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Fetal aberrant right subclavian artery in normal and Down syndrome fetuses

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KEYWORDS: aberrant right subclavian artery; Down syndrome; fetal echocardiography

ABSTRACT

Objectives *To evaluate the prevalence of fetal aberrant right subclavian artery (ARSA) in a low-risk population and compare it with that among Down syndrome fetuses, in order to estimate its potential as a marker in Down syndrome screening.*

Methods *Women undergoing routine fetal sonographic examination between 13 and 26 weeks of gestation were evaluated once for the presence of ARSA using either a transvaginal multifrequency 5–9-MHz probe or a transabdominal 4–8-MHz probe as appropriate. Early pregnancy outcome was obtained in all cases.*

Results *Nine hundred and twenty-four fetuses were recruited. An ARSA was detected in 13 fetuses (1.4%) with normal karyotype. During the study period, eight fetuses with Down syndrome referred either with known karyotype or with signs suspicious for Down syndrome were evaluated by the same protocol. Three of eight fetuses (37.5%) were found to have an ARSA. In none of these cases was ARSA an isolated finding. The odds ratio for ARSA in Down syndrome compared with normal fetuses was 42.04 (95% CI, 9.08–194.6).*

Conclusions *An ARSA was found in 1.4% of the normal population. In the small group of Down syndrome fetuses we observed a trend towards a higher rate of ARSA than in normal fetuses. In none of the Down syndrome fetuses was ARSA an isolated finding. Larger prospective studies are needed to examine the significance of ARSA as an isolated finding and the potential of ARSA as a marker in Down syndrome screening. Copyright © 2007 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Antenatal risk assessment for Down syndrome is based on screening for an ever-growing number of sonographic signs, so-called 'soft markers' that are found more frequently in the Down syndrome fetal population. Vascular 'signs' for chromosomal abnormalities have recently been added to the list of 'markers' for chromosomal aberrations. Their non-proven benefit, considerable false-positive rate and often negative impact on the prospective parents' state of mind can reflect poorly on a professional's reliability and on the relationship between patient and healthcare provider[1,2].

Fetuses with trisomy 21 have been reported to have a higher rate of anatomical abnormalities; in the cardiovascular system these include complex heart defects, isolated ventricular septal defects, isolated and/or multiple intracardiac echogenic focus, pericardial effusion, tricuspid regurgitation, and aberrant subclavian artery[3]. An aberrant right subclavian artery (ARSA) arising from the left aortic arch is one of the congenital cardiovascular abnormalities associated with Down syndrome[3,4]. Postnatal radiographic studies have shown that an ARSA is present in 16–35%[5,6] of infants or adults with Down syndrome, and in 0.4–2.3% of the general population[4,7–10]. Chaoui *et al.* reported a prenatal incidence of ARSA in Down syndrome fetuses of 35.7%[11].

Malformations are frequently found in fetuses with a high potential risk, although the real prevalence of these findings in the low-risk general population or the implications of these findings in risk assessment for aneuploidy are not known. Therefore, the aims of this study were to evaluate the prevalence of ARSA among normal fetuses, to compare it with the rate among Down syndrome fetuses, and to evaluate the potential value of ARSA as a prenatal screening tool for trisomy 21.

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METHODS

A cross-sectional study was performed to establish the prevalence of ARSA in the general population. The Institutional Review Board of the Chaim Sheba Medical Center approved the study.

Women with a singleton fetus and with no known risk factors who presented for routine fetal ultrasound examination between 13 and 26 weeks of gestation, to the Obstetric Ultrasound Unit, Chaim Sheba Medical Center, Tel Hashomer, Israel, were invited to participate. Most of the examinations were performed during routine first- or second-trimester malformation screening. Each patient was examined only once during the study and all fetuses were examined by two operators (Y.Z., Z.K.). Only patients with known gestational age, determined from the last menstrual period and confirmed by first-trimester ultrasound dating, were included in the study. Fetuses with abnormal nuchal translucency, intrauterine growth disorders or amniotic fluid volume disturbances were not included. Examinations were performed either transvaginally with a 5–9-MHz probe or transabdominally with a 4–8-MHz probe (Voluson 730 Expert system, GE Medical Systems, Zipf, Austria) as appropriate.

In the normal fetus, the right subclavian artery (RSA) courses right and anterior to the trachea and esophagus, whereas in cases with ARSA it crosses from the left thorax, behind the trachea, to the right hemithorax towards the right arm. The method for evaluation of the position of the RSA was adopted from that described by Chaoui *et al.*[11]. The three vessels and trachea view was first visualized as described by Yagel *et al.*[12] (Figure 1).

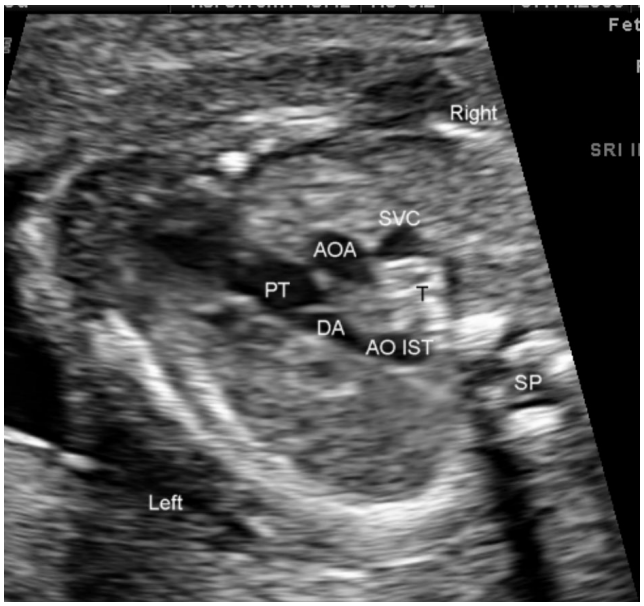

Figure 1 Three vessels and trachea view showing the aortic isthmus (AO IST) in a position as close as possible to 90° to the presumed course of the aberrant right subclavian artery in the retroesophagotracheal space. AOA, aortic arch; DA, ductus arteriosus; PT, pulmonary trunk; SP, spine; SVC, superior vena cava; T, trachea.

The plane was then adjusted to a position in which the pulmonary artery–ductus arteriosus–aortic arch axis was less than 60° relative to the presumed location of the ARSA. Color Doppler mapping was then applied over the region between the aortic isthmus and the retrotracheal area, with the velocity setting decreased to between 15 and 30 cm/s (Figure 2). In order to minimize false-positive diagnoses, we further applied direct visualization of the RSA by maintaining a transverse plane while tilting the probe cephalad and to the right until the RSA was visualized in both the transverse and longitudinal planes (Figure 3a and 3b). Visualization of the normal RSA helped avoid possible misidentification of normal vessels of the retroesophageal–tracheal space (such as the azygos vein) or other vascular abnormalities (Figure 4).

During the study period eight fetuses with Down syndrome, including two cases referred with suspicious sonographic findings but before amniocentesis results were known and six with known Down syndrome, were also examined for the presence of ARSA.

RESULTS

Nine hundred and twenty-four morphologically normal singleton fetuses of low-risk pregnant women, between 13 and 26 weeks of gestation, were examined for the presence of an ARSA during routine pregnancy sonographic follow-up. An ARSA was diagnosed when the vessel arose separately from the aortic arch behind the trachea, instead of from the brachiocephalic trunk. ARSA was detected in 13 cases (1.4%) (Figure 5). In six cases the ARSA was an isolated finding, whereas in the others it was accompanied by soft sonographic markers such as echogenic bowel, intracardiac echogenic focus (ICEF), single umbilical

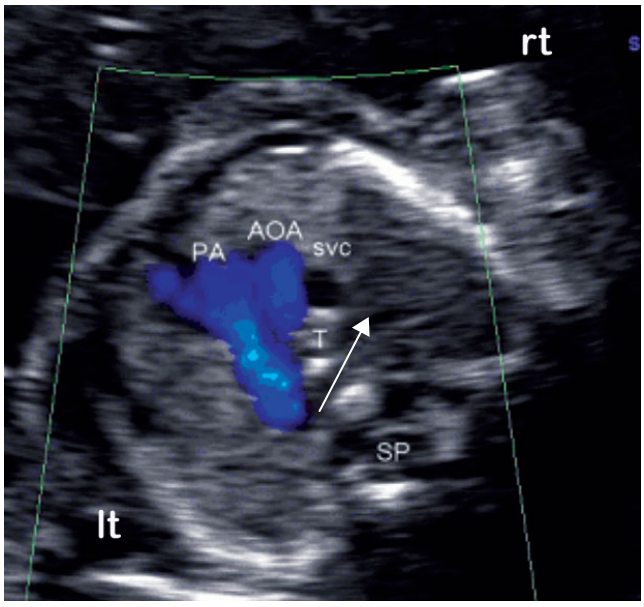

Figure 2 Three vessels and trachea view with color Doppler mapping. Arrow indicates the expected site of origin of the aberrant right subclavian artery. AOA, aortic arch; lt, left; rt, right; PA, pulmonary artery; SP, spine; SVC, superior vena cava; T, trachea.

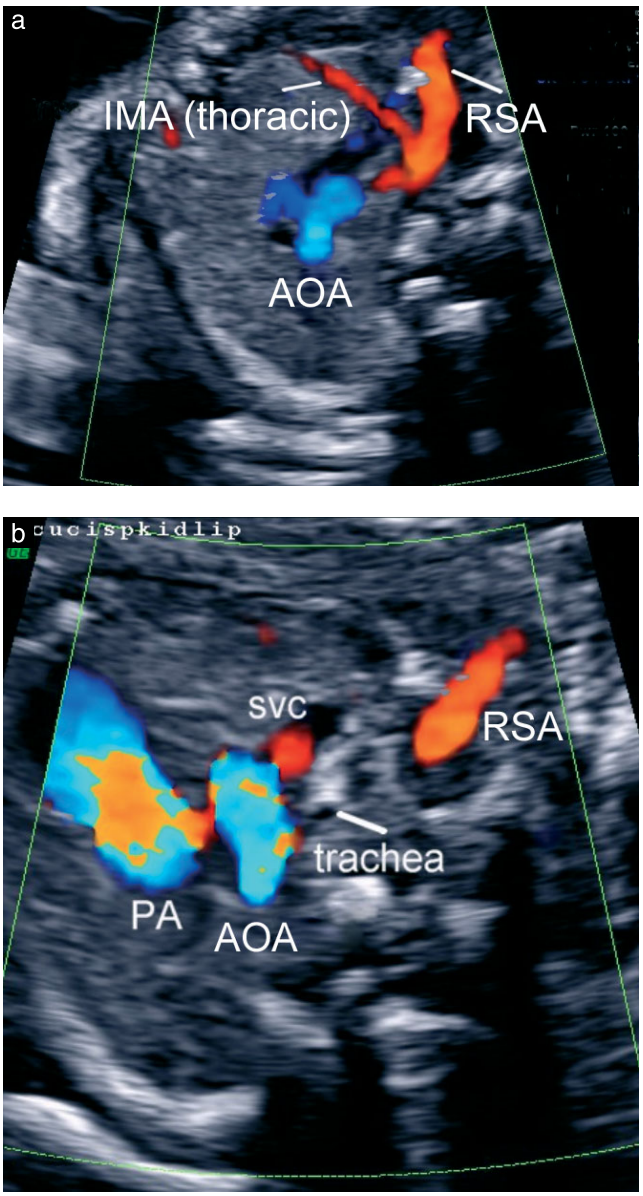

Figure 3 Direct visualization of the right subclavian artery (RSA) with (a) or without (b) the internal mammary artery (IMA) by color Doppler imaging. AOA, aortic arch; PA, pulmonary artery; SVC, superior vena cava.

artery, pyelectasis, cervical cysts and absence of the middle phalanx of the fifth digit, or other abnormalities such as 13 ribs and unilateral dysplastic kidney.

Amniocentesis revealed a normal karyotype in all 13 cases. Early pregnancy outcome confirmed normality in all subjects with the exception of a fetus with a dysplastic kidney; in this case the couple opted to terminate the pregnancy as there were early signs of a degenerative process in the contralateral kidney. Details of the findings in these 13 cases are presented in Table 1.

Among the eight fetuses with Down syndrome, three cases presented with ARSA (37.5%). In all three an ARSA was found in combination with other sonographic markers: persistent left superior vena cava (Case 3); cystic hygroma with tricuspid regurgitation and ICEF (Case 1), and bilateral choroid plexus cysts, hyperechogenic bowel

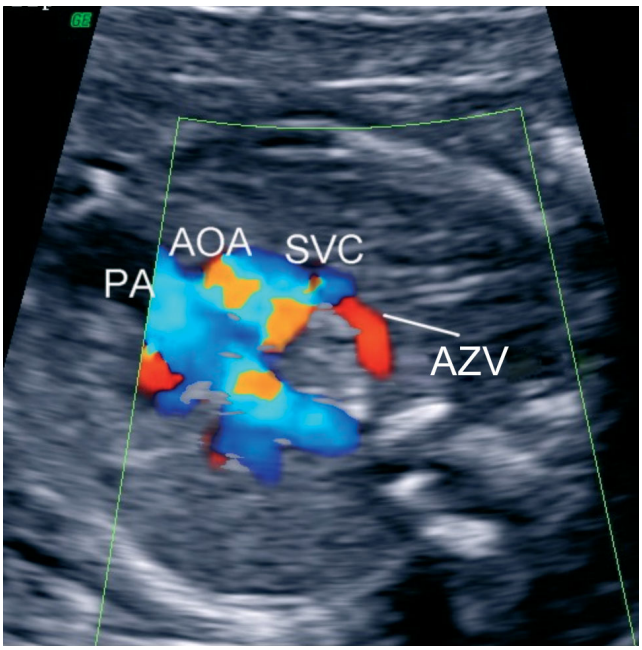

Figure 4 Color Doppler mapping showing azygos vein (AZV) connection to the superior vena cava (SVC). Note the right, retrotracheal and posteroanterior course of the azygos vein, compared with the retrotracheal, left-to-right course of the aberrant right subclavian artery in Figure 5. AOA, aortic arch; PA, pulmonary artery.

with polyhydramnios and ventricular septal defect (Case 2). Clinical features of all Down syndrome cases are presented in Table 2.

The odds ratio for ARSA in Down syndrome compared with normal fetuses was 42.04 (95% CI, 9.08–194.6). ARSA was an isolated finding in 6/924 (0.65%) normal fetuses, whereas in the Down syndrome fetuses it was always found in combination with other markers for Down syndrome.

DISCUSSION

Embryologically, the RSA originates from the aortic sac and is composed of three segments, in a proximal to distal order: the right fourth arch, the short segment of the right dorsal aorta and the right seventh intersegmental artery[13]. The normal RSA arises as the first vessel from the brachiocephalic artery of the aortic arch, and is located at the junction of the sternum and right clavicle (Figure 3a). The most common aortic arch anomaly is an ARSA[4]. It arises distal to the left subclavian artery of the normal left aortic arch, as the fourth branch, as a separate vessel from the aortic isthmus, and crosses the mediastinum obliquely from left to right, posterior to the esophagus and trachea[13,14] (Figure 5a and b). In 60% of cases, its origin in the thoracic aorta is saccular, known as the diverticulum of Kommerell[15]. The ARSA results from abnormal regression of the right fourth aortic arch, coupled with retention of a segment of the right dorsal aorta, which connects to the right seventh intersegmental artery, distal to the origin of the left seventh intersegmental artery[13].

Table 1 Details of findings in fetuses with aberrant right subclavian artery and normal karyotype

Gestational age at diagnosis (weeks)	*Maternal age (years)*	*Additional findings*	*Karyotype*	*Outcome*
15 + 1	25	Echogenic bowel	46,XX	Healthy
15 + 2	27	None	46,XY	Healthy
15 + 3	29	Bilateral cervical cysts	46,XX	Healthy
15 + 6	25	None	46,XX	Healthy
16 + 2	38	SUA, IUGR, absent MPFD	46,XY	Healthy
22 + 1	32	None	46,XX	Healthy
23 + 1	34	None	46,XX	Healthy
23 + 2	27	None	46,XY	Healthy
23 + 4	29	ICEF	46,XX	Healthy
24 + 5	30	None	46,XY	Healthy
25 + 2	28	Dysplastic kidney	46,XY	TOP
25 + 4	34	13 ribs	45,XX	Healthy
26 + 0	25	Pyelectasis	46,XY	Healthy

ICEF, intracardiac echogenic focus; IUGR, intrauterine growth restriction; MPFD, middle phalanx of fifth digit; SUA, single umbilical artery; TOP, termination of pregnancy.

Table 2 Aberrant right subclavian artery (ARSA) in cases of Down syndrome: details of screening and sonographic findings

Case	*GA at examination (weeks)*	*Maternal age (years)*	*Parity*	*NT thickness (mm)*	*Calculated risk for Down syndrome*	*ARSA*	*Additional sonographic findings*
1	15	34	Gravida 3 para 2	2.0	1:130	Yes	Cystic hygroma 4 mm at 15 weeks, TR, ICEF, cervical cysts
2	21	31	Gravida 3 para 2	—	—	Yes	Bilateral CPC, hyperechogenic bowel, VSD
3	26	23	Gravida 1 para 0	1.7	1:941	Yes	PLSVC
4	18	31	Gravida 2 para 1	2.6	1:16	No	None
5	19	33	Gravida 3 para 2	1.6	1:13	No	None
6	20	34	Gravida 5 para 4	—	1:241	No	None (PS at 39 weeks)
7	21	36	Gravida 1 para 0	1.5	1:230	No	PRUV
8	22	46	Gravida 5 para 4	3.8	1:9	No	None

CPC, choroid plexus cysts; GA, gestational age; ICEF, intracardiac echogenic focus; NT, nuchal translucency (measured in the first trimester); PLSVC, persistent left superior vena cava; PRUV, persistent right umbilical vein; PS, pulmonary stenosis; TR, tricuspid regurgitation; VSD, ventricular septal defect.

In a preliminary study, Chaoui *et al.* found an ARSA in 37.5% of 14 cases of Down syndrome[11]. The same group later published a series of 906 fetuses examined between 15 and 34 weeks' gestation[16]. The RSA was aberrant in 14 cases, one of which was diagnosed with trisomy 21. This fetus had an additional intracardiac echogenic focus. The authors found a prevalence of 1.4% (13/905) in the normal population. Similarly, we have shown that the prevalence of fetal ARSA in our low-risk population is 1.4%. Our results are also concordant with reports concerning the higher prevalence of ARSA among Down syndrome fetuses than in an unaffected population. In our Down syndrome fetuses it was 35.7%, with an odds ratio of 42.04 and likelihood ratio of 26.5.

ARSA was an isolated finding in 6/13 fetuses with a normal karyotype. The other seven were diagnosed with mostly minor abnormal findings (soft signs). Only one case was associated with progressive dysplastic kidneys and the pregnancy was terminated (Table 1).

In the group of eight fetuses with Down syndrome, two mothers were older than 35 years. In the three Down syndrome cases in which ARSA was found the nuchal translucency thickness was less than 3 mm in the two cases in which it was measured. The combined calculated risk for Down syndrome (based on either nuchal translucency at 12 weeks or the triple test at 17 weeks) was correctly indicative in 6/7 cases in which it was performed. None of these fetuses presented with ARSA as an isolated finding. Interestingly, Chaoui *et al.* also described the combination of ARSA and ICEF in their only case of Down syndrome detected among a screened population[16], and, in a study of 14 Down syndrome fetuses, they found ICEF in (3/5) cases with an ARSA[11]. They also described a case of Down syndrome in which the only abnormal finding was an ARSA[11]. This raises the difficult question of counseling parents of a fetus with ARSA, especially as an isolated finding. The relatively high incidence of ARSA in the normal population in which the outcome is good, even when associated with other abnormal sonographic findings, and, on the other hand, the presence of additional markers in all cases of Down syndrome, limits our

capacity to evaluate ARSA as an isolated finding and, as a consequence, our counseling task with regard to karyotyping. This is similar to the counseling dilemma that arises when a fetus is diagnosed with isolated right-sided aortic arch. Whether to offer an invasive procedure under such circumstances, to exclude 22q11 microdeletion, is a matter of debate. Zidere *et al.* do not recommend this unless extracardiac malformations are found[17].

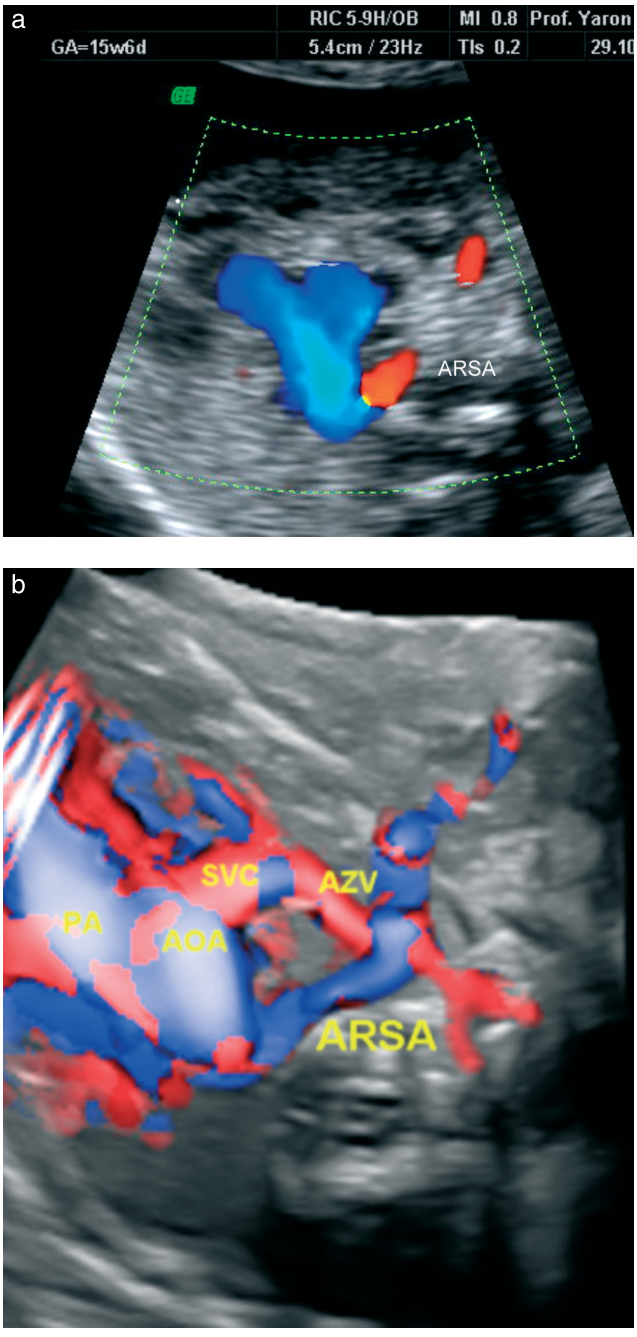

Figure 5 Two-dimensional (a) and three-dimensional (b) visualization of aberrant right subclavian artery (ARSA) using color Doppler imaging. AOA, aortic arch; PA, pulmonary artery; SVC, superior vena cava, AZV, azygos vein.

In summary, the prevalence of ARSA in our normal low-risk population was 1.4% and, based on a small group, the prevalence in fetuses with Down syndrome was 37.5%. These results concur with earlier prenatal, pediatric and adult studies of the prevalence of this aberration in such populations[18]. An extensive anatomical sonographic evaluation, as well as fetal echocardiography, is mandatory before defining ARSA an isolated finding. The implications of this increased prevalence in Down syndrome fetuses for prenatal screening programs should be investigated in a large well powered prospective study.

REFERENCES

1. Benacerraf BR, Gelman R, Frigoletto FD Jr. Sonographic identification of second-trimester fetuses with Down's syndrome. *N Engl J Med* 1987; **317**: 1371–1376.
2. Filly RA. Obstetrical sonography: the best way to terrify a pregnant woman. *J Ultrasound Med* 2000; **19**: 1–5.
3. Jones KL. In *Smith's Recognizable Patterns of Human Malformations* (5th edn). W. B. Saunders: Philadelphia, PA, 1997; 8–13.
4. Edwards JE. Malformations of the aortic arch system manifested as vascular rings. *Lab Invest* 1953; **2**: 56–75.
5. Lo NS, Leung PM, Lau KC, Yeung CY. Congenital cardiovascular malformations in Chinese children with Down's syndrome. *Chin Med J (Engl)* 1989; **102**: 382–386.
6. Goldstein WB. Aberrant right subclavian artery in mongolism. *Am J Roentgenol Radium Ther Nucl Med* 1965; **95**: 131–134.
7. Zapata H, Edwards JE, Titus JL. Aberrant right subclavian artery with left aortic-arch: associated cardiac anomalies. *Pediatr Cardiol* 1993; **14**: 159–161.
8. Raider L. Aberrant right subclavian artery. *South Med J* 1967; **60**: 145–151.
9. Nguyen KT, Vas W, Zylak CJ. Diagnosis of an aberrant right subclavian artery on CT. *J Comput Tomogr* 1981; **5**: 38–40.
10. Hara M, Satake M, Itoh M, Ogino H, Shiraki N, Taniguchi H, Shibamoto Y. Radiographic findings of aberrant right subclavian artery initially depicted on CT. *Radiat Med* 2003; **21**: 161–165.
11. Chaoui R, Heling KS, Sarioglu N, Schwabe M, Dankof A, Bollmann R. Aberrant right subclavian artery as a new cardiac sign in second- and third-trimester fetuses with Down syndrome. *Am J Obstet Gynecol* 2005; **192**: 257–263.
12. Yagel S, Arbel R, Anteby EY, Raveh D, Achiron R. The three vessels and trachea view (3VT) in fetal cardiac scanning. *Ultrasound Obstet Gynecol* 2002; **20**: 340–345.
13. Larsen WJ. Development of the vasculature. In *Essentials of Human Embryology* (2nd edn). Churchill Livingstone: New York, 1998; 123–149.
14. Freed K, Low VH. The aberrant subclavian artery. *AJR Am J Roentgenol* 1997; **168**: 481–484.
15. Davidian M, Kee ST, Kato N, Semba CP, Razavi MK, Mitchell RS, Dake MD. Aneurysm of an aberrant right subclavian artery: treatment with PTFE covered stentgraft. *J Vasc Surg* 1998; **28**: 335–339.
16. Chaoui R, Thiel G, Heling KS. Prevalence of an aberrant right subclavian artery (ARSA) in normal fetuses: a new soft marker for trisomy 21 risk assessment. *Ultrasound Obstet Gynecol* 2005; **26**: 356.
17. Zidere V, Tsapakis EG, Huggon IC, Allan LD. Right aortic arch in the fetus. *Ultrasound Obstet Gynecol* 2006; **28**: 876–881.
18. Freed K, Low VH. The aberrant subclavian artery. *AJR Am J Roentgenol* 1997; **168**: 481–484.