Spontaneous onset extensive aortic thrombosis in a Sri Lankan neonate treated successfully using recombinant tissue plasminogen activator (rTPA)

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Introduction

Neonatal thrombosis is commonly associated with vascular access devices[1]. However, spontaneous thrombotic events, with or without an underlying thrombophilic disease, are also reported[2], with aortic thrombosis being the rarest[1]. A review of reported cases spanning from 1980 to 2009 revealed only 80 spontaneous aortic thromboses[2]. Treatment includes early administration of anticoagulants and thrombolytic agents such as recombinant tissue plasminogen activator (rTPA)[3]. We report probably the first case in Sri Lanka of a neonate with extensive, spontaneous aortic thrombosis recovering completely with the use of rTPA therapy.

Case report

A baby girl, delivered at term, weighing 3300g at birth, with a normal Apgar score, was noted to have cyanosis of the lower limbs with absent femoral pulses at the sixth hour of life. Lower limb saturation was 60% in air while her upper limb saturation read 98% in air. An urgent 2D echocardiography excluded coarctation of the aorta. Doppler flow study of abdominal vessels revealed an extensive, acute aortic thrombosis just below the renal artery extending to the iliac bifurcation with minimal distal reformation of flow via the left external iliac artery.

At the twentieth hour of life, she was commenced on anti-thrombolytic agent, rTPA. Prior to starting therapy her prothrombin time (PT) was normal with an International Normalised Ratio (INR) of 1.05. Her activated partial thromboplastin time (APTT) was 35 seconds and the platelet count was 225 x 10^9/L. Contra-indications for starting rTPA, which include intra-cranial bleeding, seizures, coagulopathy, platelet count below 100 x 10^9/L or asphyxia were excluded. The infusion of rTPA was commenced at 50 micrograms/kg/hr. After 12 hours the infusion was increased to 100 micrograms/kg/hr. Treatment was monitored by the fibrinogen level, PT, INR and APTT and full blood count. Ultrasound scan of the brain and Doppler studies of the aorta were performed to exclude bleeding complications related to the rTPA therapy. The target was to keep the fibrinogen level between 1-1.2g/L and have normal clotting screen with platelet count above 100 x 10^9/L.

The rTPA infusion was stopped at 72 hours as Doppler studies revealed complete absence of thrombus and intravenous unfractionated heparin was commenced for the next 48 hours. APTT levels were measured 6 hourly targeting a ratio from 1.5 – 2.5. After 48 hours, heparin infusion was discontinued and subcutaneous enoxaparin sodium was commenced at a dose of 1.5 mg/kg twice daily for two weeks followed by a single daily dose for 4 weeks. Parental screening for possible abnormal anticoagulants revealed normal protein C and S levels. Protein C and S levels of the child read at 73 (67– 150%) and 70 (55 – 123%) respectively. Factor V Leiden mutation, factor II (prothrombin) mutation and MTHFR C677T mutation were not detected in the baby. She did not experience any further thrombotic events and had normal development during infancy.

Discussion

The incidence of symptomatic neonatal aortic thrombosis has been reported as 0.1-1.0 in 100, 000[4]. Failure to intervene early results in significant morbidity in the form of loss of a limb or organ failure and ultimately loss of a life. Arterial lines, sepsis, placental abnormalities, gestational diabetes mellitus, polycythaemia, hypernatraemic dehydration and inherited hypercoagulable states are some of the commonly reported risk factors[1,5]. The new-born baby described in the case report was evaluated for a probable predisposing cause but none were found.

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Therapeutic options available for neonatal thrombosis include commencement of un-fractionated heparin infusion, thrombolysis and micro-surgery for resistant thrombi[3,6]. rTPA has been used for neonates as a thrombolytic agent with varying levels of success[7]. The use of rTPA in neonates has been limited for extensive thrombosis or thrombosis which places life, organ or limb in danger due to the potential risk of haemorrhage[3]. Different dosing regimens exist but the most recommended dosing regime was 50 micrograms/kg/hr continuing for 3 days[8,9]. Higher doses or longer duration have been associated with increased risk of haemorrhage rather than increased efficacy[10]. The Doppler studies performed in our newborn demonstrated complete resolution of thrombus at the end of day 3 of rTPA therapy.

The availability of rTPA, a thrombolytic therapy, was life-saving for this neonate with arterial thrombosis in a resource limited setting such as Sri Lanka, where specialized micro-surgery is not readily available for neonates.

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