Intracardiac thrombus formation with rapidly progressive heart failure in the neonate: treatment with tissue type plasminogen activator

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Abstract

A newborn is described in whom the use of a central venous line was complicated by septicaemia and by intracardiac thrombus formation with tricuspid valve insufficiency and heart failure. Besides antibiotics, treatment consisted of tissue type plasminogen activator (tPA) for three days. This treatment resulted in the disappearance of the thrombus and the tricuspid insufficiency. No adverse effects were noted. Treatment with tPA should be considered in intracardiac thrombus formation with rapidly progressive heart failure in the neonate.

As central catheters are used extensively in neonates for parenteral nutrition or administration of medication, formation of both infected and non-infected thrombi on the endocardium is increasingly observed. Especially in neonates with very low birth weight such thrombus formation may lead to life threatening situations. Treatment of these cases is difficult.[1–3]

We report on our experience with tissue type plasminogen activator (tPA), a new thrombolytic agent, in a newborn with rapidly progressive heart failure due to thrombus formation on the tricuspid valve.

Case report

The patient was a girl with intrauterine growth retardation who was born by caesarean section because of fetal distress. Gestational age was 32 weeks, birth weight 900 g, and height 35 cm. Apgar scores were 8 and 8 at 1 and 5 minutes respectively. On the second day a central venous line was introduced via the right brachial vein for parenteral nutrition. On chest radiography, the tip of the catheter was located at the entrance of the right atrium. No umbilical catheters were used. There were no problems until the 10th day when lethargy, mottling of the skin, increasingly frequent episodes of apnoea and bradycardia, and increasing oxygen demand developed.

The suspected diagnosis of septicaemia was confirmed later by growth of coagulase negative staphylococcus in three bottles from two separate peripheral blood cultures. These staphylococci all had the same susceptibility profile to antibiotics. Treatment with cefotaxime, amikacin, and vancomycin and supportive medication was started.

On the 12th day of life the clinical situation again deteriorated with impaired peripheral circulation, tachycardia, tachypnoea, generalised oedema, and hepatosplenomegaly. Auscultation revealed a gallop rhythm, an additional click that could be differentiated from the third heart sound, and a holosystolic grade III murmur that had been absent previously and was situated parasternally in the left fourth intercostal space. Acute heart failure was diagnosed. Echocardiography showed no congenital heart disease but a vegetation on the atrial side of the septal leaflet of the tricuspid valve, measuring 2×3 mm (fig 1). The right atrium was dilated. Echo Doppler revealed moderate tricupsid valve insufficiency with the jet lining the free margin of the vegetation.

Laboratory investigations showed microscopic haematuria, thrombocytopenia with a platelet count of 28×10^9/l, white cell count of 5×10^9/l with 39% polymorphonuclear neutrophils, haemoglobin concentration of 104 g/l, and a packed cell volume of 0·35. C reactive protein was increased to 92 mg/l (normal value is <5 mg/l). There was a slight metabolic acidosis but no other electrolyte disturbances.

Because of the acutely deteriorating clinical condition it was decided to attempt lysis of the vegetation. Tissue type plasminogen activator (tPA, Actilyse, Boehringer Ingelheim) was administered through the central venous line in a dose of 0·5 mg/kg during 10 minutes followed by a continuous infusion of 0·2 mg/kg/hour. The antibiotic treatment was continued. The patient's general condition rapidly improved and tachycardia and generalised oedema disappeared. One day after the start of the treatment with tPA, the holosystolic murmur disappeared, two dimensional echocardiography showed a diminution of the vegetation on the tricuspid valve, and echo Doppler showed a decrease of the tricuspid valve insufficiency. However, an echodense mass seen on the septum in the right ventricle, probably a

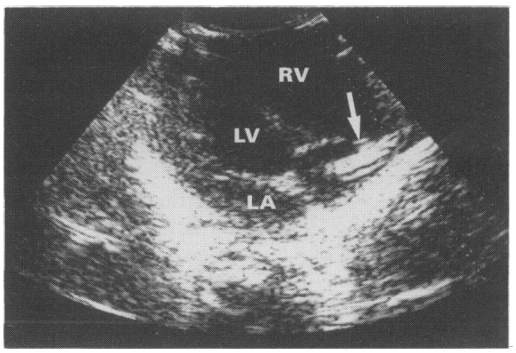

Figure 1 Ultrasound four chamber view of the heart showing the vegetation (arrow) on the tricuspid valve. LV=left ventricle, RV=right ventricle, LA=left atrium.

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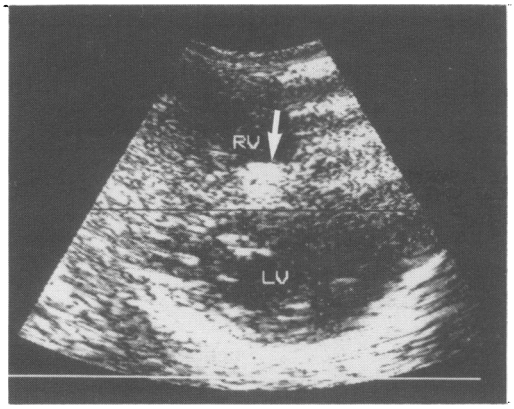

Figure 2 Ultrasound parasternal view of the heart showing the mass (arrow) in the right ventricle on the septum. LV=left ventricle, RV=right ventricle.

detached and entrapped part of the original vegetation (fig 2). On the third day of treatment with tPA, this thrombus had disappeared; the original vegetation was hardly visible. One day later no thrombi could be demonstrated and the tricuspid regurgitation had disappeared completely. Infusion of tPA was then stopped. During this treatment no bleeding tendency at puncture sites was observed, there were no respiratory disturbances, no ecchymoses or purpura appeared, and transfontanellar echography showed no intraventricular haemorrhages. Activated partial thromboplastin time, prothrombin time, and plasma fibrinogen concentration remained normal. Hepatosplenomegaly disappeared during the days after cessation of treatment. The central venous catheter was removed on the 37th day of life: bacterial culture of the tip remained negative. Antibiotic treatment was continued for a total of six weeks. Echocardiography after three weeks and three months was normal; electrocardiography and transfontanellar echography always remained normal.

Discussion

Since central catheters have been used in neonates septicaemia, mainly by coagulase negative staphylococcus, and thrombus formation are increasingly seen as complications.[1-3] When thrombi develop on the endocardium they may lead to life threatening situations such as dissemination of emboli in the lungs or the systemic circulation, obstruction of the valves, or valvular insufficiency. The latter may result in serious functional disturbances and heart failure. Endocardial vegetations of more than 1–2 mm can be diagnosed by two dimensional sector echocardiography, the accompanying functional disturbances such as valvular regurgitation by combined Doppler investigation. The treatment of thrombus formation with haemodynamic implications remains a difficult decision. The most radical treatment consists of the surgical removal of the thrombus: such treatment is, however, not without risks when the patient's condition is precarious.[4-6] An alternative which has only exceptionally been tried in infants is lysis of the thrombus by pharmacologic agents.[7]

In our patient there were sufficient indications for septicaemia by coagulase negative staphylococcus and this was treated with antibiotics and supportive measures. Intracardiac thrombus formation was suspected when the general condition again deteriorated, a heart murmur appeared, and heart failure developed. The diagnosis was confirmed and its functional implications established by echography. Surgical removal of the thrombus was not considered for three main reasons: presence of a severe infection, haemodynamic instability, and small body size. We instead decided to use thrombolytic treatment, being well aware of the risks such treatment could engender in this critically ill patient. The main problem was the possibility of dissemination of a probably infected thrombus. We could, however, expect that the thrombolytic agent would also dissolve the disseminated thrombi.

We opted for tPA, which is a recently introduced specific thrombolytic agent obtained by DNA recombination and which is identical with the endogenous human glycoprotein.[8] Compared with the first generation thrombolytic agents urokinase and streptokinase, tPA has several theoretical advantages.[9] First, it exerts its action on fibrin locally without activating the plasminogen in the circulation and therefore without causing generalised thrombolysis. Furthermore, because of its identity with the human endogenous glycoprotein, it has no immunising capacity and has identical biochemical and kinetic properties. Finally, it has a short half life time of approximately five minutes, allowing an easier monitoring of the treatment. In our patient the treatment resulted in the diminution of the vegetation on the tricuspid valve and a decrease of the tricuspid insufficiency with improvement of the haemodynamic situation after one day. After three days no thrombi could be demonstrated and the thrombolytic treatment could be interrupted. No complications, more specifically no bleeding tendency or further dissemination of the thrombus, were observed. These results were confirmed during a follow up of three months.

tPA has been used extensively in adults but in children and certainly in neonates the experience is very limited. It has been used, apparently with success, in the treatment of aortic thrombosis in a 4 day old premature infant[10] and of a pulmonary embolism in a 19 month old boy.[11] Recently, successful treatment with tPA of various thromboembolic conditions in children from different age groups was described and dosage schemes were proposed.[12] If our experience is confirmed intracardiac thrombus formation with rapidly progressive cardiac failure should be added to the list of indications for tPA treatment.

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