CASE REPORT

Successful use of Recombinant Tissue Plasminogen Activator in the Treatment of Aortic Thrombosis in a Premature Neonate

J. Torkington*, R. Hitchcock, K. Wilkinson and E. Kiely

Department of Paediatric Surgery, Great Ormond Street Hospital for Children, London WC1N 3JH, U.K.

Introduction

Thrombolysis has been used in children and infants in the treatment of atrial thrombosis, aortic thrombosis, pulmonary embolism, prosthetic valve and shunt thrombosis and renal vein thrombosis.1 In neonates, surgical thrombectomy is technically hazardous in large vessels and may be complicated in peripheral vessels by endothelial damage, stenosis of vessels and also by incomplete clot removal. The best treatment for limb- or life-threatening thromboses in neonates is therefore not well defined.1

We report the use of the second generation thrombolytic agent recombinant tissue plasminogen activator (rTPA; Actilyse® Boehringer Ingelheim) in the treatment of an acute aortoiliac thrombosis associated with umbilical artery catheterisation in a premature neonate.

Case Report

A 31 week gestation female infant weighing 1.25 kg underwent intubation and mechanical ventilation at 24 h for respiratory distress syndrome. An umbilical artery catheter (UAC) was inserted, the tip being positioned at the level of the 10th thoracic vertebra. The UAC had been used for monitoring only and no hyperosmolar fluids had been instilled through it.

Thirty six hours after insertion of the UAC, the right leg was cyanosed but femoral pulses were palpable and the UAC was removed. Over the succeeding 48 h both legs became increasingly cyanosed and mottled and the femoral pulses became impalpable.

The baby was transferred to this hospital with critical ischaemia of both legs. Colour duplex ultrasound scanning demonstrated aortic thrombosis with bilateral femoral artery occlusions. It was decided to treat this patient with rTPA systemically via peripheral intravenous infusion according to the regimen shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Dose regimen employed.</th>
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<td>1.5 mg/kg rTPA once daily for 3 days.</td>
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<td>Each dose is divided and given as follows</td>
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<td>initially 10% i.v. stat over 1–2 min</td>
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<td>then 50% as infusion over 1 h</td>
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<td>then 40% as infusion over 2 h</td>
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There was an initial improvement. After a single dose of rTPA both legs became pink, with the exception of the right hallux which remained cyanosed. The femoral pulses, however, remained impalpable.

Daily colour duplex scans were used to monitor treatment and cranial ultrasound scans used to check for bleeding complications. Electrolyte and clotting screens were performed daily to monitor renal function and any coagulopathy.

After the first 3 days of lysis aortic thrombosis was still present from below the origin of the superior mesenteric artery to the femoral arteries (Fig. 1).

In view of this a further 3 day course of rTPA was given. This was successful in clearing the thrombosis completely on duplex scan and restoring the femoral pulses and viability of the right hallux.

The baby was given intravenous heparin, monitored with an activated partial thromboplastin time at twice the normal value and then managed with systemic heparinisation.

The baby made a full recovery and was discharged home at 3 month corrected age. Follow up duplex ultrasound scans performed at 1 year and 3 months of age showed no residual aortic thrombosis.

* Please address all correspondence to: Mr J. Torkington, Department of General Surgery, West Wales General Hospital, Carmarthen, Carmarthenshire, Wales SA31 2AF, U.K.
to three times normal, measured twice a day. This was continued for a further 3 days as an empirical measure in order to prevent recurrence of the thrombosis.

Two days after the final infusion of rTPA she had an episode of melaena and bile stained nasogastric aspirates. Necrotising enterocolitis was diagnosed, she was treated appropriately with antibiotics and parenteral feeding and her symptoms settled.

Follow-up of the infant at 5 months showed her to have normal symmetrical limb growth, a full complement of pulses and no neurological deficit.

Discussion

Mild asymptomatic to severe aortic thrombosis is a recognised complication of UACs, detected by duplex scanning in around 26% of cases. Despite this UACs are commonly placed in premature infants for the purpose of monitoring. Removal of the UAC may be sufficient to prevent progression. The question of how to treat those that become symptomatic has not been settled. A surgical solution in the form of trans-abdominal aortotomy and thrombectomy has been reported in normal gestation and weight neonates but not without mortality and long-term morbidity. Peripheral ischaemia due to aortic thrombosis has been treated with streptokinase or urokinase often with mixed results. This is only the third case report of the use of rTPA in aortic thrombosis associated with a UAC. The functional outcome in the first case was associated with the loss of four toes. In their patient a shorter course and no heparin was used. The second case was more similar to ours but the thrombus was less extensive, sparing the renal arteries and requiring 10 h of rTPA infusion compared with a total of 18 h (6 x 3 h infusions) for complete resolution. The message when reviewing the three cases together is that thrombolysis should be continued until clot resolution is confirmed by duplex ultrasound and not simply on clinical grounds. Also there may be value in post-thrombolysis heparinisation.

The interesting factor in this case is the early resolution of symptoms, after the first dose, but the persistence of duplex detectable thrombus and absent pulses. In addition with thrombus extending to beneath the superior mesenteric artery gut and renal perfusion must have been affected early. It may be that the initial dose of rTPA was enough to open up collaterals and the melaena after the treatment finished was also a reflection of this. However, renal function at no time appeared affected.

The patient in this report was haemodynamically stable throughout; whether this treatment is safe in situations of fluctuating blood pressure is not established. A lower dose schedule delivered at the thrombus itself might be effective but access may be a problem. Obviously where a UAC is in situ then thrombolysis may be infused directly into the thrombosis; however, as the UAC is the aetiologic factor its early removal is indicated. In addition, many will wish to avoid arterial puncture for intra-arterial lysis when treating complications of such intervention.

Our experience suggests that rTPA at these doses systemically can be used safely and with no significant haemorrhagic side effects and should be considered when major arterial thrombosis has occurred in neonates.

References


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