

Intracardiac Thrombus Treated Non-Invasively by Anticoagulant Therapy in a Child with Tay-Sachs Disease

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Abstract

We presented a four-year-old girl with Tay-Sachs disease who had thrombus in the right atrium. The patient was admitted to hospital with cardiopulmonary arrest and aspiration pneumonia was diagnosed. Intracardiac thrombus was detected during routine echocardiographic examination. There was no underlying genetic prothrombotic predisposition in this patient. The guidelines of treatment for intracardiac thrombus in children are lacking in the literature and the experience in managing these patients is limited. We aimed to discuss the treatment approaches to intracardiac thrombi and to emphasize that, development of intracardiac thrombus is common in critically ill children and can be treated successfully by non-invasive anticoagulation with heparin.

Keywords: Anticoagulant Therapy; Child; G(M2) Ganglioside; Intracardiac Thrombosis

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intracardiac thrombus is uncommon; the frequency has increased in recent years with the increasing numbers of applications in intensive care units [1, 2]. The guidelines of treatment for intracardiac thrombus in children are lacking in the literature and the experience in managing these patients is limited. Here, we aimed to discuss the treatment approaches on intracardiac thrombus in children.

Case Report

A four-year-old girl with Tay-Sachs disease was brought to hospital as cardiopulmonary arrest. She was weighing 11 kg (<3 percentile) and height was 109 cm (<3 percentile). It was learned that she had complaints of vomiting and cough for a few days. She was diagnosed as aspiration pneumonia. In her history, she was using oxcarbamazepin for epilepsy and she was hospitalized many times due to recurrent pulmonary infections. In the family history, her brother and sister had died with diagnosis of Tay-Sachs disease. Subject's parents gave informed consent to participate in our case report. She was admitted to pediatric intensive care unit where she was intubated and mechanically ventilated. On physical examination she was in poor general condition, her pupils were miotic and cherry red spots on retina were present. As evidence of pneumonia bilateral crackles and 2/6 systolic murmur was auscultated. She had developmental delay and vital signs were body temperature: 38.6 °C, Heart rate: 168/min, TA: 80/60 mmHg. On laboratory tests; hemoglobin was 10.6 g/dL, white blood cell count 14,700/mm³, platelet 202,000/mm³, aspartate transaminase 668 U/L, alanine transaminase 256 U/L, blood urea nitrogen 120 mg/dL, creatinine 2.5 mg/dL, uric acid

Introduction

Tay-Sachs disease (also known as GM2 gangliosidosis) is a rare autosomal recessive metabolic disorder of sphingolipids caused by deficiency of hexosaminidase A. Although Tay-Sachs is not a risk factor for children and

23.4 mg/dL. Elevation of liver enzymes was bound to be affected by post-cardiopulmoner arrest and infection. The patient's liver enzymes decreased at follow up. Blood gas analysis was revealed normal. Activated Partial Thromboplastin Time (aPTT) was 26.6 sec, prothrombin time 24.4 sec and "international normalized ratio" was 1.7. Serum homocystein levels revealed normal.

Parenteral antimicrobial therapy was administered to patient for pneumonia. During routine echocardiographic examination 18x16 mm thrombus in the right atrium was detected (Figure 1). She had normal systolic function, her ejection fraction was 65%, did not require inotropes and no arrhythmia was observed. Her central venous line was removed after echocardiographic diagnosis of thrombus.

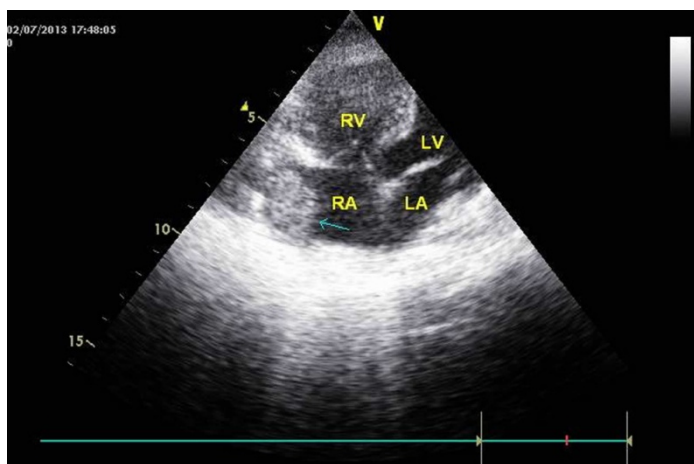


Figure 1: Echocardiographic image showing 18x16 mm thrombus in the right atrium

Intracardiac thrombus was thought to occur secondary to central venous line catheter. Although infections are very important in the etiology of thrombus retention, specific etiological agent could not be detected in the laboratory tests. Recurrent pulmonary infections due to tay sachs disease and immobilization of the patient may predispose to thrombosis. Unfractionated heparin infusion was instituted in addition to antibiotic treatment as soon as the diagnosis was made. The coagulation factors 8, 9, 11, 12, 13, protein C, protein S, antithrombin 3 and lipoprotein A levels were within normal

limits. There was no blood culture positivity. Heparin was started at a dose of 20 U/kg/hr after a loading dose of 75 U/kg and administered for two days. The dose of heparin was regulated according to aPTT (60-85 sec). The therapy then continued with low molecular weight (LMW) heparin at a dose of 100 U/kg every 12 hours. The dose of LMW heparin was regulated according to anti-factor Xa level (0.5-1 U/mL). On serial echocardiographies thrombus was found to show resolution after 11th day of the anticoagulant therapy and disappeared completely one month later (Figure 2). She is now followed at outpatient clinic and is uneventful for eight months. The echocardiographic evaluations are normal and LMW heparin treatment is planned to discontinue after four months. A 4-year-old patient with a neurometabolic disorder such as Tay Sachs, pneumonia and catheter-related thrombus was successfully treated with heparin therapy. We want to emphasize that non-invasive heparin therapy in intracardiac thrombus is very important in critically ill children.

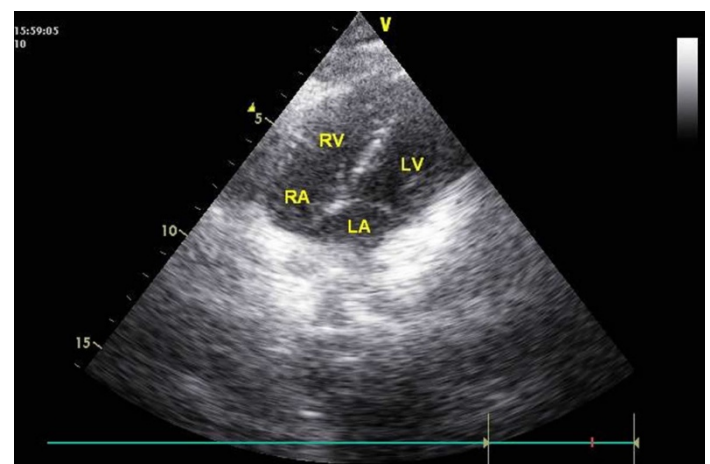


Figure 2: Echocardiographic image showing the thrombus disappeared after treatment

Discussion

Intracardiac thrombus is uncommon in children. It is mostly seen in ischemic heart disease in adults, but in children, it is frequent in patients with dilated cardiomyopathy and after cardiac operations. Central venous catheter, cyanotic congenital heart disease, endocarditis with vegetation, respiratory distress

syndrome, polycythemia and persistent fetal circulation are the risk factors of thrombosis in children. Unlike adults thromboembolic complications in children are mostly due to hereditary thrombophilic factors [3]. Therefore children presenting with thromboembolic events should be investigated for prothrombotic risk factors [4, 5]. In children the most predisposing genetic risk factor of thrombosis is factor V Leiden (FVL) mutations leading to activated protein C resistance [6, 7]. Other inherited diseases are G20210A mutation, deficiency of protein C, protein S and antithrombin III, homocysteinemia and more uncommon diseases are dysfibrinogenemie, dysplasminogenemie and sickle cell anemia [4, 5].

Besides genetic factors other acquired risk factors may be also responsible for the etiology of intracardiac thrombus. These acquired factors are; presence of a serious disease (malignancy, infection, nephrotic syndrome), an acquired inhibitor deficiency or a central venous line [7-9]. In a study of Gürgey et al. in 68% of pediatric patients with thrombosis there was an underlying infection even though these patients had no central venous lines [6]. Wasay et al. have shown that infections play a triggering role in nearly 75% of children in their patient series with thrombosis. They advised that, medical treatment must consist of both antimicrobial and anticoagulant medications [10]. Therefore broad spectrum antibiotics must be initiated to patients with positive blood cultures [11].

Thrombosis is a multi factorial entity. In addition to genetic factors, the introduction of the environmental factors has effects on the frequency and severity of thrombosis. Such as, in another study the association between infections, usage of central venous lines and thrombosis is detected in 76% of cases in childhood [6, 8]. An inherited disorder can be displayed only in 25 to 56% of patients [12]. Treatment of these cases is difficult and there are many controversy opinions about therapy in the literature. According to some authors, in case of asymptomatic right heart localized and infected thrombus only the treatment of the infection might be sufficient to dissolve the thrombus [13]. However, some other authors think that, infected thrombus require more prolonged therapy and anticoagulation is

often added to the treatment [1, 11, 14]. According to our opinion, anticoagulation therapy should be given to all symptomatic patients and to patients with a history or possibility of acute thrombus. The central venous catheters must be removed if possible. The natural history of intracardiac thrombus is resolution. For that reason, thrombolytic therapy and surgical thrombectomy are rarely preferred due to significant complications and should be considered individually [11, 13]. Again, according to our opinion, thrombolytic therapy must be preferred for only symptomatic, hemodynamically important right or left heart localized, unpediculated thrombus. However, surgical treatment must be preferred for only symptomatic, hemodynamically important, right or left heart localized, pediculated and large (≥ 2 cm) thrombus with a high risk of embolization.

Conclusion

Improvement of facilities in intensive care units, increasing life span of complicated patients and widespread use of non-invasive imaging methods increased frequency of the diagnosis of intracardiac thrombus. In patients with concomitant risk factors, cardiac thrombosis should be kept in mind. Experience in managing these patients is limited, because the literature concentrates on case reports of intracardiac thrombi treated with thrombolytic medications. In patients with intracardiac thrombus, selection of anticoagulant therapy may decrease the risk of complications. Surgery is rarely required and thrombolytics are not usually necessary for resolution of thrombus.

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