Cardiology in the Young (2013), **23**, 271–273
doi:10.1017/S1047951112000789

Brief Report

Successful treatment of neonatal pulmonary thrombosis in congenital nephrotic syndrome

Krit Makonkawkeyoon,[1] Suchaya Silvilairat,[1] Wattana Chartapisak[2]

[1]*Division of Pediatric Cardiology;* [2]*Division of Pediatric Nephrology, Faculty of Medicine, Department of Pediatrics, Chiang Mai University, Chiang Mai, Thailand*

Abstract The incidence of neonatal thrombosis has been increasing in recent times because of the use of a central venous catheter. A treatment modality consisting of fibrinolytic agents has been administered for this life-threatening condition. This case report presents the successful management of a pulmonary artery thrombosis with a recombinant tissue-type plasminogen activator in a patient with neonatal congenital nephrotic syndrome.

Keywords: Recombinant tissue-type plasminogen activator; fibrinolytic agent; pulmonary arterial thrombosis

Received: 7 December 2011; Accepted: 28 April 2012; First published online: 25 May 2012

CONGENITAL NEPHROTIC SYNDROME IS A RARE disease that presents earlier than 3 months of life and carries a poor prognosis. It is characterised by massive proteinuria, hypoalbuminaemia, oedema, hyperlipidaemia, and hypercoagulability. The goal of management is to diminish protein loss, maximise growth, and minimise infectious and thrombotic complications.[1] Thrombosis in congenital nephritic syndrome results from the renal loss of anti-thrombin. Neonatal thrombosis is a relatively rare complication. The incidence of thrombosis, however, has increased with widespread use of intravascular catheters. A low level of anti-thrombin, protein C, and protein S in neonates, patients suffering from asphyxia, infants of diabetic mothers, patients suffering from dehydration, and those suffering from renal disease, as well as alteration of the anti-thrombosis mechanism from infection, may be risk factors.[2] The primary treatment modality consists of fibrinolytic agents or surgery for a life-threatening condition. Surgical removal of the thrombus is an invasive procedure and carries a high rate of mortality. To our knowledge, no previous studies on the use of a recombinant tissue-type plasminogen activator for the treatment of pulmonary arterial thrombosis in congenital nephrotic syndrome have been reported. This case report presents the successful management of a case of neonatal pulmonary thrombosis using a recombinant tissue-type plasminogen activator.

Correspondence to: Dr S. Silvilairat, MD, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand. Tel: 66 89 761 2855; Fax: 66 53 94 6461; E-mail: ssamana@med.cmu.ac.th

Case report

An 18-day-old preterm male newborn of a gestational age of 34 weeks and birth weight 2250 grams was referred from a primary care hospital with a 1-day history of sudden cyanosis. There was no history of an umbilical catheterisation. Cyanosis suddenly developed with an oxygen saturation of 70% in room air at the age of 18 days. Arterial blood gas analysis showed hypoxia and metabolic acidosis. He was intubated and transferred to the neonatal intensive care unit in Chiang Mai University Hospital.

This infant had central cyanosis with oxygen saturation of 60% in FiO_2 1.0. Physical examination revealed blood pressure 80/50 millimetres of mercury, heart rate 180 per minute, no heart murmur, normal heart sound, and no hepatomegaly. Chest radiography showed no cardiomegaly with decreased pulmonary vascular marking. Echocardiogram revealed patent foramen ovale with a right to left shunt, a large thrombus occluding nearly the entire main pulmonary artery, which extended to the proximal portion of the left and right

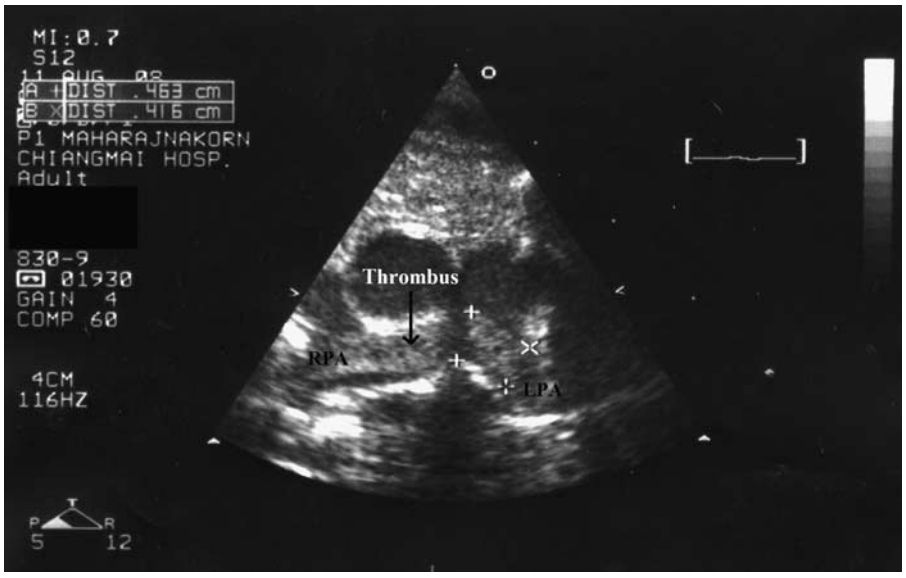

Figure 1.
Echocardiogram reveals extensive thrombus in right and left pulmonary arteries. RPA = right pulmonary artery; LPA = left pulmonary artery.

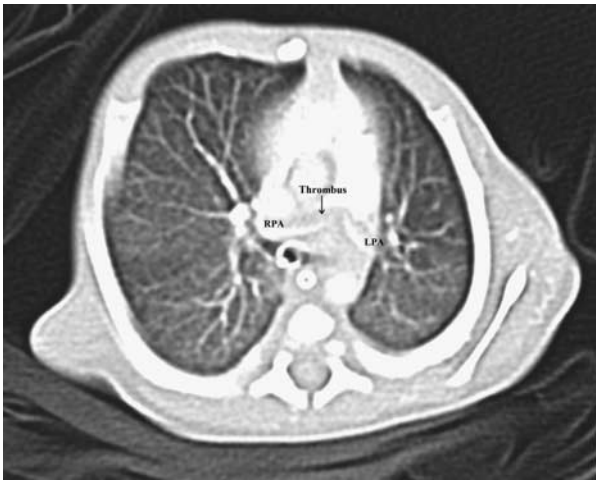

Figure 2.
Computed tomography angiogram shows a filling defect in right and left pulmonary arteries. RPA = right pulmonary artery; LPA = left pulmonary artery.

pulmonary arteries, and decreased right ventricular function (Fig 1). Computed tomography angiogram revealed a filling defect in the main, right, and left pulmonary arteries (Fig 2). This patient was diagnosed with pulmonary arterial thrombosis and respiratory failure. Treatment consisted of a recombinant tissue-type plasminogen activator 0.7 milligrams per kilogram loading, and then at 0.1 milligrams per kilogram per hour with low-dose heparin at 5 units per kilogram per hour. Fresh frozen plasma was given before the plasminogen activator was administered. The condition of the patient improved markedly with an oxygen saturation of 96% in FiO_2 0.25. The echocardiogram 12 hours after treatment with the plasminogen activator revealed a disappearance of the thrombus in the pulmonary artery and patent foramen ovale with a left-to-right shunt. Continuous administration of plasminogen activator and low-dose heparin followed for 24 hours. Heparin was increased to 20 units per kilogram per hour after 2 days to maintain a partial thromboplastin time 2 to 2.5 times the normal value after which the patient was transitioned to enoxaparin 1.5 milligrams per kilogram per dose every 12 hours. No adverse effects occurred.

Laboratory investigation showed protein C 75.4% (70–130%), protein S 67.6% (60–140%), and anti-thrombin 22.2% (70–106%). Urine examination showed a urine protein count of 4+. A spot urine protein/urine creatinine analysis showed a concentration of 74.3, and 24-hour urine protein concentration was 3.6 grams per square metre per hour. Additional laboratory results are as follows: serum albumin 1.3 grams per decilitre, serum globulin 0.9 grams per decilitre, and cholesterol 267 milligrams per decilitre. The renal Doppler ultrasound showed no renal artery or renal vein thrombosis. Therefore, congenital nephrotic syndrome was suspected. Prednisolone and enalapril were given to reduce proteinuria. A maternal blood test showed negative results for syphilis, hepatitis B, cytomegalovirus, rubella, and human immunodeficiency virus. Unfortunately, this patient had severe sepsis and died at the age of 30 days. A suspected diagnosis of congenital nephrotic syndrome of the Finnish type was finally made at autopsy.

https://doi.org/10.1017/S1047951112000789 Published online by Cambridge University Press

Discussion

This report presents a successful management of a case of pulmonary arterial thrombosis in an infant with congenital nephrotic syndrome using a recombinant tissue-type plasminogen activator. To our knowledge, there are no previous studies on the treatment of pulmonary arterial thrombosis in congenital nephrotic syndrome using a plasminogen activator. This case had a sudden severe onset of cyanosis and respiratory failure requiring endotracheal intubation. Pulmonary arterial thrombosis was diagnosed by echocardiography and computed tomography angiography. Plasminogen activator and heparin were administered during emergency management with a completely resolved thrombosis within 12 hours after plasminogen activator infusion.

Most of the literature has reported the successful treatment of an intra-cardiac thrombus related to central venous catheterisation using a fibrinolytic agent and heparin.[2–5] Ferrari et al[3] reported that 5% of patients developed catheter-related intracardiac thrombosis in the first few days of life. The right atrium was the most common site for a thrombus.[2] Successful treatment of a right pulmonary arterial thrombosis using urokinase was reported.[4] Kändler et al[5] reported that the use of plasminogen activator and heparin for treatment of caval thrombosis can be achieved in patients with congenital nephrotic syndrome.

Recombinant tissue-type plasminogen activator was recently used for treatment of intra-cardiac thrombosis in a neonate.[2–5] The tissue plasminogen activator converts the plasminogen directly to plasmin, which is the activate serum protease. Major advantages are high fibrin specificity, short half-life, and reverse hypo-coagulable state, leading to low risk of haemorrhagic complications and low anti-genicity.[2]

Low-dose heparin was concomitantly given with the plasminogen activator for increasing the efficacy of thrombus lysis. Low-molecular-weight heparin was administered after complete clot dissolution to prevent formation of a new thrombus.

Medical treatment was preferred rather than surgery in a newborn, especially in a preterm infant, because the cardiopulmonary bypass technique and the small vessel sizes were major problems.[4] In this case report, early detection of the thrombosis with prompt administration of the activator and low-dose heparin successfully and safely treated a patient with congenital nephrotic syndrome.

Acknowledgement

The authors thank Dr. Pannee Visrutaratna, Department of Radiology for the assistance with computed tomography angiogram, and Dr. Rungrote Natesirinikul, Division of Pediatric Hematology/Oncology, Chiang Mai University for suggestions.

References

1. Papez KE, Smoyer WE. Recent advances in congenital nephrotic syndrome. Curr Opin Pediatr 2004; 16: 165–170.
2. Hartmann J, Hussein A, Trowitzsch E, Becker J, Hennecke KH. Treatment of neonatal thrombus formation with recombinant tissue plasminogen activator: six years experience and review of the literature. Arch Dis Child Fetal Neonatal Ed 2001; 85: F18–F22.
3. Ferrari F, Vagnarelli F, Gargano G, et al. Early intracardiac thrombosis in preterm infants and thrombolysis with recombinant tissue type plasminogen activator. Arch Dis Child Fetal Neonatal Ed 2001; 85: F66–F69.
4. Alkalay AL, Mazkereth R, Santulli Jr T, Pomerance JJ. Central venous line thrombosis in premature infants: a case management and literature review. Am J Perinatol 1993; 10: 323–326.
5. Kändler C, Ries M, Rupprecht T, Ruder H, Harms D. Successful systemic low-dose lysis of a caval thrombus by rt-PA in a neonate with congenital nephrotic syndrome. J Pediatr Hematol Oncol 1997; 19: 348–350.