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Case Report

PDA Aneurysm in a Neonate with ACTA 2 Mutation

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Abstract

ACTA2 (actin, alpha 2, smooth muscle) mutation associated with PDA aneurysm rarely presents with heart failure in neonates. Survival is poor with impaired quality of life due to strokes, aneurysms and thrombotic-ischemic events.

We describe a neonate with ACTA2 mutation found to have a 3 cm arterial duct aneurysm (PDA) extending into the distal arch and proximal main pulmonary artery (MPA) with impaired left ventricular systolic function. She underwent excision of the aneurysm and repair of distal arch under deep hypothermic circulatory arrest (DHCA) with good immediate outcome.

Introduction

ACTA2 (actin, alpha 2, smooth muscle) is a gene encoding for a protein which belongs to the actin family, playing a significant role in cell motility, structure and integrity [1-3].

Smooth Muscle Cell (SMC) contractile force requires cyclic interactions between SMC -actin (encoded by ACTA2) and the -myosin heavy chain (encoded by MYH11). Missense mutations in ACTA2 are responsible for a syndrome characterised by dysfunction of SMCs throughout the body leading to cerebrovascular disease, fixed dilated pupils, hypotonic bladder, hypoperistalsis of gut and pulmonary hypertension [1,3,4].

This mutation is also implicated in 14% of inherited ascending Thoracic Aortic Aneurysms And Dissections (TAAD) in adults [2,3]. Other vascular anomalies include early onset Coronary Artery Disease (CAD) and strokes [3].

We describe a neonate with ACTA2 mutation and found to have a huge arterial duct aneurysm extending into the MPA with significant risk of rupture.

Case Report

A 38+2 weeks neonate was admitted to unit for respiratory distress requiring intubation and ventilation soon after birth. A CXR showed enlarged heart and increased pulmonary vascularity (Figure 1). A transthoracic echocardiogram showed significant pulmonary hypertension with large aneurysm of Patent Ductus Arteriosus (PDA), Mitral Regurgitation (MR), Tricuspid Regurgitation (TR), Mild Left Ventricle (LV) dysfunction and hypertrophy. She required inotropic support with milrinone and dobutamine for haemodynamic instability. A cardiac fluoroscopy (Figure 2a) and then a CT cardiac angiogram (Figure 2b) confirmed the presence of a very large PDA aneurysm.

She was also noted to have fixed dilated pupils; hence was reviewed by neurologist and ophthalmologists. Fundoscopy revealed partial anidria and hypoplastic iris with tortuous vasculature. Samples were sent for genetic testing with suspect of ACTA2 mutation.

Due to the ongoing heart failure and inability to wean from ventilator, a decision was made to surgically resect the PDA aneurysm. A CT scan of the brain was performed to rule out cerebral bleeding.

The operation was performed via a median sternotomy. A large PDA aneurysm was found impinging upon the bifurcation of the main pulmonary artery. The aneurysm had obscured the descending aorta making distal control impossible. We therefore decided to repair the aneurysm under deep hypothermia and circulatory arrest. Standard Cardiopulmonary Bypass (CPB) was instituted. The baby was cooled and the circulation was arrested at 18 °C. The aneurysm was excised. The residual gap in both the MPA and the aortic arch were repaired using pulmonary homograft patches sutured with continuous stitches (Polypropylene 7-0). After restarting the circulation, the patient was rewarmed and weaned from CPB in sinus rhythm with good hae-modynamics.

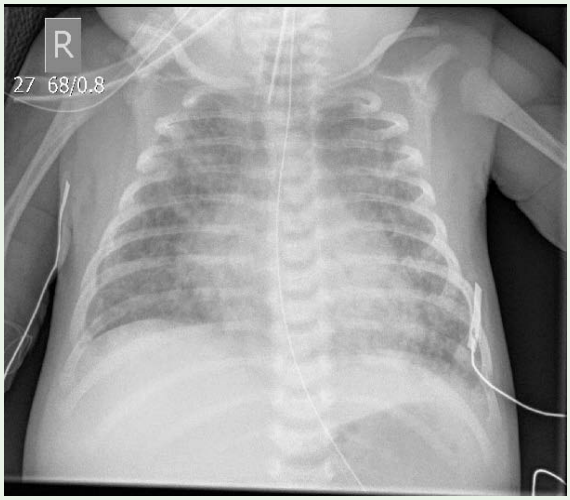

Figure 1: X-ray of the chest showing enlarged heart and increased pulmonary vascularity.

During the first few days the patient required further inotropic support for impaired LV function. She was extubated 48 hours after operation. Once extubated she came gradually off cardiovascular support and subsequently needed oral captopril for blood pressure control. The baby was electively reintubated for ongoing respiratory distress and oxygen dependence despite falling pulmonary pressure. A bronchogram was performed and ruled out tracheobronchial malacia. A raised left hemi-diaphragm and limited movement of contrast within the left airway were found. Plication of left hemi-diaphragm was performed following which the baby was successfully extubated the following day.

Genetic test results showed an ACTA2 mutation as well as 3q29 duplication.

The baby was then discharged; however, 5 months after the operation the child died at home. A post mortem showed that the death was due to a myocardial infarction secondary to diffuse intracoronary smooth cell proliferation.

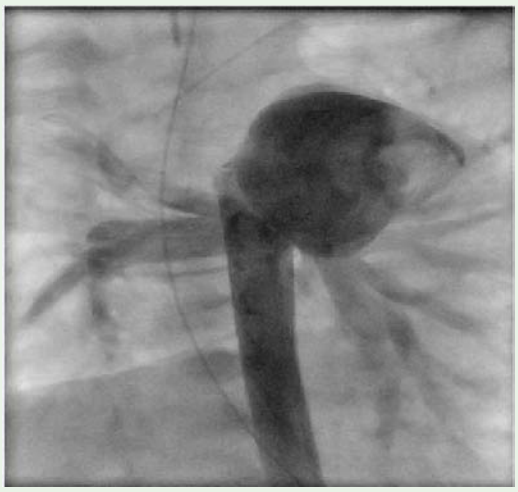

Figure 2a: Cardiac fluoroscopy showing large arterial duct aneurysm (PDA).

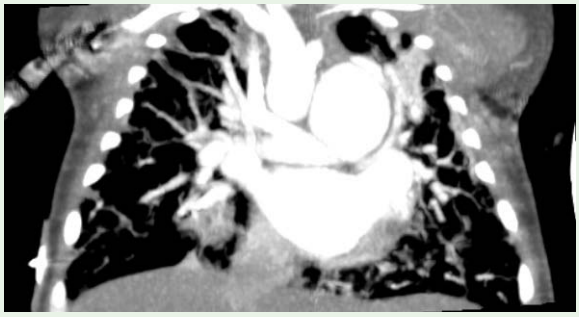

Figure 2b: CT cardiac angiogram showing large arterial duct aneurysm (PDA).

Comment

ACTA2 mutation associated with PDA aneurysm, pulmonary hypertension and impaired left ventricular function presenting in the first week of life is rare. Very few cases have been reported in neonates. Survival is poor with impaired quality of life due to strokes, aneurysms and thrombotic-ischemic events. The diagnosis of this rare condition has been made on the basis of clinical features in keeping with the syndrome. The evidence of fixed pupils without any other neurological deficit prompted review by neurologist and ophthalmologist. Diagnosis of this rare condition is not possible without involvement of experts from multiple disciplines.

Surgery in neonates with this condition is associated with high mortality and morbidity. Incidence of postoperative bleeding is high due to tissue fragility. However, the clinical condition of the neonate warranted an urgent surgical intervention. In our opinion a CT scan head is crucial to exclude neurological abnormalities such as haemorrhage and cerebral arteriopathy which may have a significant impact on the management plan.

Our experience suggests that the surgical option is possible and can achieve a good immediate result. It is crucial to handle tissue minimally and gently to avoid surgical trauma. The decision to perform the operation under circulatory arrest was made because the dimension of the aneurysm precluded clamping of aorta. Pulmonary hypertension made safe dissection without rupture impossible. There was also a concern regarding clamps causing trauma to fragile tissues and bleeding. Bleeding can be a significant issue leading to haemodynamic instability and need for re-exploration. Delayed sternal closure was hence performed. Except for reintervention on the left hemi-diapragm the early post-operative recovery was reasonably smooth.

Conclusion

Surgery can be safely performed in neonates with this rare condition without bleeding related complications.

Despite the good surgical result, the outcome of the patient can still be very poor in a mid- or long-term follow up.

Compliance with ethical standards

Research involving human participants and/or animals: This article does not contain any studies with human participants or animals performed by any of the authors.

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