

# VACTERL-H syndrome: first trimester diagnosis

## *İlk trimester tanısı konan VACTERL-H Sendromu*

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### Abstract

We present two consecutive female fetuses with identical upper limb anomalies. The first of the cases was found to have ventriculomegaly, atrial septal defect, anal atresia, narrowing of the duodenal lumen and unilateral renal agenesis at the end of the second trimester. These abnormalities were characteristic of autosomal recessive VACTERL-H syndrome. The second case was diagnosed to have absent radii and thumbs at 11 weeks. Detailed examination of fetal limbs in the first trimester screening in cases with high risk is useful for early detection of this malformation.

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**Key words:** VACTERL-H syndrome, radial aplasia, first trimester diagnosis

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### Özet

Bu sunumda benzer üst ekstremité anomalisi saptanan iki kardeş fetus takdim edilmektedir. İlk vakada ventrikülomegali, atriyal septal defekt, anal atrezi, duodenum lümeninde daralma ve unilateral renal agenezi tanısı ikinci trimester sonunda konmuştur. Bu anomaliler otozomal resesif geçişli VACTERL-H sendromunun karakteristik belirtilerindedir. İkinci vakada 11. haftada radius ve baş parmak yokluğu ultrasonografi ile tanı konmuştur. İlk trimester taramasında fetal ekstremitelerin detaylı incelemesi bu nadir malformasyonun erken tanısının konmasını sağlayabilir.

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**Anahtar kelimeler:** VACTERL-H sendromu, radial aplazi, ilk trimester tanı

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### Introduction

VACTERL association is defined as a combination of vertebral, anal, cardiac, tracheoesophageal, renal and limb anomalies. VACTERL cases are defined as having 2 or more of these anomalies and the majority (>90%) of these patients have two or three (1). The combination of VACTERL anomalies with hydrocephalus (VACTERL-H) was suggested to be a specific entity (2, 3). Patients with VACTERL-H syndrome often have bilateral and symmetrical radial ray abnormalities especially radial aplasia, imperforate anus and genital anomalies (4). X-linked (5-7) sporadic (8), and autosomal recessive (9) inheritance of this association were described in previous reports. There is only one case of VACTERL syndrome detected in the first trimester in the literature, which presented with megalourethra and hyperechogenic kidney (10).

In this case report we aimed to point out the importance of first trimester screening in cases with high risk of the familial form of this malformation.

### Case Reports

#### Case 1

It was the first pregnancy of the mother (26-years), who was married to her cousin. First trimester screening was performed at 12 weeks of gestation and the patient was included in the high risk group (nuchal translucency: 2.1mm, PAPP-A:

0.3 MoM, Free Beta HCG 0.29 MoM). The lateral ventricle of the fetus was 11mm and double bubble sign was remarkable in the second trimester (at 19 weeks of gestation). Karyotype analysis from the fetal blood at 22 weeks was normal (46, XX), no chromosome breakage was found. At 23 weeks, ventriculomegaly was more prominent (14 mm). The parents opted for termination. At birth (24 weeks), the female fetus weighed 420 g, length was 35 cm (Figure 1). Autopsy findings included ventriculomegaly, unilateral radial aplasia, contralateral hypoplasia, bilateral absence of the thumbs (Figure 2), anorectal atresia, narrowing of the duodenal lumen, absence of the right kidney and pelvic location of the left one and atrial septal defect.

#### Case 2

In the second pregnancy the mother was admitted to our department at 11 weeks of gestation (CRL: 40.9 mm). At a detailed sonographic examination, bilateral absence of the radii and thumbs were detected (Figure 3a, 3b). After two weeks, the nuchal translucency was 1.6 mm, anomalies of upper limbs were more prominent and the fetus did not have any associated malformation at the sonographic examination (Figure 4). The parents opted for termination at 13 weeks of gestation. Autopsy findings were only bilateral radial aplasia and bilateral aplasia of the thumbs (Figure 5). The karyotype of the fetus was normal (46, XX). Analysis for chromosome breakage was not performed. The parents were informed about the 25% risk of recurrence and the availability of prenatal diagnosis.

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### Discussion

Phenotypic manifestations of the autosomal recessive form of VACTERL-H syndrome and the X linked recessive form have been reported to be almost identical, and Lurie et al. suggested that the only exception might be the absence of cardiovascular malformations in cases with X linked inheritance (11). Atrial septal defect was one of the associated anomalies of our first case, as in other cases with the autosomal recessive form.

Lurie et al. reported also that patients with autosomal recessive inheritance and sporadic cases of VACTERL-H associa-

tion showed two differences: Firstly, radial bone involvement occurred in all familial but only in some sporadic cases. Secondly, cardiovascular malformations were more severe in patients with autosomal recessive inheritance (11). As proposed by the authors, both of our cases had radial aplasia as in other familial cases.

Kovacs et al. presented two consecutive mid trimester fetuses in a family, which had ventriculomegaly with radial and renal defects (12). Progressive ventriculomegaly served the basis for prenatal diagnosis in their cases, as in our first case. Since this was not a prominent finding before 19 weeks of gestation, it could not be useful in early detection in the second case.

In a review of 12 cases, Harris et al. reported that the dilatation of the colon in anal atresia may be related to gestational age and is more likely to be present beyond 27 weeks (13). However, Lam et al. reported a case of anorectal malformation (ARM) which illustrated that a dilated colon may be present in association with anal atresia as early as 12 weeks (14). Even in multiple associated anomalies, prenatal detection of ARM by fetal ultrasonographic examination was found to have a low sensitivity (36%) (15). The presence of anorectal atresia was not detected prenatally in the first case because of the absence of dilated colon at 23 weeks.



Figure 1. Macroscopic appearance of the first case



Figure 2. Absence of the thumb

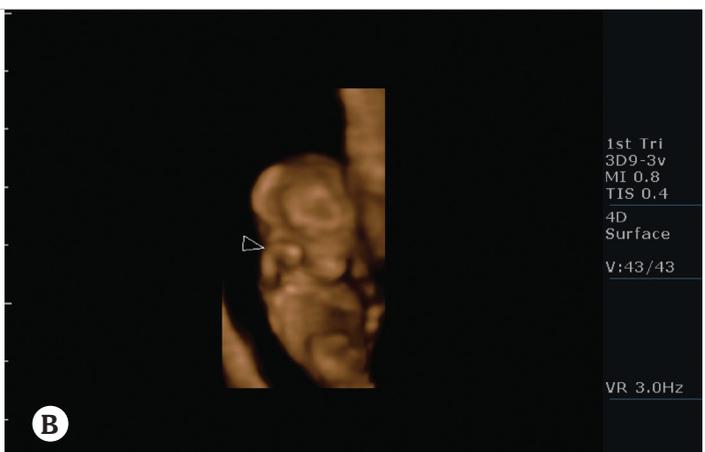


Figure 3. A) Absence of radius and thumb at 11 weeks (CRL 40.9 mm), B) 3D sonographic appearance of the hand (note the position of the fingers)



**Figure 4.** Absence of the radius and thumb at 12 weeks 4 days (CRL 65 mm)



**Figure 5.** Macroscopic appearance of the second case

The presence of duodenal atresia in cases of VACTERL syndrome have been reported (16, 17). Fujishiro et al. proposed that, in the absence of limb anomalies, signs of esophageal atresia and renal anomalies, the diagnosis might be very difficult. The detection of characteristic findings of duodenal atresia (double bubble: enlarged stomach and duodenum) was suggested to be useful for the prenatal diagnosis of such cases (17). Although in the first case the presence of double bubble at 19 weeks was a prominent sign, it could only be detected during the late second trimester.

The VACTERL-H phenotype is recognized to be a severe manifestation of autosomal recessive Fanconi anaemia. Although Lomas et al. did not show any increased chromosome breakage in amniocytes from affected cases when challenged with mitomycin C (18), Wang et al. found that chromosomes from males with VACTERL-H syndrome had increased spontaneous breakages and sensitivity to mitomycin C (19). Mutations in *FANCB* gene are reported to be the cause of X linked VACTERL-H syndrome (19, 20). Both of our cases were female and in the first case we did not find any chromosome breakage. Analysis of the parents and their relatives might reveal new forms of mutations.

In a review of 44 VACTERL association cases, Kolon et al reported a 100% survival rate (21). The prognosis of VACTERL-H syndrome is reported to be poor because of the severity of the malformations (5, 22-24). However the survivors require significant surgical treatment and care (25, 26). Early detection of this anomaly provides the option of termination. Unfortunately some of the major components could not be detected until the end of the second trimester with ultrasonography. Detailed examination of upper limbs in the first trimester screening may be a useful sign in the detection of familial cases.

#### Conflict of interest

No conflict of interest was declared by the authors.

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