Psychomotor Retardation and Agenesis of Vena Cava Inferior and Sacrum Associated with Unusual Features of VACTERL Anomalies

Psikomotor Retardasyon, Vena Cava İİnferior ve Sakrum Agenezi İle İlişkili VACTERl Anomalisinin Nadir Özellikleri

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ABSTRACT

We report a 3-year-old female. Her malformations included facial and limb abnormalities, sacral agenesis, ASD, VUR and the absence of inferior vena cava. Vena cava inferior agenesis association with VACTERL has not been reported in the literature before. Newborn or infants with limb anomalies should be better evaluated for the other anomalies.

Key Words: Sacral agenesis, VACTERL, Vena cava inferior

ÖZET

Bu makalede yüz ve ekstremite anomalileri, sakral agenezi, ASD, VUR ve vena kava inferior yokluğu olan 3 yaşındaki kız hasta sunulmaktadır. VACTERL anomalisi ile ilişkili vena kava inferior agenezisi literatürde daha önce tanımlanmamıştır. Ekstremite anomalileri ile doğan yeni doğanların ve infantların diğer anomaliler açısından daha iyi incelenmesi faydalı olacaktır.

Anahtar Sözcükler: Sakral agenezi, VACTERL, Vena kava inferior

INTRODUCTION

We report a 3-year-old girl affected by reflux nephropathy, skeleton and vascular abnormalities, atrial septal defect (ASD), retardation of growth and development. Although the pattern of malformation overlaps some syndromes such as Holt-Oram and Fanconi, differential diagnosis was made with other several syndromes including acral and renal anomalies. One of the situations including these anomalies is the VACTERL association. The VATER association diagnostic criteria are three or more of the following: vertebral defects, anal atresia, esophageal atresia and/or tracheoesophageal fistula, and radial-ray limb anomalies (1). The two other defects including renal and cardiac anomalies were subsequently added to the list of major defects in this association. Recently vascular defects were noted in a high proportion of their own and previously reported VATER association cases and their inclusion in the spectrum of malformations was proposed (2). Studies have estimated the VACTERL frequency to be approximately <1-9/100,000 infants (3,4). The etiologies of VACTERL association remain largely unknown. Reported causes of features seen in VACTERL association in patients are mitochondrial dysfunction, pathogenic copy number variations, heterozygous mutations in HOXD13, and heterozygous/hemizygous mutations in ZIC3 (4). Reported environmental influences include maternal diabetes, infertility treatment, in utero exposure to estrogen and/or progesterone-containing compounds, statins, and lead (4).

CASE REPORT

The patient was a 3-year-old girl, and was born by uneventful delivery from unconsanguineous healthy parents at 36th weeks of gestational age and a birth weight of 2600 g. There was no information about maternal diabetes or other disease because the mother had no prenatal care. In her family history, her grandfather had died at the age of 57 from renal failure. None of the family members had a dysmorphologic appearance.
Because of hip dysplasia and bilateral equinovarus deformity she was operated when 6 months old (Figure 1). At the age of 7 months, treatment was started for recurrent urinary tract infections and constipation. When she was 3 years old, she was sent to our hospital for further evaluation.

At the admission, her weight, length and head circumferences were under the 3rd percentiles. She has radial deviation of both wrists, clinodactyly of fifth finger of left hand, rudimentation and ulnar deviation of first finger of left hand, aplasia of the first finger of the right hand with facial dysmorphism; long face, frontal bossing, temporal depression and asymmetric ears. The right ear was 5 mm smaller and lower than the left one (Figure 2). She could not stand or sit without support.

The patient had bilateral grade V vesicoureteral reflux on voiding cystourethrography (VCUG) and bilateral hydronephrosis with ultrasonographic study. Magnetic resonance (MR) imaging confirmed the hydronephrosis and sacral agenesis, and also demonstrated small capacity urinary bladder (Figure 3). Contrast enhanced abdominal computed tomography (CT) revealed the ageneses of inferior vena cava and azygos continuation. Vesicostomy was performed as the patient was younger than 5 years and the parents could not perform clean intermittent catheterization.

She was diagnosed with psychomotor retardation with the Denver Developmental Screening Test II as a result of delayed personal section, language and gross motor section. EMG examination demonstrated bilateral significant lumbosacral plexiopathy.

Her blood pressure was high (115/75 mmHg) and was treated with amlodipine and captopril. A systolic murmur on the left site of the sternum was related to ASD of ostium secundum type that was demonstrated by echocardiography. Ulnar deviation and rudimentary first phalanx of left hand (Figure 4), aplasia of first phalanx of right hand, aplasia of fifth phalanx of left leg and bilaterally radial hypoplasia and widespread ostopenia were seen on x-ray (Figure 5). The cytogenetic analysis revealed a normal 46,XX karyotype. The DEB (diepoxybutane) test was normal.
DISCUSSION

When we checked out the literature for our patient’s findings, we found some cases that were reported with limb and urinary system anomalies. Limb and urinary system anomalies occur together as a single developmental field defect or as a component of several malformation syndromes such as trisomy 18 (5,6). In 1964, Lash first proposed the concept of developmental field and demonstrated the influence of the mesonephron on limb’s bud development in organ culture (7). The combination of acral and renal abnormalities is the best interpreted as a developmental field complex defect (8). With these findings, the patient could match some syndromes such as Holt-Oram, Goldenhar, VACTERL and Fanconi. Because she had limb anomalies and ASD, Holt-Oram could be matched in which mutation located on HO Sm gene. Growth failure, hypoplastic radius, absent thumb, developmental hip dysplasia, equinovarus, microcephaly, and asymmetric ears could match Fanconi, but the DEB test was normal. The girl had frontal bossing, temporal depression, aplasia of first finger of right hand, hypoplasia of first finger of left hand and asymmetric ears as in OAV (oculoauriculaverterbral or Goldenhar syndrome) complexes too.

In addition these anomalies belong to the spectrum of anomalies seen in VACTERL. Diagnosis of the VACTERL association is made on clinical grounds, based on the presence of the congenital malformations most (but not all). Because of sacral agenesis, and cardiac and limb anomalies this patient is compatible with VACTERL. Vertebral components of this syndrome have been reported in approximately 60-80% of patients (9-11) and mostly are tethered cord, syringomyelia, hemivertebrae, scoliosis, hypoplastic and deformed lumbar spine and sacrum. Sacral agenesis is a rare malformation as a part of VACTERL syndrome, together with it was reported in rare cases. Cardiac malformations have been reported in approximately 40-80% of patients with VACTERL association (9-11). Structural heart anomalies are common in the VACTERL association. Similarly, the reported case has ASD. Renal anomalies are reported in approximately 50-80% of patients (9-11). Unlike many other features of VACTERL association, which are relatively clinically obvious, renal anomalies may be less apparent unless careful imaging is performed. Potential medical complications of the renal anomalies are vesicoureteral reflux, hydronephrosis, urinary tract infections, nephrolithiasis, and impaired renal function (12). Our patient was referred for recurrent urinary tract infections, and in her evaluation she was diagnosed with bilateral grade V vesicoureteral reflux and hydronephrosis. In the future, these malformations may result in significant morbidity. Limb malformations have been reported in approximately 40-50% of patients (9,10). These anomalies include thumb aplasia/hypoplasia, polydactyly and many other limb anomalies. Radial hypoplasia was reported with VACTERL but not together with bilaterally radial hypoplasia and sacral agenesis previously. In the literature, some vascular anomalies in association with VACTERL such as left superior vena cava have been reported (13). To the best of our knowledge there are no reported case with aplasia of vena cava inferior and the VACTERL complex. Although we did not have any information about the prenatal history such as maternal diabetes and we could not perform microarray analysis, all these finding together supported VACTERL with unusual features.

In 1998 and 1999 some authors postulated that the VACTERL association is another polytopic developmental field defect (14,15). In 2004 a multi-center study was designed for identified in a large group of cases with congenital renal anomalies and a limb deficiency (2). They selected the 197 cases that had both limb anomaly and renal or urinary tract anomaly. In about 50% of these cases a diagnosis or a recognized phenotype was reported, with chromosomal aberrations and VACTERL being most frequent.

All above data indicate that limb and urinary tract anomalies can occur together without other anomalies, as well as be part of different syndromes and known multiple congenital anomalies pattern, with different known and unknown etiologies.
In conclusion we suggest that newborn or infants with limb anomalies should be better evaluated for especially urinary tract anomalies. Early diagnosis is crucial in such cases as potential targeted therapy (either surgical or conservative) might prevent irreversible damage of renal parenchyma.

REFERENCES