Cardiol Young 2001; 11: 355–356

ISSN 1047-9511

Brief Report

The role of tissue plasminogen activator in the successful treatment of infected cardiac thrombus in children

Eli Zalzstein, Nili Zucker, Aviva Levitas

Pediatric Cardiology Unit, Cardiology Department, Soroka University Medical Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel

Abstract Infected cardiac thrombus is rare in children, with antibiotic or antifungal agents used as the first line of treatment. Persistence is an indication for surgical intervention. We describe two children who were treated successfully with a combination of antibiotic and antithrombotic agents. Use of antithrombotic agents promotes degeneration of fibrin, thus reducing the mass and facilitating the diffusion of the antibiotic and/or antifungal agents.

Keywords: Infected cardiac thrombus; plasminogen

INFECTED CARDIAC THROMBUS IS RARE IN CHILDREN. Patients with immunosuppressive disorders, drug abusers, and patients with prolonged indwelling central lines comprise the population at risk for thrombus development.[1] Infected vegetations are associated with substantial mortality in all age groups and, in the presence of persistent sepsis, surgical resection of the mass has been required in from one-third to three-quarters of cases (2, 3). We report on two children who were diagnosed with infected cardiac thrombus, and who were treated successfully with a combined regimen of antithrombotic and antibiotic agents. Such combined therapy may reduce the need for surgical intervention in future cases.

Patient 1

A 3-year-old received hyperalimentation through a central line because of protracted diarrhea from the age of 2 months. The line was inserted through the jugular vein, and the tip of the catheter was located at the superior caval.vein The patient developed fever, and blood cultures drawn at that time were positive for *Staphylococcus epidermidis* and *Candida albicans*. An echocardiographic examination revealed a 10 mm × 7 mm mass on the anterosuperior leaflet of the tricuspid valve. Treatment was commenced with vancomycin and amphotericin, but the fever persisted. Repeat echocardiographic evaluations performed twice weekly revealed no change in the size of the mass. Cultures of blood and urine continued to be positive. An echocardiogram performed on the twelfth day showed that the mass had grown to a size of 11 mm × 10 mm. Mild regurgitation of the tricuspid valve was detected by color flow. The results of blood tests for platelet count, prothrombin time and partial thromboplastin time were within normal limits. In light of the protracted diarrhea that necessitated continuous intravenous hyperalimentation, lysis of the mass was considered. After the potential risk of thrombolytic therapy was discussed with the parents, we administered tissue plasminogen activator for 3 successive days at a dose of 0.5 mg/kg/h for 6 hours. At the conclusion of each course of treatment, we reevaluated the echocardiographic findings. After the 3rd course of treatment, there was no echocardiographic evidence of the mass, and cultures of blood and urine became negative. Treatment with amphotericin-B and vancomycin was continued for an additional two weeks. There were no adverse effects such as excessive bleeding or peripheral embolization. Throughout the follow-up period of 24 months, there was no evidence of recurrence.

Correspondence to: Eli Zalzstein, MD, Pediatric Cardiology Unit, Cardiology Department, Soroka University Medical Center, POB 151, Beer Sheva, 84105, Israel. Tel: 972–8–6403050; Fax: 972–8–6400665; E-mail: eliz@ bgumail.bgu.ac.il

Accepted for publication13 December 2000

https://doi.org/10.1017/S1047951101000403 Published online by Cambridge University Press

Patient 2

A 3-month-old baby was treated for intractable diarrhea by hyperalimentation through a central line. The line was inserted via the jugular vein, and the tip of the catheter was located at the junction of the superior caval vein with the right atrium. On the 14th day of hospitalization, the patient developed fever. The results of blood tests showed leukocytosis with a shift to the left, and an elevated sedimentation rate. Treatment was initiated with cefotaxime. When cultures of blood and urine were positive for *Candida albicans*, amphothericin was added to the therapeutic regimen. An echocardiographic examination demonstrated two masses, one measuring 2 mm × 4 mm in the superior caval vein, and the other, measuring 3 mm × 3 mm, was attached to the right atrial wall. Lysis of the masses was considered, and following parental consent, tissue plasminogen activator was given at a dose of 0.5mg/kg/h for 6 hours. On the second day, after two courses of thrombolysis were completed, an echocardiographic examination revealed lysis of both masses. Cultures of blood and urine were negative on the fifth day. Ampotericin was continued for another 2 weeks. Follow-up echocardiography on the seventeenth day revealed complete resolution of the masses without evidence of embolization to any part of the heart or the great vessels, including the peripheral pulmonary arteries. Throughout the follow-up period of 20 months, there was no evidence of recurrence.

Discussion

Insertion of catheters centrally is often indicated in severely ill babies and, as a result, formation of thrombus is increasingly seen as a complication.[4,5] Treatment of infected thrombus includes the intravenous administration of antibiotics, and in cases with hemodynamic compromise, surgical removal of the thrombus. Such radical treatment is not without risks because of the basic unstable condition of the patient. An alternative therapy is pharmacologic lysis of the thrombus.[6] Antithrombotic agents promote degradation of fibrin, reducing the mass of the vegetation and facilitating the diffusion of antibiotic antifungal agents. Although both patients described here were treated with antibiotic and antifungal agents, cultures of blood and urine remained positive. The addition of tissue plasminogen activator to the regimen of treatment improved the clinical course. The thrombus decreased in size, and cultures of blood and urine became negative. No adverse effects were seen.

The use of anticoagulants such as heparin or coumadin to stop the growth of vegetations in native valves is complicated by increased rates of bleeding.[7] We chose tissue plasminogen activator because of its clinical advantage. Although it has a high affinity for fibrin, the activator has a low affinity for circulating plasminogen, thus reducing its systemic effects. Its elimination half time is short, decreasing the risk of bleeding complications.[8] Successful treatment in this fashion was described in a neonate leading to lysis of vascular thrombus,[9] an intracardiac thrombus,[4] and an infected cardiac thrombus in a premature infant.[10] We conclude that combined treatment using an antithrombotic agent together with antibiotic and antifungal agents may be a viable alternative to surgery in some of these critically ill infants.

Acknowledgement

We acknowledge with thanks the significant clinical contribution of Joseph Kapeluchnick, MD in working with our patients.

References

1. Melamed R, Leibovitz E, Abramson O, Levitas A, Zucker N, Gorodisher R. Successful non-surgical treatment of Candida tropicalis endocarditis with liposomal amphotericin-B (AmBisome). Scand J Infect Dis 2000; 32: 86–89
2. Citak M, Rees A, Mavroudis C. Surgical management of infective endocarditis in children. Ann Thorac Surg 1992; 54: 755–760
3. Nomura F, Penny DJ, Menahem S, Pawade A, Karl TR. Surgical intervention for infective endocarditis in infancy and childhood. Ann Thorac Surg 1995; 60: 90–95
4. Noel GJ, O'Loughlin JE, Edelson PJ. Neonatal Staphylococcus epidermidis right-sided endocarditis: description of five catheterized infants. Pediatrics 1988; 82: 234–239
5. Schmidt B, Zipursky A. Thrombotic disease in newborn infants. Clin Perinatol 1984; 11: 461–488
6. Delaplane D, Scott JP, Riggs TW, Silverman BL, Hunt CE. Urokinase therapy for a catheter-related right atrial thrombus. J Pediatr 1982; 100: 149–152
7. Van Overmeire B, Van Reemots PJ, Van Acker KG. Intracardiac thrombus formation with rapidly progressive heart failure in the neonate: treatment with tissue plasminogen activator. Arch Dis Child 1992; 65: 443–445
8. Levy M, Benson LN, Burrows P, Bentur Y, Strong DK, Smith J, Johnson D, Jacobson D, Jacobson S, Koren G. Tisue plasminogen activator for the treatment of thromboembolism in infants and children. J Pediatr 1991; 118: 467–472
9. Dillon PW, Fox PS, Berg CJ, Cardella JF, Krummel TM. Recombinant tissue plasminogen activator for neonatal and pediatric vascular thrombolytic therapy. J Pediatr Surg 1993; 28: 1264–1268
10. Fleming RE, Barenkamp SJ, Jureidini SB. Successful treatment of a staphylococcal vegetation with tissue plasminogen activator. J Pediatr 1998; 132: 535–537

https://doi.org/10.1017/S1047951101000403 Published online by Cambridge University Press