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### **Case Report**

# Local thrombolytic treatment of Cerebral Venous Thrombosis in three paediatric patients

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#### **Abstract**

There is increasing evidence that local thrombolysis can be used with relative safety and efficacy in adults with superior sagittal sinus thrombosis (SSST). However, little data is available on the use of local thrombolysis in children with SSST. We report three patients who received local thrombolysis for dural sinus thrombosis. Two patients received urokinase and one patient received urokinase followed by local TPA infusion. Recanalization was achieved in two patients.

#### Introduction

Superior sagittal sinus thrombosis (SST) is uncommon in children. Several treatment protocols have been used for treatment of paediatric SST, including hydration, antibiotics, steroids, diuretics, osmotic agents, antiplatelet therapy, systemic anticoagulation and systemic and local thrombolysis. <sup>1-3</sup> The use of TPA in paediatric SST has not been reported but there are a few reported cases of urokinase thrombolysis in these patients. We report three patients with dural sinus thrombosis. Two patients received locally administered urokinase and the other was treated with local TPA infusion. One of these patients was referred to briefly in a recent large series.<sup>4</sup>

#### **Case Report**

Patient 1: A four-year-old boy with nephrotic syndrome presented with headache and irritability. General physical and neurologic examinations were unremarkable except for lethargy. Head CT showed hyperdensity of the superior sagittal sinus (SSS) and straight sinus (StS). MRI with MR venography (MRV) showed thrombosis of the SSS and the straight sinus (StS). Catheter angiography confirmed thrombosis of SSS, StS and left transverse sinus (TS). An angiographic catheter was placed into internal jugular vein via transfemoral catheterization. A Tracker -18 microcatheter (Target Therapeutics, CA) was advanced through angiographic catheter into the superior sagittal sinus. The patient received a bolus of urokinase (50,000 units) into SSS. The catheter was retained in the SSS and urokinase was infused continuously at 5000 units per hour. A repeat angiogram 20 hours later showed patency of SSS. There were no complications. Patient was subsequently started on oral warfarin. He was discharged with a normal neurologic status.

Patient 2: A 12-year-old girl with systemic lupus erythematosus and lupus nephritis presented with headache and difficulty with ambulation. Neurologic examination showed papilloedema and gait ataxia. Her laboratory evaluation was unremarkable except for an elevated prothrombin time (23.8 seconds) and positive antiphospholipid antibodies. Brain MRI/MRV showed small bilateral subdural haematomas and thrombosis of superior sagittal sinus, straight sinus and right transverse sinus. Catheter angiography confirmed the MRV findings. Intravenous heparin was started but there was no neurologic improvement after 24 hours. A 5F angiographic catheter was placed through femoral vein catheterization. A Tracker-18 microcatheter was advanced into SSS through the angiographic catheter. The patient received a bolus of urokinase (250,000 units) into the SSS followed by continuous infusion at 60,000 units per hour for 41 hours. A repeat angiogram showed recanalization of SSS. She required blood transfusion due to falling haematocrit. She was discharged home on warfarin with a normal neurologic exam but still had papilloedema.

Patient 3: A 3-1/2 week old boy who had prolonged hypoglycaemia at birth was admitted with lethargy and poor oral intake. Initial neurologic examination was unremarkable except for lethargy. The hospital course was complicated by sepsis, acute renal failure, disseminated intravascular coagulation (DIC), myocarditis and seizures. Head CT scan showed a right frontal intraparenchymal haemorrhage. Cerebral angiography showed thrombosis of the Superior Sagittal Sinus, Transverse Sinus, Sigmoid sinus, and internal jugular vein. A Tracker-18 catheter was advanced into SSS through transfemoral angiographic catheter. He received a bolus of urokinase (30,000 units) into the SSS followed by local TPA infusion at 0.5 mg/kg/hour. Recanalization was not achieved. The patient died six hours after TPA infusion. An autopsy showed cardiomyopathy, extensive dural venous sinus thrombosis and pulmonary artery thrombosis, without evidence of haemorrhagic complications.

#### **Discussion**

A growing body of evidence suggests that local

urokinase thrombolysis is relatively safe and effective in adult patients with cerebral venous thrombosis (CVT). Horowitz et al.<sup>3</sup> reported 13 patients including a 12-year-old boy treated with local urokinase thrombolysis. In a review of 20 patients with SSST, Wasay et al.<sup>4</sup> found local urokinase thrombolysis to be relatively safe and effective. Local thrombolysis using recombinant tissue plasminogen activator (TPA) has been suggested recently as an alternative to urokinase. Kim et al.<sup>5</sup> reported nine adult patients with dural sinus thrombosis treated with local TPA with excellent outcome. Frey et al.<sup>6</sup> summarized 12 adult patients with cerebral venous thrombosis who were treated with combined intrathrombus rtPa and intravenous heparin. Nine patients had significant clinical improvement. Two patients showed worsening of haemorrhage.

CVT in children causes significant morbidity and mortality. One literature review found a16% mortality and 22% with long term disability in paediatric patients with CVT. Supportive care without anticoagulation is the mainstay of treatment in most cases characterized by limited thrombosis.<sup>7</sup> A recent study of 22 paediatric patients with CVT showed intravenous heparin or low molecular weight heparin (LMWH) to be safe and effective.<sup>2</sup> The experience with thrombolytic therapy in paediatric CVT is limited to a few case reports.8-10 Griesmer et al8 reported a 10-year-old boy with SSST, TST, StS and sigmiod sinus thrombosis. Due to progressive neurological deterioration he was treated with local Urokinase thrombolysis with dramatic improvement. Wong et al.9 reported a one-day-old neonate with parasagittal haemorrhage due to cortical vein thrombosis. The patient recovered completely after local urokinase thrombolysis. Gebara et al. 10 reported a nine-week old girl with dural sinus thrombosis secondary to subclavian vein catheterization. She had complete recovery after local urokinase thrombolysis.

Anticoagulation is commonly used for adult patients with SSST; however anticoagulation may not ensure neurologic recovery. There is a growing interest in the use of local thrombolysis with urokinase or TPA for CVT. More than 90 adult cases of CVT treated with local thrombolysis have been reported in literature.<sup>4</sup> Because of important maturational differences in cerebrovascular and coagulational systems of infants and children compared with adults, therapies that had been proven to be safe and effective in adult patients may not be directly extrapolated to the paediatric age group.

One of our children had nephrotic syndrome and another had lupus nephritis. A hypercoaguable state in nephrotic syndrome is probably related to functional anti-thrombin III deficiency. Because mechanism of heparin is based on anti-thrombin III activity, its effects are variable in patients with

nephrotic syndrome. Due to extensive thrombosis and comorbidity, local thrombolytic therapy was chosen.

Collagen vascular disease is a well-known risk factor for CVT. Local thrombolytic therapy has been used previously in adult patients with SLE. Despite the presence of small SDH, thrombolysis was used in the second patient because of progressive neurological deterioration despite heparinization. Her symptoms improved after local thrombolysis.

The third patient had extensive comorbidity and thromboses of multiple dural sinuses. When patency of SSS was not achieved with urokinase bolus he was switched to tPa infusion. His death was unrelated to either his dural sinus thrombosis or to the thrombolytic therapy but it was due to his overwhelming systemic illness. No new intracranial haemorrhage or worsening of frontal haematoma was identified on autopsy.

Our study shows the safety of local urokinase thrombolysis in three children with CVT despite the presence of preexisting intracranial haemorrhages in two patients. The thrombolysis led to recanalization and neurologic recovery in two cases. The poor outcome in the third patient was most likely due to the underlying systemic illness. Local thrombolysis appears to be reasonably safe in children with CVT and deteriorating neurologic status. However, firm conclusions should await further experience and prospective randomized trials.

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