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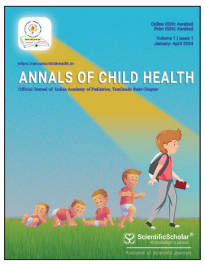

Case Series

Two Unusual Cases of Spontaneous Thrombosis in Neonates: Management and Outcome

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ABSTRACT

Neonatal thrombosis usually occur as a complication of an indwelling central vascular catheter. Here we report two unusual cases of spontaneous thrombosis in neonates. In case 1, baby had a left atrial thrombus diagnosed soon after birth serendipitously by echocardiography. Since the thrombus was highly mobile with risk of embolization, he was given thrombolytic therapy. Thrombolysis resulted in prompt resolution of the thrombus without any complication. In case 2, baby had a chronic left axillary artery thrombosis that had occurred in utero. He presented at birth with features of limb ischemia. He was given anticoagulant therapy for three months. Though the limb perfusion and movements normalized, he developed shortening of the limb due to chronic ischemia. To conclude, due to non-availability of standard guidelines and scarcity of existing literature, management of these neonates is arbitrary. Owing to the rapidly expanding neonatal intensive care that contemplates more such cases, it is time to formulate separate guidelines for the management of thrombosis in neonates.

Keywords: Neonate, Spontaneous thrombosis, Thrombolysis, Anticoagulant therapy, Recombinant tissue plasminogen activator

INTRODUCTION

Most of the arterial and venous thrombi in neonates develop as complications of central vascular catheters(CVCs).[1] Spontaneous thrombosis in neonates is rarely reported.[2] Here, we describe two unusual cases of spontaneous thrombosis in neonates and discuss their management and outcome.

CASE SERIES

Case 1

The baby boy was born at 33 weeks gestation with 1280 g birth weight to a 29-year-old primigravida mother by cesarean section. Indications for delivery were pre-eclampsia, fetal growth restriction, and non-reassuring non-stress test. The baby did not cry at birth and required resuscitation with positive pressure ventilation (PPV) and intubation. He had persistent bradycardia with a heart rate between 60 and 100 beats/min until 5 min of life. He also had low oxygen saturations <90% until 20 min of life despite PPV with 100% oxygen.

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The baby was shifted to the neonatal intensive care unit and started on invasive mechanical ventilation. Echocardiography performed at 1 h of life showed a 3 × 3 mm thrombus in the left atrium that was moving freely into the right atrium and left ventricle through the patent foramen ovale and mitral valve, respectively [Figure 1]. He also had myocardial dysfunction with an ejection fraction of 45%.

Since the thrombus was highly mobile, the risk of embolization was considered high, and it was decided to initiate thrombolytic therapy. Recombinant tissue plasminogen activator (rTPA) was started as 0.02 mg/kg/h infusion. The baby was also started on dobutamine for myocardial dysfunction, and ventilator support was continued. Repeat echocardiography after 6 h of rTPA infusion showed a significant reduction in the size of the thrombus, with only a thin rim of thrombus left behind. Repeat echocardiography at 8 h showed complete resolution of the thrombus, and rTPA infusion was stopped. Myocardial function also had normalized. Dobutamine was tapered and stopped, and the baby was extubated to room air. Subsequent anticoagulant therapy was not given, as repeat echocardiograms performed on days 3 and 7 showed no evidence of thrombus.

The coagulation profile and cranial ultrasound performed both before and after the thrombolysis were normal. Clinical exome sequencing did not identify any mutation suggestive of a hereditary prothrombotic state. The baby was discharged home on day 12 of life. The baby is on regular follow-up and has normal growth and development.

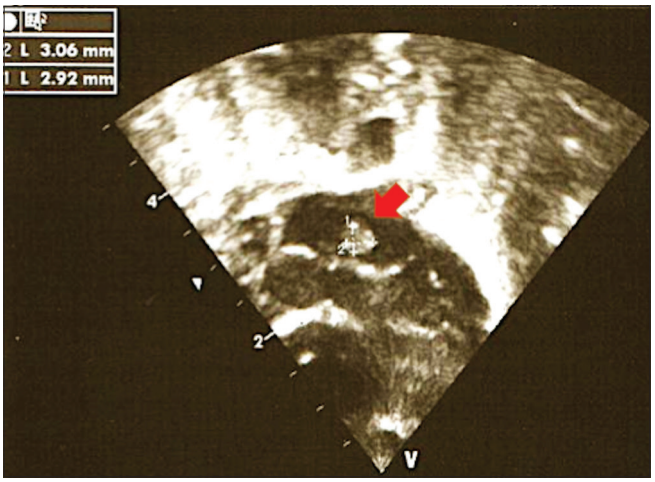

Figure 1: Echocardiographic image showing left atrial thrombus (red arrow).

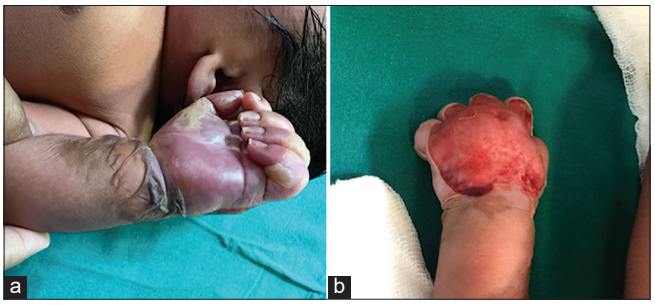

Figure 2: Clinical images of the baby showing features of acute limb ischemia. (a) ventral surface and (b) dorsal surface.

Case 2

The baby boy was born at 38 weeks gestation with a 3580 g birth weight to a primigravida mother with an uneventful antenatal period. At birth, his left upper limb was found to be swollen, cyanosed, and limp [Figure 2]. There was a superficial necrotic skin lesion on the dorsum of the left hand. The fingertips had discoloration suggestive of early ischemic necrosis. Brachial, radial, and ulnar pulses were not palpable. He was otherwise stable and had no other external anomalies.

Ultrasound Doppler showed normal blood flow in the left subclavian artery, low-velocity monophasic tardus parvus flow in axillary and brachial arteries, and absent blood flow in distal ulnar and radial arteries. High-resolution computed tomography (CT) angiography revealed a complete occlusion of the left axillary artery for a length of 13 mm with the formation of multiple collaterals around the occlusion. The subclavian, brachial, and radial arteries showed normal opacification, while there were multiple segments of filling defects in the ulnar artery. A diagnosis of chronic *in utero* axillary artery thrombosis was considered with a recent occlusion of the ulnar artery, probably due to distal embolization.

The baby was started on unfractionated heparin (UFH) infusion with a loading dose of 75 U/kg/h followed by 50 U/kg/h. Glyceryl trinitrate patch 6.25 mg was applied topically on the dorsum of the hand. Local wound care and antiseptic dressings were performed regularly. Color and perfusion of the limb gradually improved. Brachial pulse became palpable, while radial and ulnar pulses were not palpable. Repeat Doppler after 48 h showed improvement in blood flow in all the arteries, including the ulnar artery. The baby was started on subcutaneous injections of low-molecular-weight (LMW) heparin (2 mg/kg/dose 12th hourly), and UFH infusion was stopped by 72 h. COVID-19 polymerase chain reaction and echocardiography were normal. Cranial ultrasound and coagulation profile were normal. Genetic evaluation for a hereditary prothrombotic state could not be done due to financial constraints.

Repeat CT angiogram after one month showed near-complete recanalization of the axillary artery, while the multiple segments of non-opacification of the ulnar artery were persistent. LMW heparin therapy was given for three months. The wound on the dorsum of the hand healed with scarring, causing flexion contractures of the fingers, for

which regular physiotherapy was initiated. On follow-up at six months, the baby had shortening of the left upper limb, causing limb length discrepancy. Perfusion, tone, power, and movement of the limb was otherwise normal.

DISCUSSION

We describe two unusual cases of spontaneous thrombosis in neonates: One was a left atrial thrombus diagnosed soon after birth, and the other was an *in utero* axillary artery thrombosis. The former was an acute thrombus managed with thrombolysis resulting in prompt resolution without any complication. The latter was a chronic thrombus managed with anticoagulant therapy. Although the limb perfusion and movements improved gradually, there were residual effects due to chronic limb ischemia.

Atrial thrombi occur most often as a complication of indwelling CVC, which usually occurs in the right atrium.[3,4] Our baby had a left atrial thrombus that developed without a CVC. The thrombus was diagnosed soon after birth. It is difficult to say whether it was an antenatal thrombus that hindered the transition at birth, making the baby hypoxic and bradycardic, requiring prolonged resuscitation, or the thrombus developed postnatally during the period of bradycardia in the delivery room.

Most of the intracardiac thrombi in neonates are asymptomatic.[3] In our baby also, the thrombus was identified incidentally when echocardiography was performed as part of the evaluation of asphyxia and shock.

Although the size of the thrombus was small in our baby, the highly mobile nature of the thrombus suggested a greater risk of embolization.[3] Dissemination of emboli to any vital organ can be lethal. The risk of administering thrombolytic therapy to neonates is considered high, more so in preterm neonates in the first week of life due to the risk of major hemorrhages such as intraventricular hemorrhage and pulmonary hemorrhage. However, the available limited data show that the risk of major hemorrhage and related mortality following thrombolysis in neonates is low.[4,5]

The American Society of Hematologists 2018 gives recommendations on the use of thrombolytics for intracardiac thrombus in children based on the size and mobility of the thrombus, the patient's hemodynamic status, and bleeding risk.[6] There are no standard guidelines for the management of thrombi in neonates. The existing literature shows varied treatment approaches for neonatal thrombosis with expectant management, anticoagulant therapy, or thrombolysis.[3,4] The choice of drug for thrombolysis, the dosage regimen, and the duration of therapy are also highly variable.[3-5] In our case, low-dose rTPA infusion for 8 h resulted in complete resolution of the thrombus without causing any hemorrhagic complication.[5]

In case 2, the presence of collaterals suggested that the axillary artery thrombus was chronic and had happened *in utero*. Hence, we chose to give anticoagulant therapy alone without thrombolysis. Although there are guidelines for thrombosis causing acute limb ischemia,[7] there are no standard recommendations for the management of chronic thrombosis in neonates or children. Despite anticoagulant therapy for 3 months, the baby had limb shortening, probably due to chronic *in utero* ischemia. Fortunately, limb length discrepancy of upper limbs does not cause significant functional impairment. Since the movements and functionality of the limb are normal, the baby may not need any reconstructive surgery.

CONCLUSION

We report two cases of spontaneous thrombosis in neonates, an entity that is rarely reported. Due to the non-availability of standard guidelines and scarcity of existing literature, the management of these neonates is arbitrary. Due to the rapidly expanding neonatal intensive care that contemplates more such cases, it is time to formulate separate guidelines for the management of thrombosis in neonates.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

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