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Research Letter

Prenatal ultrasound demonstration of scoliosis, absence of one rib, a radial club hand, congenital heart defects and absent stomach in a fetus with VACTERL association

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A 34-year-old, gravida 4, para 1, woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Cytogenetic analysis revealed a karyotype of 46,XY. The woman's husband was 49 years old. She and her husband were non-consanguineous, and there was no family history of congenital malformations. The woman did not have diabetes mellitus during this pregnancy. Level II ultrasound at 22 weeks of gestation demonstrated absent stomach (Fig. 1), double outlet of right ventricle (Fig. 2), ventricular septal defect (Fig. 3), scoliosis with absence of the one rib (Fig. 4) and a radial club hand (Fig. 5). A diagnosis of VACTERL association was made. The parents elected to terminate the pregnancy. A 525-g male fetus was delivered with a radial club

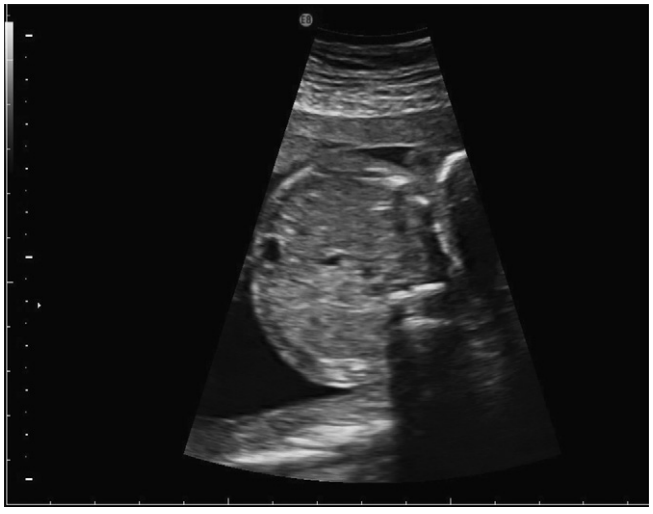

Fig. 1. Prenatal ultrasound demonstration of absent stomach.

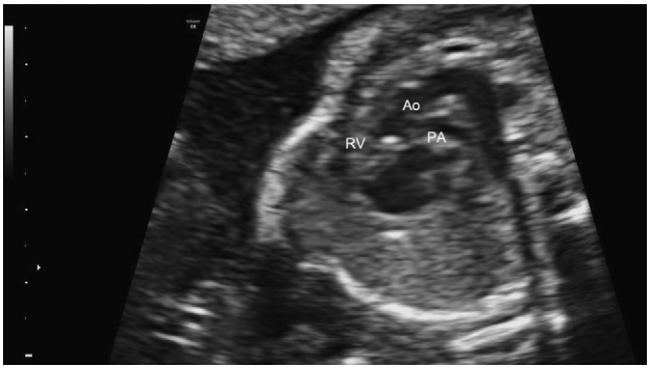

Fig. 2. Prenatal ultrasound demonstration of double outlet of right ventricle. Ao = aorta; RV = right ventricle; PA = pulmonary artery.

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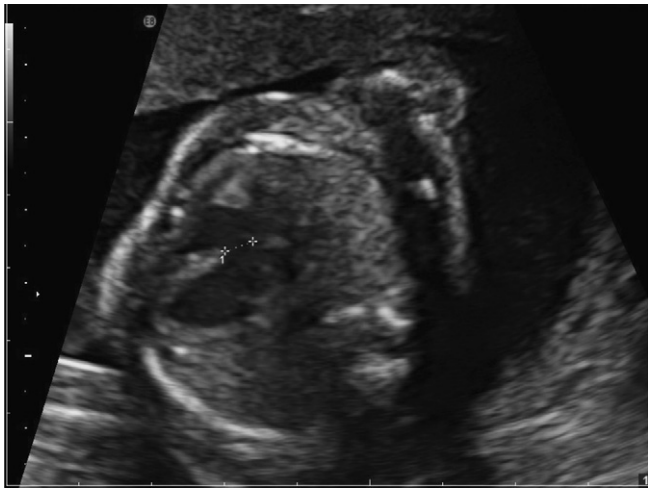

Fig. 3. Prenatal ultrasound demonstration of ventricular septal defect.

hand (Fig. 6). X-ray showed a gracile radius and reduced first metacarpal and phalanges of the right thumb (Fig. 7) and hypoplastic vertebral bodies of T10 to T12 causing scoliosis with convexity to the left (Fig. 8). Array comparative genomic hybridization analysis of fetal tissues revealed no genomic imbalances.

VACTERL association (OMIM 192350) is an acronym to describe nonrandom association with at least three of seven core abnormalities including vertebral defects (V), anal atresia (A), cardiac defects (C), tracheo-esophageal fistula (TE), renal anomalies (R) and limb defects (L). VACTERL association has an incidence of 1/10,000∼1/40,000 in live-born infants [1]. Prenatal diagnosis of VACTERL association should include a differential diagnosis of Alagille syndrome, Baller−Gerold syndrome, CHARGE syndrome, Currarino syndrome, 22q11.2 deletion syndrome (DiGeorge syndrome), Fanconi anemia, Feingold syndrome, Fryns syndrome, Holt-Oram syndrome, MURCS association, oculo-auriculo-vertebral syndrome, Opitz G/BBB syndrome, Pallister−Hall syndrome, Townes−Brocks syndrome and VACTERL-H, which have clinical

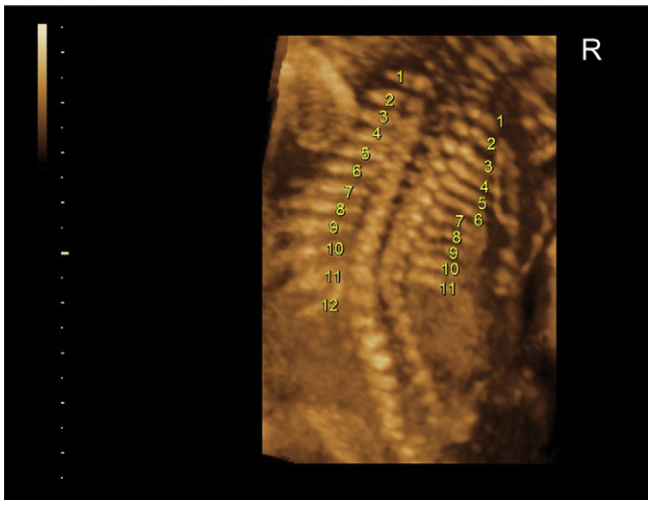

Fig. 4. Three-dimensional ultrasound demonstration of scoliosis with absence of one rib.

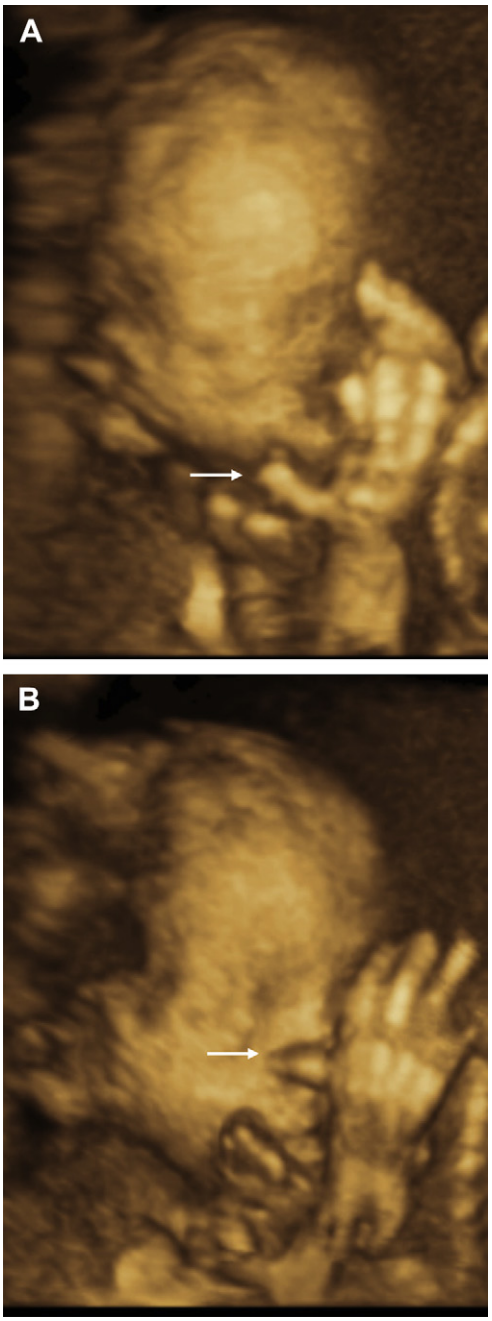

Fig. 5. Three-dimensional ultrasound demonstration of a radial club hand (arrows).

features in common with VACTERL association [1]. VACTERL association has been reported to be associated with unilateral pulmonary agenesis, unilateral aplasia of the humerus and partial hemihypoplasia [2,3].

Although approximately 90% of the cases of VACTERL association occur sporadically, there is evidence for familial inheritance in the other 10% of the cases, suggestive of genetic factors in the etiology of VACTERL association [4]. Reported genetic factors associated with VACTERL association include mitochondrial dysfunction and respiratory chain deficiency [5−9], genomic imbalances with various deletions or duplications [10−14], mutations in the *HOXD13* gene [15−17],

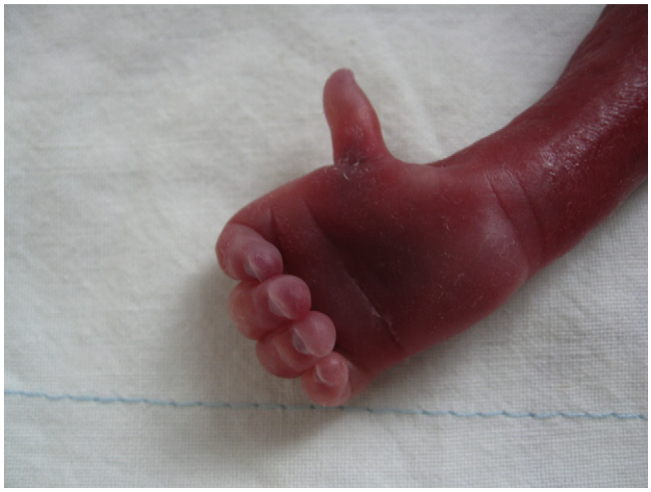

Fig. 6. Radial club hand at birth.

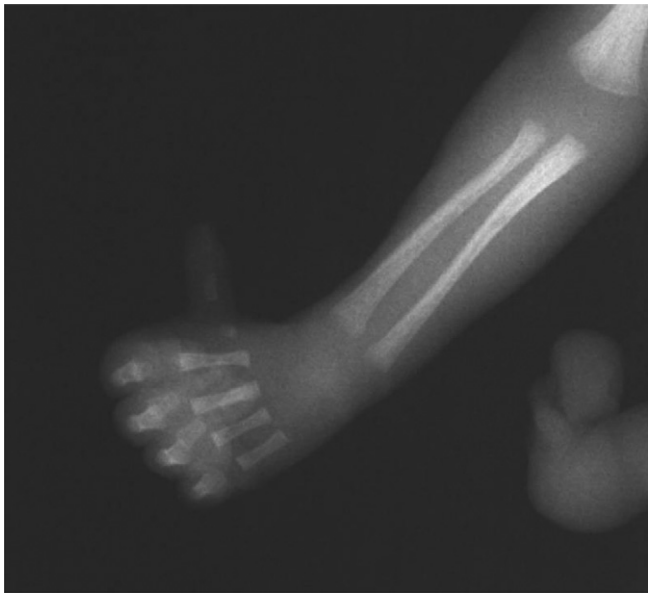

Fig. 7. X-ray shows a gracile radius and reduced first metacarpal and phalanges of the right thumb.

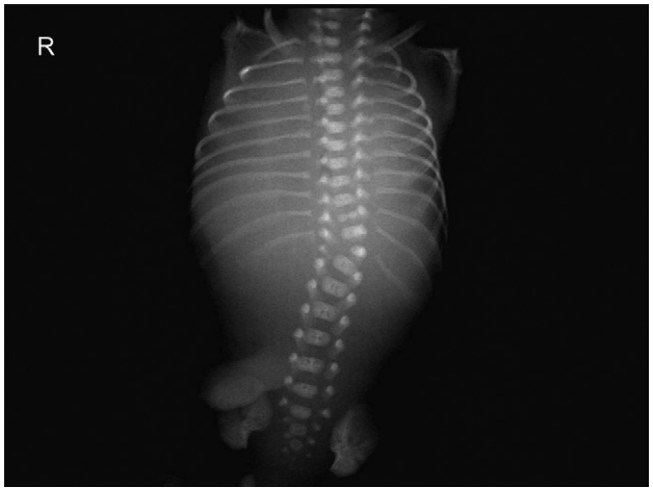

Fig. 8. X-ray shows hypoplastic vertebral bodies of T10 to T12 causing scoliosis with convexity to the left.

mutations in the *ZIC3* gene [18–21], mutations in the *PTEN* gene [22], and mutations in the *FOXF1* gene and the *FOX* gene cluster [23–25].

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