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CASE REPORT

Isomerism of the atrial appendages associated with 22q11 deletion in a fetus

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Abstract

There is a strong association between prenatally diagnosed structural heart disease and fetal chromosomal abnormalities. Isomerism of the atrial appendages is an exception to this because the fetal karyotype is usually normal in this condition. A case of atrial isomerism diagnosed antenatally with a normal female karyotype but with a microdeletion of chromosome 22q11 is reported.

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Keywords: atrial isomerism; chromosome 22q11; fetal karyotype; microdeletion

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Isomerism of the atrial appendages, when diagnosed prenatally, is frequently associated with structural heart disease but the fetal karyotype is usually normal.[1]

We report a case of isomerism of the left atrial appendages associated with an atrioventricular septal defect in a fetus in whom routine chromosome analysis demonstrated a normal karyotype but more detailed testing revealed a microdeletion of chromosome 22q11.

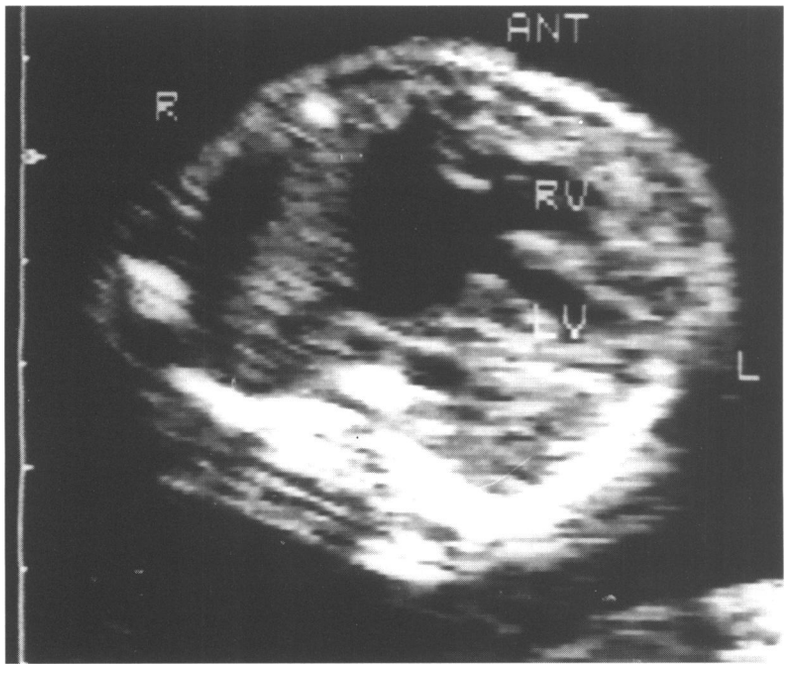

Figure 1 Four chamber view through the fetal thorax showing complete atrioventricular septal defect with right ventricular dominance. RV, right ventricle; LV, left ventricle; ANT, anterior.

Case report

A 19 year old primigravida was referred for a detailed fetal echocardiogram. She was about 23 weeks pregnant. There was no family history of congenital heart disease and the couple were not consanguineous.

Ultrasound imaging showed the fetal heart in the left side of the thorax and the stomach on the right side of the abdomen. This finding suggested intestinal malrotation. The left renal pelvis was dilated and polyhydramnios was present.

The fetal heart rate was 80–100 beats per minute and analysis of atrial and ventricular wall contraction indicated complete heart block. There was a complete atrioventricular septal defect (fig 1) and both great arteries arose from the right ventricle with the aorta to the right and running alongside the pulmonary artery. At the level of the fetal diaphragm there was interruption of the inferior caval vein and right sided azygous continuation (fig 2). The arrangement of the great vessels in the abdomen of this fetus suggested isomerism of the atrial appendages.

An amniocentesis was performed to establish the fetal karyotype because dilatation of the renal pelvis was also present. On G banding, the karyotype was that of a normal female 46 XX, but fluorescent in situ hybridisation (FISH) showed a microdeletion of the 22q11 region.

In view of the complex nature of the cardiac defect and the chromosomal abnormality, the mother chose to terminate the pregnancy. A complete fetal postmortem was performed.

The fetus was a female with a few dysmorphic features including mild hypertelorism, downfolding of the upper helix of the right ear, and a sacral tuft.

The thymus was not present and no ectopic thymic tissue could be found. Both lungs were bi-lobed with bronchi that were bilaterally long and hyparterial. The heart was situated in the left chest with the apex to the left. Both atria were morphologically of the left type with

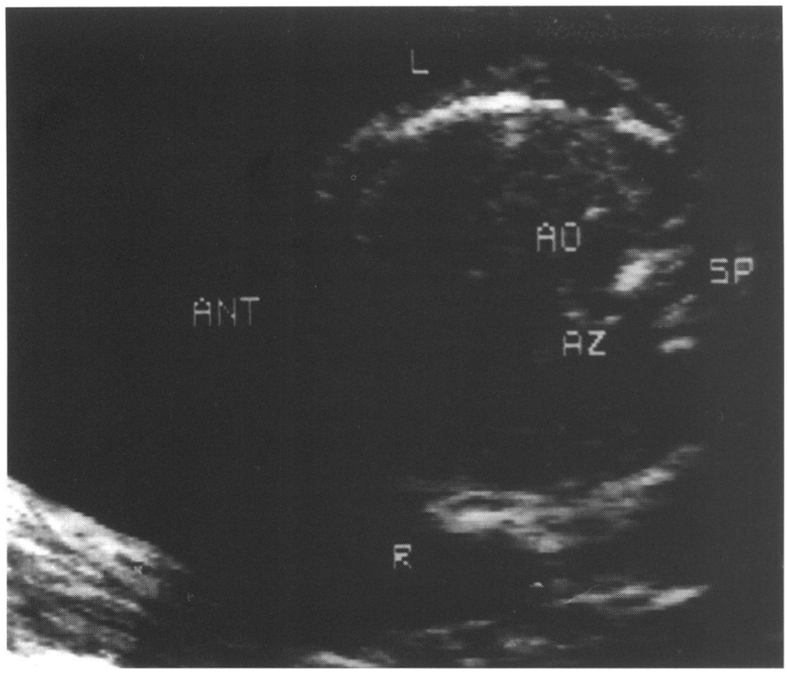

Figure 2 Cross section through the fetal thorax at the level of the diaphragm showing the azygos vein posterior and to the right of the aorta. AO, aorta; AZ, azygos; SP, spine; ANT, anterior.

dilatation of the right-sided left-type atrium. There was right ventricular dominance with a right to left ratio of 2:1. Both great arteries were side by side with the aorta to the right. The aorta continued as a left-sided aortic arch. There was a single right-sided superior caval vein with interruption of the inferior caval vein and drainage of the hepatic veins directly into the right-sided atrium. The pulmonary veins drained bilaterally, two to each atrium. The atrioventricular junction was guarded by a common valve. This confirmed a complete atrioventricular septal defect. The right-sided left-type atrium led into a right ventricle and the right ventricular outflow tract led into the pulmonary trunk and into the aortic root (double outlet right ventricle). The left sided left-type atrium led into a finely trabeculated left ventricle.

In the abdomen, the stomach was situated on the right with malrotation of the intestines. The liver was normal and present on the right side. There were multiple spleens on the right side adjacent to the stomach. The left kidney was enlarged and was shown to be cystic on sectioning. The remainder of the fetal post mortem was normal and consistent with gestational age.

Discussion

Isomerism of the atrial appendages and abnormalities of visceral situs during fetal life have been shown to be associated with a normal fetal karyotype.[2] Also, the high incidence of recurrence in siblings and the association of parental consanguinity with atrial isomerism, supports the view that this condition arises because of various single gene defects which are recessively inherited.[3,4] The chromosomal location of several of these genes has been established and some disease-causing mutations in specific genes identified.[5,6]

To our knowledge, this is the first reported case of atrial isomerism associated with with a deletion in chromosome 22q11. A clear association between deletions in the chromosome 22q11 region and congenital heart defects, particularly conotruncal anomalies, has been reported.[7-9]

Chromosome 22q11 deletion is also associated with extracardiac abnormalities.[10] The presence of a cardiac defect, the absence of a thymus gland, and the hypertelorism present in this fetus are features which are consistent with chromosome 22q11 deletion phenotype. Isomerism of the atrial appendages with the associated intestinal malrotation and polysplenia are not known associations. The conotruncal abnormality which was present in this fetus may be a feature of either the left atrial isomerism or of the chromosome 22q11 deletion. Thus the influence of the 22q11 deletion in the formation of the complex cardiac defect in this fetus remains unclear.

In conclusion, although the risk of aneuploidy in association with atrial isomerism remains low, chromosomal defects may occasionally be present. This report reinforces the need to consider fetal karyotyping in all fetuses with a structural cardiac defect detected prenatally, especially if there are additional extracardiac abnormalities. This first reported observation of left atrial isomerism with a deletion of chromosome region 22q11 now needs further analysis to establish whether this is a consistent finding or an unfortunate coincidence.

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1 Cook AC, Allan LD, Anderson RH, Sharland GK, Fagg NL. Atrioventricular septal defect in fetal life—a clinicopathological correlation. *Cardiol Young* 1991;**1**:334–43.
2 Brown DL, Emerson DS, Shulman LP, Doubilet PM, Felker R, Van Praagh S. Predicting aneuploidy in fetuses with cardiac anomalies: significance of visceral situs and non-cardiac anomalies. *J Ultrasound Med* 1993;**12**: 153–61.
3 Rose V, Lzukawa T, Moes CAF. Syndromes of asplenia and polysplenia. A review of cardiac and non cardiac malformations in 60 cases with special reference to diagnosis and prognosis. *Br Heart J* 1975;**37**:840–52.
4 Gatrad AR, Read AP, Watson GH. Consanguinity and complex cardiac anomalies with situs ambiguus. *Arch Dis Child* 1984;**59**:242–5.
5 Casey B, Devoto M, Jones KL, Ballabio A. Mapping a gene for familial situs abnormalities to human chromosome Xq24-q27·1. *Nature Genet* 1993;**5**:403–7.
6 Britz-Cunningham SH, Shah MM, Zuppan CW, Fletcher WH. Mutations of the connexion 43 gap junction gene in patients with heart malformations and defects of laterality. *N Engl J Med* 1995;**332**:1323–9.
7 Goldmuntz E, Driscoll D, Budarf ML, Zackai EH, McDonald-McGinn DM, Biegel JA, *et al.* Microdeletions of chromosomal region 22q11 in patients with conotruncal cardiac defects. *J Med Genet* 1993;**30**:807–12.
8 Greenburg F. DiGeorge syndrome: an historic review of clinical and cytogenetic features. *J Med Genet.* 1993;**30**: 803–6.
9 Melchionda S, Diglio MC, Mingarelli R, Novelli G, Scambler P, Marino B, *et al.* Transposition of the great arteries associated with deletion of chromosome 22q11. *Am J Cardiol* 1995;**75**:95–8.
10 Driscoll D, Salvin J, Sellinger B, Budarf ML, McDonald-McGinn DM, Zackai EH, *et al.* Prevalence of 22q11 microdeletions in DiGeorge and velocardiofacial syndromes: implications for genetic counselling and prenatal diagnosis. *J Med Genet* 1993;**30**:813–7.