A large intracardiac fungus ball in a premature infant

Filiz Ekici[1], Birgül Varan[2], Berna Şaylan-Çevik[1], Murat Özkan[3], Alev Ok-Atılgan[4], Ayla Oktay[2]

[1]Department of Pediatric Cardiology, Ankara Children's, Hematology and Oncology Hospital, and Departments of [2]Pediatric Cardiology, [3]Cardiovascular Surgery, and [4]Pathology, Başkent University Faculty of Medicine, Ankara, Turkey

SUMMARY: Ekici F, Varan B, Şaylan-Çevik B, Özkan M, Ok-Atılgan A, Oktay A. A large intracardiac fungus ball in a premature infant. Turk J Pediatr 2011; 53: 325-327.

We present a premature infant with large intracardiac mass. She had a history of sepsis and umbilical venous catheterization in the neonatal period. Twenty-seven days after withdrawal of the catheter, a precordial murmur was noted. A large right atrial highly mobile mass suspected to be thrombus was detected by echocardiography. C-reactive protein was elevated. Three blood cultures were negative. Anticoagulation treatment was started. After one week, no resolution of the thrombus was observed. The mass was surgically resected and diagnosis of thrombus infected by fungi was made on histopathological examination. Early screening of cardiac chambers by echocardiography is recommended in all preterms with intravascular catheterization.

Key words: intracardiac thrombosis, umbilical catheterization, preterm infants.

Thromboses in neonates are usually associated with central catheterization and occur in both arterial and venous systems[1-4]. Such thrombi may persist or be detected after catheter removal and can lead to life-threatening complications[1-4]. An increasing number of very tiny babies are surviving the first week of life, thus increasing the likelihood of colonization of fungi. The immature immune system in these sick preterm infants may be less capable of dealing with the vascular candidiasis. We present a 72-day-old very low birth weight premature infant with a large right atrial infected thrombus. The treatment strategies for intracardiac thrombosis are also reviewed.

Case Report

A 72-day-old premature female infant was admitted to our hospital for cyanosis while feeding. She was born at the 29th gestational week and had a very low birth weight (970 g). She had a history of *Staphylococcus aureus* sepsis and respiratory distress syndrome, and was treated with mechanical ventilation, and a broad-spectrum antibiotic therapy, parenteral nutrition, and blood transfusion via umbilical venous catheterization in a local hospital. A transient thrombocytopenia (platelet count: 21,000/mm^3) was also observed during the treatment of sepsis. On physical examination, weight and length were 1900 g and 43.5 cm (<3rd percentile), respectively. Heart rate was 150 beats/minute, blood pressure was 70/28 mmHg and respiratory rate was 48/minute. Her general condition was well; a precordial second-degree murmur was detected on physical examination. Respiratory sounds were normal, and peripheral pulses were palpable. Laboratory findings were as follows: hemoglobin 9.2 g/dl, hematocrit 27.9%, platelet count 64,000/mm^3, and leukocyte count 8,800/mm^3. Biochemical tests and urinary analysis were normal. C-reactive protein was high, at 4.34 mg/dl [N: 0-0.4 mg/dl]. Activated partial thromboplastin time, prothrombin time and international normalized ratio were normal. Cranial and abdominal ultrasonographic examinations were normal. Three blood cultures were negative. An echocardiography was performed, and a large right atrial highly mobile mass with a suspicion of thrombosis was detected. Patent foramen ovale and a small patent ductus arteriosus were also present. The lesion measured 10 x 13 mm, filled the right atrial cavity, and had an irregular and heterogeneous appearance, containing echolucent areas (Figs. 1A, 1B). The lesion was attached to the ostium of the inferior

vena cava (Fig. 1C) and middle part of the atrial septum by a stalk (Fig. 1A). The mobile mass was prolapsing through the tricuspid valve during ventricular diastole and partially occluding the tricuspid valve. These clinical and echocardiographic findings suggested the diagnosis of a right atrial thrombus. We used enoxaparin (2 mg/kg q12 h) for anticoagulation. After a week of anticoagulation treatment, the large thrombus persisted in echocardiography. The mass was resected surgically. Consequently, the diagnosis of the intracardiac thrombus infected by candida species was made by histopathological examination (Fig. 2A, 2B). Antifungal treatment with amphotericin B was given for four weeks.

Discussion

The use of central venous catheter in preterm infants has led to an increased incidence of thrombotic events. Tanke et al.[3] investigated the development of central venous catheter-induced thrombosis in 193 infants in the neonatal intensive care unit, and intracardiac thrombosis was found in 25 cases (13%). Ferrari et al.[4] reported that intracardiac thrombosis developed in 5% of preterm infants (<1500 g) within one to four days after umbilical catheter insertion.

Ultrasound can be very helpful in defining the location, extent and size of such thrombi. Thrombi tend to have bright, relatively smooth borders and a homogeneous appearance. Specific regions more likely to harbor thrombi include the ventricular apex, the atrial appendages and intravascular catheters. Although most atrial thrombi are relatively fixed in position, some may be highly mobile and may mimic a left atrial myxoma[5]. Clinical cardiac signs depend on the size, hemodynamic consequences and age of the thrombus. In most of the reports, the time of the diagnosis ranged from a few hours to three days after catheter placement. Generally, preterm infants with a small size thrombus have subtle or no clinical cardiac symptoms[3,4,6].

Although the optimal treatment modalities for neonates with thrombosis are not known, administration of an antithrombotic agent is useful to prevent extension of the clot and allow normal thrombolytic processes to resolve the clot. Heparin, either unfractionated or a low molecule weight preparation, is recommended in the neonatal period[6,7]. Recombinant tissue type plasminogen activators have been recommended recently as first choice of therapy in preterm infants[2,4]. The efficacy of enoxaparin, causing partial or complete resolution, was between 59-100%. Suggested starting doses of enoxaparin are 1.2 - 1.7 mg/kg q12 h for term neonates and 2 - 3.5mg/kg q12 h for preterm neonates[7,8].

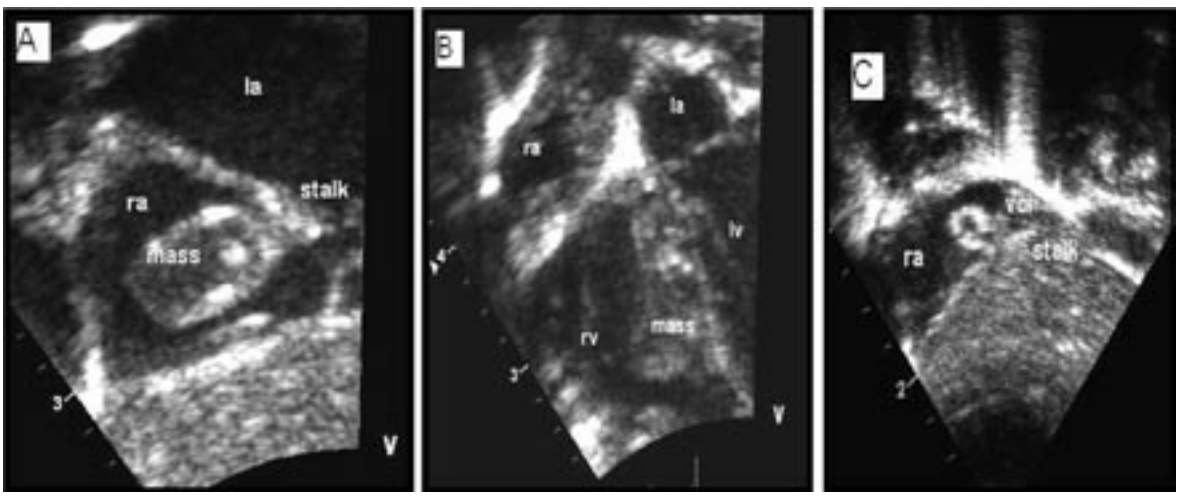

Fig. 1. The subcostal view in systole (A) and apical four-chamber view in diastole (B). The lesion is very large, filling the right atrial cavity, and the main mass of the lesion has an irregular and heterogeneous appearance, containing echolucent areas. The lesion was attached to the ostium of the inferior vena cava (C) and also partially to the right atrial free wall and middle part of the atrial septum by a stalk (A), which permitted the main mass of the lesion to move through the right ventricular cavity (la: left atrium, ra: right atrium, lv: left ventricle, rv: right ventricle).

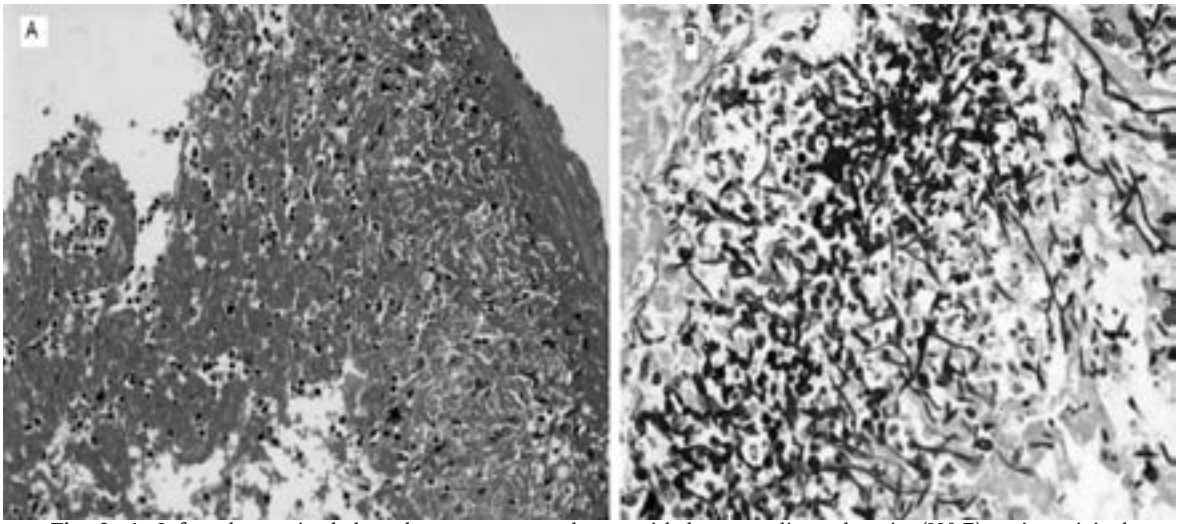

Fig. 2. A. Infected organized thrombus areas were shown with hematoxylin and eosin (H&E) stain, original magnification x 200. B: Fungus colonizations compatible with candida species were shown with histochemical periodic acid–Schiff (PAS) stain, original magnification x 200.

Newborns without structural heart disease may also acquire infective endocarditis related to the presence of intravascular catheters. The catheter may induce direct vascular endothelial damage and alter the thromboresistant endothelial surface. The organisms can enter the body along the side of the catheter, and the tip provides a nidus for colonization and subsequent embolization of candida. These infants may have multiple sites of infection, requiring a prolonged course of antifungal therapy. Removal of the infected tissue may also be necessary for complete resolution[9].

We observed that an intracardiac thrombus can enlarge and become an infected mass. Early screening of cardiac chambers by echocardiography is recommended in all preterms with umbilical catheterization.

REFERENCES

1. Novak-Göttl U, Duering C, Kempf-Bielack B, Sträter R. Thromboembolic disease in neonates and children. Pathophysiol Haemost Thromb 2003; 33: 269-274.
2. Greenway A, Massicotte MP, Monagle P. Neonatal thrombosis and its treatment. Blood Rev 2004; 18: 75-84.
3. Tanke RB, van Megen R, Daniëls O. Thrombus detection on central venous catheters in the neonatal intensive care unit. Angiology 1994; 45: 477-480.
4. 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: 66-69.
5. Feigenbaum H. Echocardiography (5th ed). Philadelphia: Lea & Febiger; 1994.
6. Beardsley DS. Venous thromboembolism in the neonatal period. Semin Perinatol 2007; 31: 250-253.
7. Michaels LA, Gurian M, Hegyi T, Drachtman RA. Low molecular weight heparin in the treatment of venous and arterial thromboses in the premature infants. Pediatrics 2004; 114: 703-707.
8. Malowany JI, Monagle P, Knoppert DC, et al. Enoxaparin for neonatal thrombosis: a call for a higher dose for neonates. Thromb Res 2008; 122: 826-830.
9. Mendoza GJB, Soto A, Brown EG. Intracardiac thrombi complicating central total parenteral nutrition: resolution without surgery or thrombolysis. J Pediatr 1986; 108: 610-613.