SHORT COMMUNICATION

Isolated pericardial effusion in the human fetus: a report of three cases

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Objective Our objective was to determine the possible underlying etiologies and outcome in isolated fetal pericardial effusion.

Methods Doppler fetal echocardiography allowed the diagnosis of pericardial effusion in three patients and revealed the etiology in two.

Results We present the findings in three cases of isolated pericardial effusion. In the first, the pericardial effusion was a manifestation of trisomy 21 associated with a myeloproliferative disorder. In the second, the pericardial fluid collection was the first sign of an autosomal recessive disease, idiopathic infantile arterial calcification. The third case was remarkable because of the spontaneous resolution of a large pericardial fluid collection.

Conclusion Isolated fetal pericardial effusion covers a wide spectrum of etiologies from severe genetic and chromosomal diseases to transient forms. Copyright © 2003 John Wiley & Sons, Ltd.

KEY WORDS: prenatal diagnosis; fetal pericardial effusion; Down syndrome; myeloproliferative disorder; idiopathic infantile arterial calcification

INTRODUCTION

Pericardial effusion (PE) is detectable during routine obstetric ultrasonography. A fluid collection greater than 2 mm is abnormal (Shenker et al., 1989; Di Salvo et al., 1994). Many cases present with other fluid collections (ascites, pleural effusion, fetal skin edema). Pericardial effusion is the result of the mechanism that produces fetal hydrops. Structural cardiac malformations and fetal cardiac arrhythmias are the most common cause of non-immune hydrops (Jauniaux et al., 1990; Santolaya et al., 1992; Van Maldergem et al., 1992; Norton, 1994; Steiner, 1995). Other conditions associated with non-immune fetal hydrops include genetic disorders, metabolic disorders, pericardial teratoma, hematologic abnormalities and congenital infections (Steiner, 1995). We report three cases of isolated PE, which are not related to structural heart abnormalities or fetal arrhythmias.

MATERIAL AND METHODS

Doppler fetal echocardiograms were performed using an Acuson 128XP and a 5-MHz linear transducer. An evaluation of the rhythm, morphology and Doppler flow velocities of the fetal heart was performed. Our definition of pericardial effusion is a fluid collection greater than 2 mm, found in all the views of the fetal heart and present around the atrioventricular groove.

RESULTS

Case 1

A 25-year-old woman, gravida 1, para 1, was referred at 31 weeks of gestation with a diagnosis of pericardial effusion. Fetal echocardiography revealed normal cardiac anatomy and rhythm. A PE of 12 mm was found with abnormal diastolic function of the fetal heart (equal velocities of the filling peaks E and A of the mitral and tricuspid valves). Amniocentesis, fetal blood sampling and pericardiocentesis were performed. Fetal karyotyping revealed 47, XY,+21. Fetal blood analysis showed a hemoglobin level of 15 g/dL, platelet count of 117 000/mm³ and white blood cell count of 123 000/mm³. Of the white blood cells, 64% were blast cells. Flow cytometric analysis revealed that they were positive for CD13 and CD33, two markers of the myeloid lineage and CD34 and CD7, two markers of immaturity in myeloid leukemia. They were negative for CD41, a platelet-related antigen that is frequently found in myeloproliferative disorders in neonates or children.
with trisomy. Finally, blast cells did not express major B- or T-lineage-related antigens. According to these results, this leukemia was classified as an acute myeloid leukemia (AML) with an FAB M0 state of differentiation. The pericardial fluid did not contain any blast cells. Viral screening in the blood and the pericardial fluid was negative. After prenatal counselling, the parents opted for termination of pregnancy at 32 + 2 weeks of gestation and they refused fetal autopsy.

Case 2

A 19-year-old woman, gravida 2, para 1, a first-degree consanguineous marriage, was referred for evaluation of a PE at 32 + 4 weeks of gestation.

Fetal echocardiography confirmed a PE of 8 mm. Cardiac anatomy, flow velocities and cardiac rhythm were normal. Amniocentesis was performed and fetal karyotyping was normal (46, XX). Viral screening was negative. Serial fetal echocardiography showed an increasing pericardial effusion. An unusual echo-dense appearance was found at the level of the pulmonary annulus, trunk and ascending aorta (Figure 1). The diagnosis of idiopathic infantile arterial calcification (IIAC) was made at 33 + 4 weeks of gestation. At 35 + 3 weeks of gestation, an emergency Caesarean section was performed for fetal distress. A female infant weighing 2680 g, length 44 cm and head circumference 31 cm was delivered. At birth, the baby was in congestive heart failure with hepatosplenomegaly and a large pericardial effusion. Pericardiocentesis was performed. Echocardiography revealed calcification of the great vessels (Figure 2) and the coronary arteries. Electrocardiography did not reveal any signs of myocardial ischemia. Further investigations including cranial ultrasound and computed tomography scan of the brain showed calcifications of the carotid, vertebral and intracranial arteries (Figure 3). The abdominal scan showed diffuse calcification of the abdominal aorta, coeliac trunk, renal, splenic, hepatic and mesenteric arteries and the arteries of the limbs (Figure 4). Angiography revealed areas of vascular narrowing of the aorta and carotids without renal artery stenosis. Periarticular calcifications were seen in both shoulders, the right elbow, both wrists, knees and ankles (Figure 5). We began treatment with diphosphonates. The baby developed arterial hypertension that was controlled with β-blockers and calcium channel inhibitors. Serial echocardiography showed the regression of the PE and the development of a progressive hypertrophic cardiomyopathy.

Case 3

A 26-year-old woman, gravida 2, para 1, was referred for evaluation of PE at 18 + 2 weeks gestation. The PE was 10 mm. Cardiac anatomy, flow velocities and rhythm were normal. Amniocentesis, fetal blood sampling and pericardiocentesis were performed. Fetal karyotyping was normal, 46, XX. Viral screening in the blood and the pericardial fluid was negative. Serial fetal echocardiography showed a decreasing PE with subsequent complete resolution at 28 + 2 weeks of gestation. The fetal growth was normal. At 38 + 2 weeks of gestation, a female infant was delivered. Her weight was 3210 g, length 47 cm and the Apgar score 10/10. She had a normal clinical examination and the post-natal echocardiography was normal too.

DISCUSSION

In two of the three cases, the isolated PE was the first sign of a chromosomal or genetic disease. In the first case, a chromosomal abnormality (trisomy 21) was found. A high incidence (31%) of karyotypic anomalies, in particular trisomy 21, has been reported in isolated prenatal pericardial effusion (Sharland and Lockhart, 1995). In the second case, IIAC was diagnosed prenatally. Children and infants with trisomy 21 have an increased risk of developing leukemia (Lange, 2000). The unique feature of acute leukemia in children with Down syndrome is the high incidence of acute myeloid leukemia and primary acute megakaryoblastic leukemia. Similar forms of hematologic abnormalities can be
observed in neonates with Down syndrome. In neonates, however, this disorder is named transient myeloproliferative disorder (TMD) since in most cases spontaneous regression is observed (Lange, 2000). Zipursky et al. (1997) estimated that at least 10% of Down newborns have TMD that usually regresses by the age of 2 or 3 months. In the rare prenatal reports of this pathology in fetuses with trisomy 21, the clinical presentation was non-immune hydrops and/or fetal hepatosplenomegaly (Smrcek et al., 2001; Macones et al., 1995). We are aware of only two other cases that have been reported previously with trisomy 21 and TMD, revealed by an isolated pericardial effusion (Strobelt et al., 1995; Hirashima et al., 2000).

In TMD, peripheral leukocyte counts are markedly elevated and circulating blast cells are present. Anemia is usually absent or is moderate. The platelet count may be normal, reduced or abnormally high. The number of peripherally circulating blast cells may be very high or barely detectable. TMD may also be seen in cytogenetically normal infants, in whom only the blast cells are trisomic. It has been postulated that aneuploid placental tissue is responsible for the abnormalities seen in fetal hematopoietic regulation (Hendricks et al., 1993). In aneuploidy, the myeloproliferative disorder may produce PE in the absence of anatomical or rhythmic abnormalities (Hendricks et al., 1993; Strobelt et al., 1995). Our case had a very elevated peripheral leukocyte count with 64% myeloblasts with an FAB M0 stage of differentiation and a diminished platelet count. These characteristics are consistent with TMD as well as true congenital leukemia. Our fetal case did not have anemia or extensive organ involvement; these features are compatible with TMD. However, the only
criteria that allows distinguishability between TMD and congenital leukemia would be the evolution. Isolated fetal PE associated with trisomy 21 and TMD is very rare, our case being the third reported one (Strobelt et al., 1995; Hirashima et al., 2000).

In IIAC, calcification (hydroxyapatite deposition) in the media of the large muscular arteries is associated with a stenosing, fibrous proliferation that is maximal in the area of the internal elastic lamina (Meradji et al., 1978; Rutsch et al., 2001). This is an autosomal recessive condition. There was consanguinity of the parents in our fetal case. The prenatal diagnosis of IIAC is rarely reported (Meradji et al., 1978; Stuart et al., 1990; Levine et al., 2001). We are aware of only one other case reported (Stuart et al., 1990) in which an isolated PE in the fetus was the first sign of IIAC. Fetal echocardiography is the only prenatal diagnostic tool. Prenatal diagnosis enables genetic counselling. In more than 160 cases of IIAC that have been reported, the disease appeared in early infancy, and was often lethal by six months of age, generally because of ischemic cardiomyopathy (Rutsch et al., 2001). Cases with long survival have also been reported (Marrott et al., 1984). In fact, this condition presents various phenotypic expressions that explain its heterogeneity ranging from spontaneous remission to rapid onset of death (Thiaville et al., 1994). The pathology of IIAC is related to decreased plasma inorganic pyrophosphate (PPI) and urinary PPI levels. Its role is to inhibit hydroxyapatite deposition in bone and cartilage (Rutsch et al., 2001). Some patients have responded to therapy with diphosphonates that are non-hydrolyzable analogues of PPI (Meradji et al., 1978; Van Dyck et al., 1989). In our case, it is still premature to draw any conclusions regarding the efficacy of bisphosphonates.

Transient isolated PE in the fetus has been reported (Shenker et al., 1989; Di Salvo et al., 1994) and it has a good prognosis. Its etiology may be related to transient abnormalities of the lymphatic circulation. A complete sonographic evaluation is necessary to exclude cardiac structural or functional abnormalities. Karyotyping and viral screening are mandatory. If all these investigations are normal, the PE is probably transitory. Serial fetal echocardiography must be performed in order to confirm its decrease and its spontaneous resolution. In our case, the PE disappeared at 28 + 2 weeks of gestation.

CONCLUSION

Isolated pericardial effusion in the fetus can vary from a benign form with spontaneous resolution to severe forms in which the PE is a manifestation of a chromosomal or a genetic disease. Therefore, a complete diagnostic work-up is mandatory comprising fetal ultrasonography, Doppler fetal echocardiography, amniocentesis and when necessary cord sampling and pericardiocentesis. The purpose is to provide optimal genetic counselling in a prenatal tertiary centre.

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REFERENCES


