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Case Report

Prenatal diagnosis of radial ray defects by ultrasound: A report of 6 cases

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ABSTRACT

Objective: All of the medical records of fetuses with the sonographic finding of radial ray defects (RRDs) between 2008 and 2015 were retrieved. The associated sonographic findings, cytogenetic results, and necropsy findings were correlated.

Case report: There were 6 cases of RRD. Three cases were bilateral and the other 3 cases were unilateral. The gestational ages at diagnosis were between 12 and 24 weeks gestation. All women carrying fetuses with RRDs opted to terminate the pregnancy. There were 2 cases of trisomy 18, one case of thrombocytopenia-absent radius syndrome, and 2 cases of isolated RRD. Both cases of trisomy 18 had other sonographic abnormalities.

Conclusion: RRD should be considered if a short radius and abnormal angulation of the wrist or thumb is noted. The use of 3-D ultrasound facilitates the diagnosis of RRD, even at early gestation, by providing a better surface appearance, panoramic views, and spatial orientation.

Introduction

Radial ray defects (RRDs) encompass partial or complete absence of the radius and/or radial ray structures [1–3]. The radial ray gives rise to the first carpal and metacarpal bones, and the phalanges of the thumbs. According to Sofer [1], the incidence is approximately 1:30,000 live births. In another Finnish population-based study, the live birth prevalence was 1.64 per 10,000 live births [3]. RRD and associated anomalies include components of various disorders. Most defects are bilateral and sporadic, while bilateral defects are more likely a part of a multiple malformation syndrome [1–7]. Isolated RRD comprises 8%–30% of the cases, and the majority of the cases are associated with other anomalies, such as trisomy 13, 18, and 22q 11.2, and anomalies, such as VACTERL associations, Holt-Oram, Fanconi anemia, and thrombocytopenia with absent radius (TAR) [2–8]. Detailed ultrasonography, including 2-D or 3-D imaging, offers an opportunity to better appreciate subtle anomalies [4–6]. The aim of this study was to report our experience over a 6-year period in a regional tertiary referral fetal medical center in Taiwan.

Case presentation

We reviewed of our ultrasound laboratory database. All of the medical records of fetuses with the sonographic findings of RRD between 2008 and 2015 were retrieved. The fetuses with a final diagnosis of skeletal dysplasia were excluded. The associated sonographic findings, cytogenetic results, and necropsy findings were correlated. There were 6 cases of RRD. Three cases were bilateral and the other three cases were unilateral (Fig. 1A,B). The gestational ages at diagnosis were between 12 and 24 weeks. There were 2 cases of trisomy 18, 1 case of thrombocytopenia-absent radius syndrome confirmed by cord blood, and 3 cases of isolated RRD. Cases 1 and 6 had regular antenatal examinations in our hospital beginning at 12 or 13 weeks gestation, and RRD was diagnosed in the subsequent routine antenatal screening ultrasound. Cases 2 and 3 were referred from other local clinics due to suspected RRD. Case 4 was noted in a referred integrated ultrasound scan. In case 5, RRD was found incidentally during a referral for amniocentesis. Cytogenic studies of cases 1–4 were performed using cord blood. The results of amniocentesis from another hospital in case 5 showed trisomy 18 and a non-invasive prenatal test on case 6 was reported to be normal. Both cases of trisomy 18 had other sonographic abnormalities, as shown in Table 1. None of the cases had family histories of heart or skeletal disease. All women carrying fetuses with RRD opted to terminate the pregnancy after counseling, including those beyond 24 weeks gestation.

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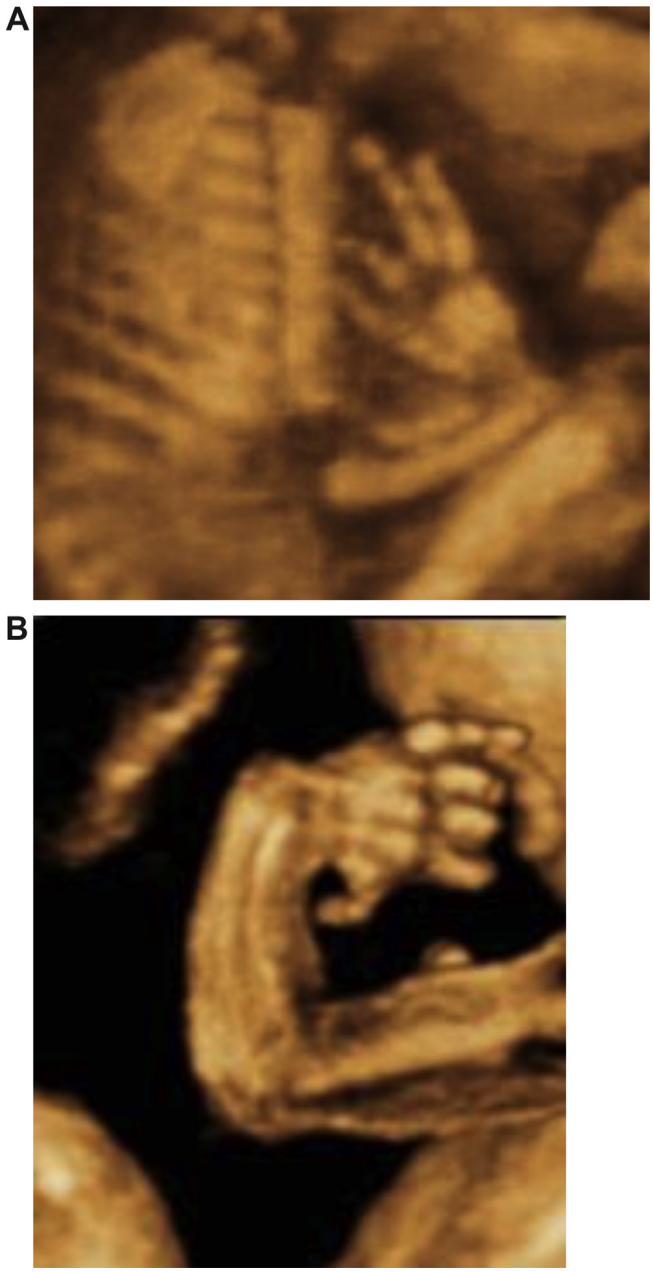

Fig. 1. 3D ultrasound images in case 1 (Figure 1A) and case 4 (Figure 1B) of RRD. RRD: radial ray defects. A: Ultrasound of Case 1 in 3D image showed short radius, absent of the thumb and radial angulation of the hand. B: Ultrasound of Case 4 in 3D image showed radial angulation of the hand.

Fig. 2A,B showed the necropsy and ultrasound images of the hands, respectively. Fig. 3 demonstrates the postmortem X-ray of case 4, which reported deformities of the hands in agreement with the ultrasound images. Table 1 shows all cases of RRD with ultrasound findings, data, and outcomes.

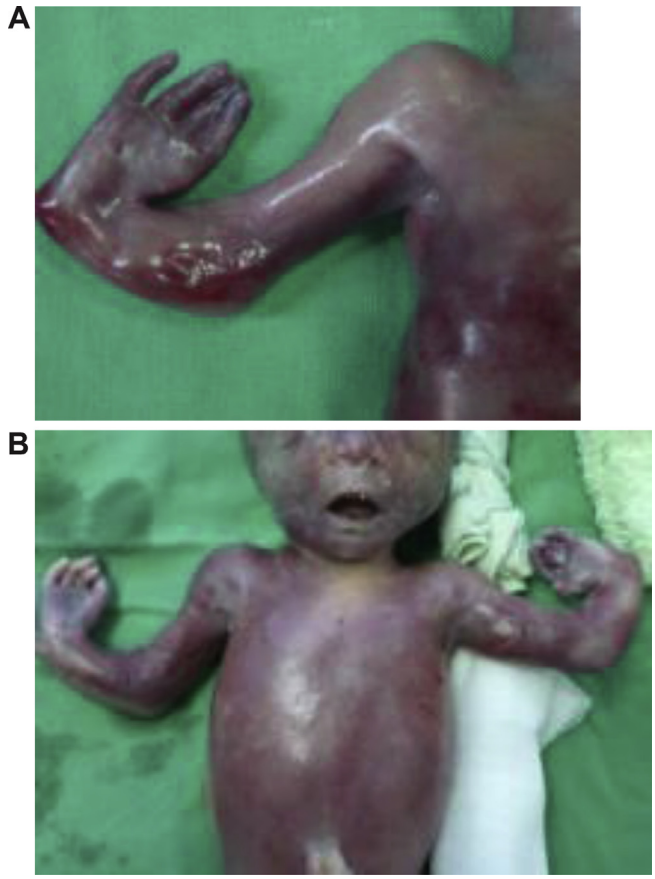

Fig. 2. Necropsy findings in case 1 (Figure 2A) and case 4 (Figure 2B) of RRD. RRD: radial ray defects. A: necropsy findings reported absence of the thumb and radial angulation of the hand in Case 1. B: necropsy findings reported shorening forearms and hands deformity with radial angulations in Case 4.

Discussion

Development of the human upper limbs is complicated and several genetic pathways and transcription factors are involved. The molecular pathway involved in limb development, includes fibroblast growth factor, sonic hedgehog, and bone morphogenic protein. In addition, the homeobox and wingless gene families, and the T-box transcription factor (TBX5) all are related [3,9–11]. Some reports indicate that isolated RRD occurs in 8%–30% of all cases [8]. The majority of associated major congenital syndromes include VACTERL associations. The phenotype is largely variable, including certain anomalies of the vertebrae and limbs. Many cases are sporadic. A strong association exists between the heart and RRD, and is evident at birth. Holt-Oram syndrome (heart anomalies, and especially preaxial limb reduction), Fanconi pancytopenia syndrome (radial hypoplasia, hyperpigmentation, and pancytopenia), Roberts syndrome (upper limb reduction anomalies and heart defects), Boller–Gerold syndrome (craniosynosis and radial aplasia),

Table 1
All cases of RRD with ultrasound findings, data, and outcomes.

CASE	1	2	3	4	5	6
Laterality	Right	Bi-	Left	Bi-	Bi-	Right
Associated anomalies	No	No	Yes (clubbed feet, CPC)	Yes (low platelet count)	Yes (CPC, omphalocele, CHD, NTDs)	Yes umbilical cord:1A1V
GA at DX	20	23	13	24	17	20
Final Dx	Isolated RRD	Isolated RRD	T-18	TAR synd.	T-18	Isolated RRD

Uni: unilateral; Bi: bilateral; CPC: choroid plexus cyst; T-18: trisomy 18; TAR: thrombocytopenia with absent radius; CHD: congenital heart disease; NTDs: neural tube defects; 1A1V: one artery and one vein; Dx: diagnosis; GA: gestational age.

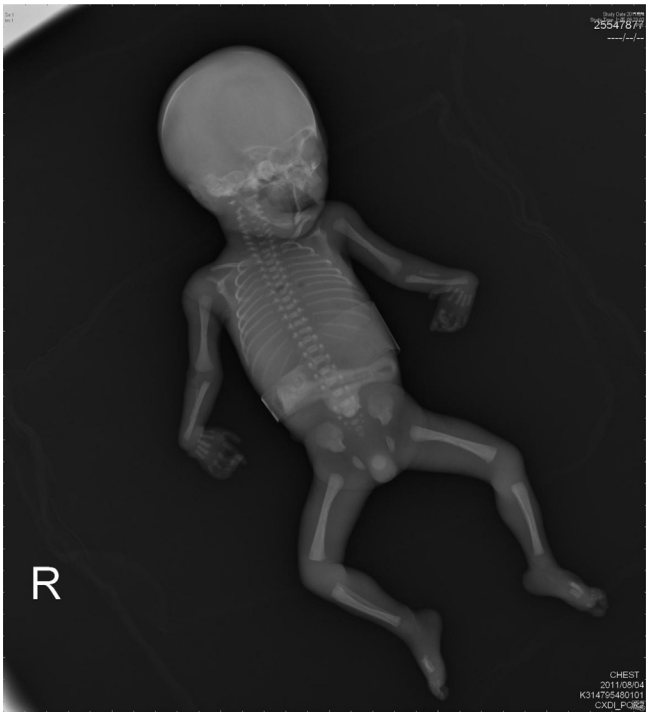

Fig. 3. Postmoterm X ray of Case 4 demonstrated shorening forearms and hands deformity with radial angulations as ultrasound image.

and Cornelia de Lange syndrome (minor limb abnormalities, heart defects, and hearing and eye problems) may be related to RRD [2–8,11]. When a radial ray anomaly is detected, these syndromes should be considered. Some reports have also proposed that valproate or thalidomide exposure might be associated with RRD [3–5]. Autosomal dominant, autosomal recessive, and X-linked inheritance have been proposed [2]. A detailed family history or exposure to a teratogen or drug should be included to obtain detailed consanguinity information.

Most previous reports or studies of RRD involve postnatally live cases [1–3,7,8,11,12]. Fetuses with RRD detected *in utero* are few in number [4–6]. Fetal screening and prenatal diagnosis, including ultrasound and maternal serum screening or a genetic approach in early pregnancy, can detect trisomy 18, 13, 22q 11.2, and other syndromes. RRD is often overlooked during obstetric ultrasound examinations because the position of the extremities is not always ideal for scanning and measurement. Measurement of the radius is not included in routine biometry. Shortening of the radial bone, not similar lengths of the radius bilaterally, the bizarre angle between the forearm and the palm or abnormal deviation of fingers, especially thumbs, was noted in conventional 2-D sonography; 3-D sonography should be applied for a more detailed survey. In four of our presenting cases, although sonographic features were present on 2D sonography, the diagnosis was made by 3D sonography first. The diagnosis was initially missed in one case referred at 13 weeks gestation. With 3D sonography, the diagnosis was made during the subsequent exam at 17 weeks gestation. The use of 3D ultrasound actually can facilitate the diagnosis of RRD, even at early gestation, because it provides a better surface appearance, panoramic view, and spatial orientation, which can be obtained to check the posture and configuration of the upper limbs. The deformity of the hands with radial angulation and loss or dysplasia of the thumb can be well-depicted on X-ray or necropsy findings. Although the number of cases in this study was limited to six, RRD can be regarded as an isolated finding only after a detailed assessment of other anomalies or other syndromes in affected fetuses.

Conflict of interest

The authors declare no conflict of interest.

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