherited mostly in an X-linked pattern in some families but autosomal recessive patterns have been described as well.[8–11] It is typically due to aqueductal stenosis often requiring surgical intervention. In some cases, branchial arch defects have been described in patients with VACTERL-H. However, cases of patients with VACTERL with brachial cleft defects without hydrocephalus have not been described in the literature to date.

VACTERL association can sometimes be difficult to differentiate from other syndromes as features characteristic of VACTERL easily crossover to other disorders. Oculo-auriculo-vertebral spectrum disorder was an entity that was initially strongly considered in this case. However, the infant did not have cardinal features of abnormalities of the cheek or jawbones and had a normal ophthalmologic examination. Other related syndromes also considered included Townes–Brocks syndrome, however, the infant did not have thumb abnormalities, polysyndactyly, syndactyly, or any other limb abnormalities.

Conclusion

The differential diagnosis for VACTERL association is broad and can be difficult to differentiate from other conditions with a similar constellation of findings. Making the correct diagnosis is essential not only for medical management and prognosis, but also for appropriate genetic testing and counseling to the families. Our patient presents a new and interesting VACTERL phenotype. In addition to meeting diagnostic criteria for VACTERL association, he also had first branchial cysts, which to date had only been described in VACTERL-H patients.

Conflict of Interest
None.

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