CASE REPORT

A dysmorphic newborn with petechiae and a 'Big Heart'

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SUMMARY

A male fetus was noted to have an isolated pericardial effusion. At birth, he had dysmorphic features of Down syndrome and extensive petechiae. He was diagnosed to have transient myeloproliferative disorder. The large pericardial effusion and TMD spontaneously resolved. At 4 years of age, he was diagnosed with acute megakaryoblastic leukaemia, underwent chemotherapy and achieved complete remission.

BACKGROUND

Down syndrome is the commonest genetic syndrome worldwide affecting 1 in 1000–1100 births. Children with Down syndrome have multisystem involvement, with cardiovascular, endocrine and haematological abnormalities. Transient myeloproliferative disorder (TMD) is a well described but less commonly recognised complication unique to newborns with Down syndrome.

In this article, we describe an unusual case where TMD was associated with an isolated large pericardial effusion. Subsequently, both abnormalities resolved spontaneously and concurrently. Later on, in early childhood, this child developed acute megakaryoblastic leukaemia (AMKL) which responded well to chemotherapy.

CASE PRESENTATION

A baby boy was born to a 42-year-old mother at 35 weeks of gestation. Antenatal scans showed the fetus to have an isolated pericardial effusion and polyhydramnios from 32 weeks of gestation, which remained stable in size. Amniocentesis was not performed. There was no associated ascites, pleural effusion or effect on the fetus growth. The baby's birth weight was 2.7 kg. He was well at birth but had dysmorphic features of Down syndrome and extensive petechiae over the face and abdomen. He did not have peripheral oedema, or evidence of pleural effusions or ascites. His liver and spleen were not enlarged. A chest X-ray, echocardiogram and full blood count was performed at birth for further evaluation.

INVESTIGATIONS

Full blood count at birth showed a total white count of $64.62 \times 10^9/L$, haemoglobin level of 14.6 g/dL with a mean corpuscular volume of 124.6 fL and a platelet count of $55 \times 10^9/L$. Chest X-ray revealed massive cardiomegaly with no pleural effusion (figure 1). The echocardiogram revealed a 22 mm×13.6 mm×12 mm pericardial effusion, normal structures and contractility

Figure 1 Chest X-ray at birth showing massive cardiomegaly.

(figure 2). Peripheral blood karyotyping confirmed the diagnosis of Down syndrome. Thyroid function test was normal.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for the bicytopenia include early onset neonatal sepsis, intrauterine TORCHES infection although pericardial effusions are less commonly seen. Viral myocarditis and hypothyroidism could cause pericardial effusion but the newborn was clinically well. Pericardial effusion could be part of the findings of hydrops fetalis (pleural effusions, ascites and subcutaneous oedema from congestive in utero heart failure) but there were no findings of heart failure in this newborn.

TREATMENT

As this child did not have any clinical or echocardiographic signs of cardiac tamponade, the large

Figure 2 Echocardiographic image shortly after birth revealing a large pericardial effusion.

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pericardial effusion was managed with expectant observation. It spontaneously resolved by 4 months of age together with the spontaneous resolution of his bicytopenia and decrease in total white count in keeping with TMD. He required treatment with a short course of low-dose cytarabine as he developed transaminitis and hyperbilirubinaemia that is also seen in cases of TMD, which if left untreated can lead to hepatic fibrosis. In this case, there was good response to treatment and there was complete recovery of the initial mild liver dysfunction.

OUTCOME AND FOLLOW-UP

At 4 years of age, pancytopenia was noted on routine blood testing during a follow-up visit. A diagnosis of AMKL was made on bone marrow aspirate and the child was started on chemotherapy. He responded well to treatment and achieved complete remission soon after starting treatment. Subsequent echocardiograms were normal and did not show any recurrence of pericardial effusion. He is cancer free now at 5 years of age.

DISCUSSION

Pericardial effusions may be seen in Down syndrome in association with other congenital cardiovascular abnormalities and hypothyroidism. However, cases of Down syndrome and TMD presenting with an isolated pericardial effusion not associated with other cardiac abnormality has rarely been reported.

Only one other case has been previously reported by Strobelt *et al*¹, where a prenatal diagnosis of pericardial effusion, TMD and Down syndrome, was made in the absence of other cardiac abnormalities. Fetal pericardiocentesis was performed at 33 weeks gestation to treat fetal hydrops due to in utero cardiac tamponade. A pericardial effusion was noted on echocardiogram at birth that resolved spontaneously at 1 month of age with the haematological abnormalities, similar to the patient in our case. As this condition has been so rarely reported, the natural history of isolated pericardial effusions in TMD is still not fully understood.

The aetiology of pericardial effusion in cases of TMD is not well described. Rougemont *et al*² found megakaryoblastic infiltration of the epicardium and pericardial lymph nodes on post-mortem examination after termination of pregnancy at 32 weeks, thus suggesting TMD as an independent cause of pericardial effusion in Down syndrome. In other cases³ where pericardiocentesis was performed, pericardial fluid analysis did not reveal any blasts and eosinophils were found in one case.⁴

It is also not known if the presence of a pericardial effusion affects the prognosis of TMD and the future development of AMKL. However, the clinical course in our case suggests a benign course of the pericardial effusion if there is concomitant TMD which is likely a causative factor.

TMD is a condition unique to infants with Down syndrome during the fetal or neonatal period, occurring in up to 10% of infants born with Down syndrome.⁵

The pathogenesis of this disorder stems from somatic mutations in the GATA1 gene, found solely in trisomy 21 cells, whose key function lies in the differentiation and proliferation of megakaryocytes. There have also been case reports of TMD in the absence of GATA1 mutations suggesting the existence of another initiating event in megakaryoblastic hyperproliferation in TMD.

Infants with TMD classically present with blood cytopenias and may have severe anaemia causing congenital hydrops. Some

cases may also involve other organs, especially the liver, spleen and heart. Megakaryoblasts can infiltrate and induce hepatic fibrosis, which is the commonest cause of mortality in these patients. Treatment with cytarabine is required in cases where there is evidence of extensive hepatic involvement to prevent the development of hepatic fibrosis. It is not known if treatment of TMD with cytarabine can prevent future development of AMKL. The child described in our case report developed AMKL despite initial treatment of TMD with low-dose cytarabine, there is no conclusive evidence at present to suggest that higher doses of cytarabine will alter the outcome of this group of children.

About 30% of patients with TMD eventually develop AMKL.⁶ GATA1 mutations alone have been unable to account for the transformation of TMD to AMKL, and is an area of active investigation. It is not known at present if treatment of TMD can prevent its transformation to AMKL. Patients with Down syndrome and AMKL have a favourable prognosis (compared with AMKL not associated with Down syndrome) with treatment on current chemotherapy protocols with a 5 year survival rate reaching 70%.

Learning points

- ▶ Transient myeloproliferative disorder is a condition present in newborns with Down syndrome that can be associated with an isolated pericardial effusion, which may resolve together with the resolution of haematological abnormalities.
- ▶ Children with transient myeloproliferative disorder require treatment if there is any evidence of liver dysfunction as hepatic fibrosis is a major cause of mortality in this group of children.
- ▶ It is important to monitor for the development of possible acute myelokaryoblastic leukaemia in children with Down syndrome, especially after resolution of transient myeloproliferative disorder in infancy.
- ▶ Acute myelokaryoblastic leukaemia in Down syndrome carries a favourable prognosis with treatment.

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Competing interests None.

Patient consent Obtained.

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