Cantú syndrome as a rare cause of pericardial effusion in a young woman

Introduction

Cantú syndrome, also recognized as hypertrichosis-osteochondrodysplasia-cardiomegaly syndrome, was originally reported by Cantú et al in 1982 and is a rare autosomal dominant condition with few reported cases worldwide. It is characterized by hypertrichosis, osteochondrodysplasia, macrocephaly, and neonatal macrosomia. Related conditions include acromegaloid facial appearance syndrome and hypertrichosis with acromegaloid facial features. Cardiac manifestations include cardiomegaly with increased ventricular mass and enlarged chambers, pericardial effusion, patent ductus arteriosus and pulmonary hypertension, with preserved cardiac function. This article describes a case of a young woman admitted with a pericardial effusion and an underlying diagnosis of Cantú syndrome.

Discussion

Cantú syndrome is a rare ATP-sensitive potassium channelopathy resulting from mutation in either the ABCC9 or KCNJ8 gene (Grange et al, 2006; van Bon et al, 2012). This gene instructs the production of sulfonylurea receptor 2 proteins, which form one subunit of potassium ion channels. The mutated gene allows the ion channels to remain open longer. While this mutation demonstrates autosomal dominant transmission, most cases occur as a result of a de novo mutation (Lazalde et al, 2000).

Cardiac manifestations of Cantú syndrome include cardiomegaly with preserved cardiac function, pericardial effusion (20%), patent ductus arteriosus (50%), aortic aneurysm and pulmonary hypertension. A large patent ductus arteriosus is often present and surgical closure may be needed in early childhood. Newborns typically exhibit hypertrichosis, macrosomia and macrocephaly. Skeletal abnormalities include scoliosis, osteopenia and hypotonia in infants. Anxiety and obsessive-compulsive disorder are recognized parts of the spectrum of the disorder (Grange et al, 2014).

Defects in the ABCC9 gene have also been related to familial atrial fibrillation and familial dilated cardiomyopathy. Patients with Cantú syndrome generally exhibit normal cardiac dimensions and myocardial function (Bienengraeber et al, 2004).

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CASE REPORT

A 29-year-old woman presented to the authors' tertiary cardiac centre for an echocardiogram after being reviewed in heart muscle clinic. The patient described a 6-month history of worsening exertional dyspnoea, reduced exercise tolerance and pleuritic chest pains. She had unintentional weight loss of 1 stone over the last 2 months. There were no symptoms of palpitations, syncope or fevers.

Her past medical history included ligation of a patent ductus arteriosus at 3 months of age, hirsutism, Asperger syndrome, attention deficit hyperactivity disorder with mild learning difficulties, and anxiety. Her mother and father had no previous medical history of note. One of her three siblings had Down syndrome. The patient was a lifelong non-smoker, who consumed no alcohol and was unemployed. Current medications were diazepam and fluoxetine to treat anxiety.

On examination, the patient had a thin build, low body mass index, and was well perfused peripherally. The jugular venous pressure was not elevated. She had coarse facial features and hirsutism as shown in *Figure 1*. There was a surgical scar on her back from her previous patent ductus arteriosus ligation. The resting heart rate was 89 beats per minute and blood pressure was 107/80 mmHg.

A 12-lead electrocardiogram showed no abnormality. The chest radiograph X-ray showed cardiomegaly.

Blood analysis showed no abnormality in full blood count, electrolytes, liver function tests, thyroid function tests, cortisol, luteinising hormone, testosterone, sex binding hormone, free androgen, progesterone and prolactin hormones.

Echocardiography demonstrated good biventricular systolic function with left ventricular ejection fraction of 65%, normal ventricular dimensions and wall thickness. The proximal ascending aorta was mildly dilated when indexed for body size to 37 mm. The left atrium was dilated (volume 70 ml). There was mild tricuspid and aortic regurgitation. There was a significant global pericardial effusion noted with Doppler evidence of tamponade physiology at right ventricular inflow. The maximal dimensions of the effusion were 4.6 cm posterior to the left ventricle, 5.0 cm around the left ventricular apical posterior level, 4.1 cm around the right atrium and 3.2 cm around the right ventricular free wall (*Figure 2*).

The patient was admitted for therapeutic pericardiocentesis and during her admission genetic tests detected a mutation in the ABCC9 gene, confirming a diagnosis of Cantú syndrome.

Pericardial drainage showed macroscopically cloudy amber fluid. Microscopically the fluid contained red bloods cells and numerous benign appearing mesothelial cells, with immunohistochemistry excluding malignancy. Acid-fast bacilli staining revealed no mycobacteria. Further cultures demonstrated no bacterial growth.

Biochemical analysis of the pericardial fluid demonstrated elevated lactate dehydrogenase levels (588 U/litre). Pericardial fluid protein measured 61.0 g/litre, which was in excess of 50% of serum protein levels, consistent with an exudative effusion.

Focused echocardiography imaging 2 months following initial pericardiocentesis showed re-accumulation of the effusion without tamponade physiology.

Figure 1. Facial features of Cantú syndrome.

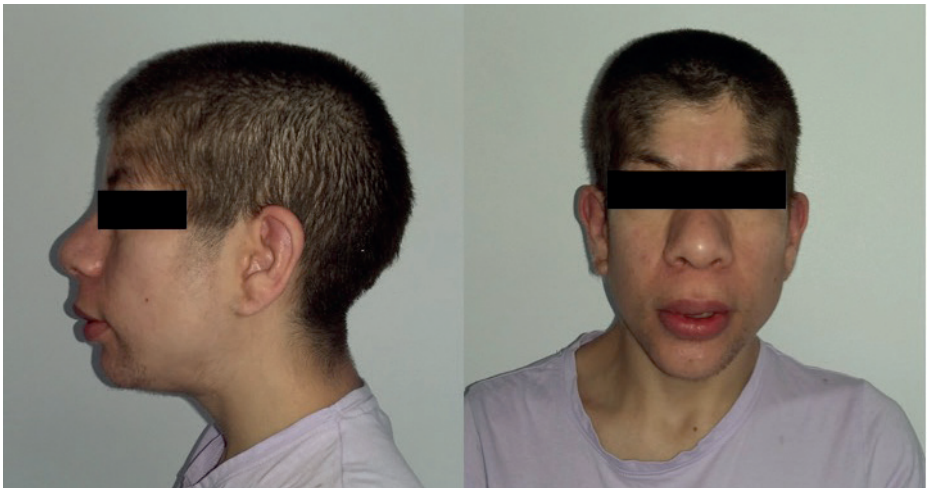
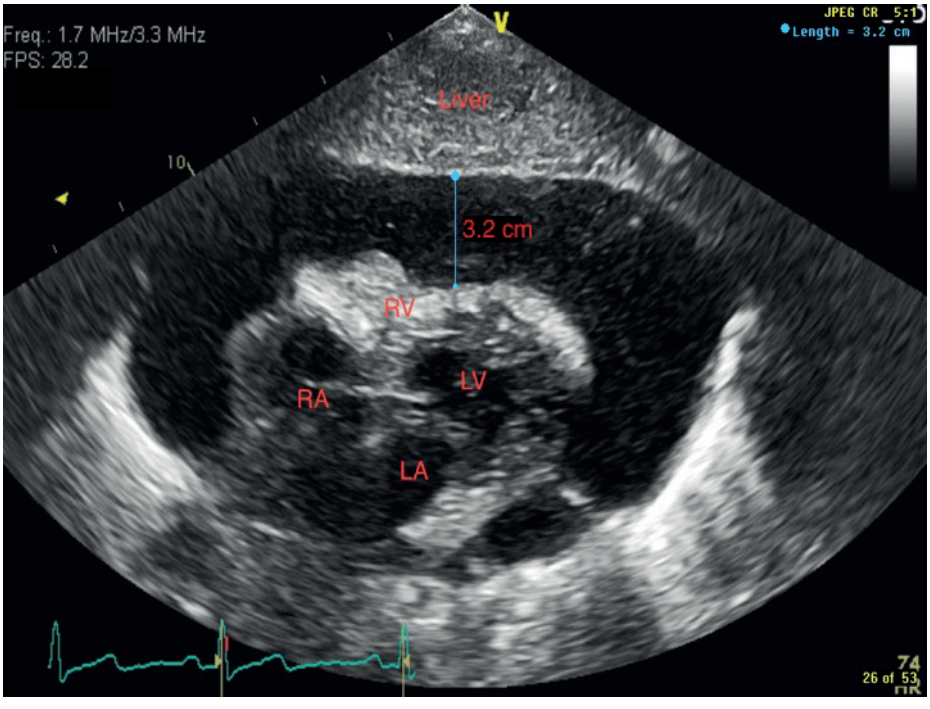


Figure 2. Subcostal view showing global pericardial effusion.



Diagnosis is made through recognition of the characteristic clinical features and detection of the variant gene ABCC9 or KCNJ84. This patient was born at a time when the genetic causation of Cantú syndrome had not been elucidated.

This patient's presentation with fatigue, reduced exercise tolerance and dyspnoea was the result of a progressive pericardial effusion, requiring pericardiocentesis. Future treatment for re-occurrence of the effusion may require repeated pericardiocentesis, or a surgical pericardial window. The aetiology of pericardial effusion in this condition is currently unknown. Pericardial fluid analysis in this case demonstrated an exudate, suggesting that this cannot simply be related to oncotic pressure gradients. Pericardial tissue biopsies in other cases of this syndrome have demonstrated evidence of mild inflammation, suggesting an underlying inflammatory process (Nevin et al, 1996; Grange et al, 2006). Cardiac evaluation is necessary with periodic echocardiographic surveillance to monitor for re-accumulation of pericardial effusion or development of cardiomyopathy (Grange et al, 2014). BJHM

LEARNING POINTS

- Cantú syndrome has many clinical manifestations including dysmorphism, macrocephaly, macrosomia, osteochondrodysplasia, hypertrichosis, scoliosis, patent ductus arteriosus, cardiomegaly, pericardial effusion and aortic dilation.
- Cantú syndrome is a potassium channelopathy caused by mutations in either the ABCC9 or KCNJ8 gene.
- Cardiac surveillance is recommended for patients affect by Cantú syndrome with yearly echocardiography and electrocardiography.

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