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Case Report

A case of inherited thrombophilia with superior vena cava syndrome: pharmacological thrombolysis

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ABSTRACT

Venous thrombosis involving vena cava is an uncommon phenomenon seen in children, even in those with inherited thrombophilia syndromes. We present a case of protein C and S deficiency with superior vena cava (SVC) thrombosis along with pyo-pericardium, treated successfully with intravenous (IV) tissue plasminogen activator (TPA) and unfractionated heparin (UFH). A 4-year, male patient presented with massive pericardial effusion (causing cardiac tamponade). Fluoroscopic and echo-guided pericardiocentesis was done. Pericardiocentesis continued for the next 2 days, after which the catheter was removed as fluid volume came down. However, the child soon showed features of SVC syndrome. Ultrasonography and CT angiogram of neck vessels showed occlusive thrombus. Systemic thrombolysis with IV alteplase was performed, followed by continuous UFH IV infusion. Blood investigations showed protein S deficiency and low protein C level. Gradually, symptoms and cardiac function improved. We discharged the patient on warfarin, aspirin and clopidogrel. On follow up, he is doing well. The development of SVC syndrome due to inherited thrombophilia syndromes like protein C and protein S deficiency is rare in children. With that, thrombolytic therapy in children has not been studied much in the past, with extrapolation of data from adult studies being made, putting into the question of its safety and efficacy. However, we successfully managed to restore blood flow in thrombus occluded areas by TPA therapy with no complication from the therapy. SVC syndrome is attached to many causes, one being protein S and C deficiency. However, it can be successfully managed with thrombolysis using TPA.

Keywords: SVC syndrome, Protein C, Protein S, Tissue plasminogen activator, Alteplase, Heparin

INTRODUCTION

Hereditary predisposition to thrombosis is a rare phenomenon in children.[1] With the advent of easy availability of genetic testing in the human population worldwide, numerous inherited risk factors for thrombosis have been identified. But, the majority of the individuals, who inherit one of these risk factors, do not necessarily develop thrombosis during their childhood years. The common heritable thrombophilias are factor V Leiden mutation, prothrombin 20210 mutation, antithrombin III deficiency, elevated factor VIII, hyperhomocysteinemia, protein C deficiency, and protein S deficiency. Protein C and protein S are glycoproteins that are predominantly synthesized in the liver, are vitamin K dependent. They are important components of the natural anticoagulant system in the body. When thrombin reaches the intact endothelium, it binds to its endothelial receptor (thrombomodulin). The thrombin-thrombomodulin complex, thus formed, converts protein C into its activated form. In the presence of co-factor protein S, the activated protein C proteolyzes and inactivates factor Va and factor VIIIa. Inactivated factor Va is a functional anticoagulant.[2] A deficiency of protein C and protein S in the body results into loss of this natural anticoagulant properties, resulting into unchecked

thrombin generation and enhanced risk of thromboembolism. Venous thrombosis involving vena cava is also an uncommon phenomenon seen in children, even in those with inherited thrombophilia syndromes.

In this case report, we describe a rare case that was encountered in our institution. We present case of protein C and S deficiency with SVC thrombosis along with pyo-pericardium, treated successfully with IV TPA and UFH.

CASE REPORT

A 4-year, male child, weighing about 15.5 kg was admitted to our institution with complaints of fever for the last 6 weeks, chest pain and shortness of breath for the last 2 weeks. All of these complaints were of insidious onset. The fever was remittent, high-grade, that resolved upon medication with sweating. The chest pain was at the middle of the chest, continuous, stabbing in nature and aggravated upon breathing fast or on body movements. The shortness of breath was gradually progressive and was of New York heart association (NYHA) class III grade at presentation. The child also had facial puffiness for the last 10 days, which was also of insidious onset and gradually progressive in nature.

On physical examination, he had periorbital oedema and neck veins were distended with child in sitting position. He had tachycardia with pulses of low volume, no special character, and no radio-radial or radio-femoral delay. He was normotensive at presentation with saturation of 94% in room air, which increased to 99% in moist oxygen inhalation. Child was tachypnoeic with chest auscultation revealing fine crepitations bilaterally and diminished vesicular breath sound on the right side accompanied by dull percussion note. Precordial inspection was unremarkable but, on palpation the apical impulse could not be localized properly on both sides of the chest. Precordial auscultation revealed muffled heart sounds.

An immediate 2D-echocardiogram followed physical examination, which showed a massive, organised pericardial collection (Figure 1); mild tricuspid regurgitation (TR); tricuspid valve inflow respiratory variation >25%; mitral valve inflow respiratory variation > 25%; IVC partially collapsing with respiration (Figure 3); collapsed right atrium and right ventricle (RV) (Figure 1); fair left ventricular (LV) function; and moderate to severe right sided pleural effusion (Figure 2).

A diagnosis of pericardial tamponade was made. The child was taken to the cardiac catheterization laboratory, where echocardiography and fluoroscopy-guided pericardiocentesis was performed under general anaesthesia with a 5F pigtail catheter, aseptically. About 300 ml. of thick purulent pericardial fluid was aspirated. Intercostal chest drain (ICD) was inserted into the right pleural space and about 120 ml. of serous, straw-coloured pleural fluid was aspirated. The 5F pigtail catheter was left into pericardial cavity. The pericardial fluid collected was sent for culture and sensitivity, biochemical and microscopic examinations. 100,000 IU streptokinase and 500 mg vancomycin was injected into the pericardial cavity. The child was shifted to the paediatric intensive care unit (PICU) in hemodynamically stable condition.

The child was started on IV antibiotics, vancomycin (40 mg/kg/day in 2 divided doses) and piperacillin-tazobactam (300 mg/kg/day in 3 divided doses), empirically, and IV infusion of furosemide (0.1 mg/kg/hour). About 240 ml. and 65 ml. of purulent and mildly haemorrhagic pericardial fluid were aspirated from the indwelling Pigtail catheter for the next 2 consecutive days, respectively. About 500 mg. of vancomycin was injected into the pericardial cavity for 3 consecutive days. The pericardial fluid analysis showed plenty of pus cells and the culture report displayed methicillin-resistant staphylococcus aureus (MRSA) that was sensitive to vancomycin. Hence IV vancomycin was continued. Gradually, the condition of the child improved and the pericardial collection amount reduced. IV infusion of furosemide was converted to interval dosages (2 mg/kg/day in 2 divided doses). The child was shifted to the paediatric general ward after 4 days. As the amounts of pleural fluid and pericardial fluid collections kept reducing, ICD and Pigtail catheter were finally taken out from the right pleural space and the pericardial space, respectively, after about 8 days of their insertion.

However, the child started developing oedema of face, chest and both the upper limbs from the day following their removal. 2D Echocardiogram was done immediately which showed no evidence of pericardial effusion; mild to moderate RV dysfunction; mild LV dysfunction; IVC partially collapsing with respiration; and, moderate right sided pleural effusion and mild left sided pleural effusion. The child was planned to undergo ultrasonogram (USG) with colour doppler study of neck vessels followed by high resolution computed tomography (HRCT) of thorax and angiogram of neck vessels, both of which showed occlusive echogenic thrombus in the whole of right internal jugular vein (IJV), in the lower half of left IJV and in the whole of left innominate vein. In view of significant pleural effusion, right sided ICD and later left sided ICD was inserted. IV infusion of furosemide (0.1 mg/kg/hour) was restarted. Blood investigations, comprising of complete blood count; prothrombin time (PT), activated partial thomboplastin time (aPTT) and INR levels; D-dimer; ANA profile; serum protein C, protein S, and antithrombin III activity levels; serum factor VIII activity; and, serum homocysteine quantitative analysis were sent. IV antibiotics were upgraded to meropenem (120 mg/kg/day in 3 divided doses) and Teicoplanin (10 mg/kg every 12 hours for 3 doses followed by 10 mg/kg/day once daily) owing to high total leucocyte count.

IV UFH 100 IU/kg stat. followed by IV infusion of UFH (20 IU/kg/hour) was started. In view of venous thrombosis of neck vessels, systemic thrombolysis with

IV Alteplase (0.5 mg/kg/day for 2 days) was performed. Over the next 5 days, oedema gradually subsided and ICD output reduced significantly. 2D echocardiogram showed improved cardiac function; no pericardial effusion; and mild pleural effusion on both sides. No features suggestive of constrictive pericarditis was noted. IV furosemide infusion was converted to interval dosages (2 mg/kg/day in 2 divided doses). Blood investigations showed no protein S activity and protein C activity was very low (only 12 IU/dL). Repeat USG with colour doppler study of the neck vessels showed thrombi in bilateral IJV; with total occlusion of right IJV (Figure 4) and, partially patent left IJV (Figure 5) and left innominate vein. Lower systemic veins were patent. As the general condition of the child improved, IV Infusion of UFH was stopped and he was started on oral medications, warfarin (3 mg once daily), aspirin (5 mg/kg/day once daily) and Clopidogrel (5 mg/kg/day once daily). As the amounts of pleural fluid collections from both sides kept reducing over the next few days, both the ICDs were finally taken out. IV furosemide was converted to oral (1 mg/kg/day in 2 divided doses) and Spironolactone (3 mg/kg/day in 2 divided doses) was added. Child was finally discharged in hemodynamically stable condition and with the above-mentioned oral medications in the same dosages. 2D echocardiogram before discharge showed, adequate biventricular systolic function with LV ejection fraction of about 56%; no significant TV and MV inflow variability with respiration; small thrombus-like mass at the right SVC; mild TR; no pericardial effusion: trace right sided pleural effusion and no left sided pleural effusion.

The child is currently on regular follow-up visits at the out-patient department with, blood INR monitoring in every 3 months; clinical examination and 2D echocardiogram in every 1 year. He is currently on warfarin and aspirin orally. In about 6 months post-discharge, the thrombi at the neck vessels had subsided. There has been no evidence of recurrence of thrombus at the neck vessels or at any other site with the current therapy till the last follow-up visit.

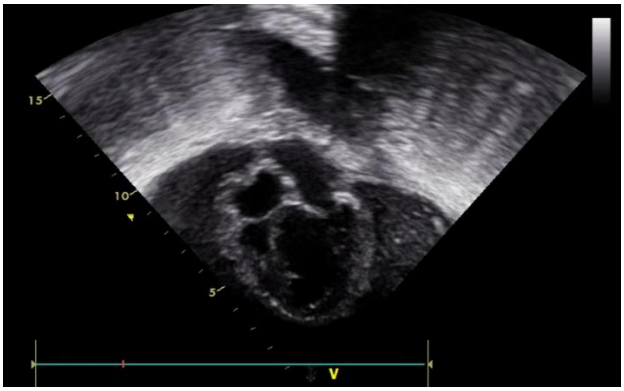

Figure 1: 2D echocardiogram showing apical 4-chamber view at end-diastole. The heart is surrounded by a massive pericardial effusion with collapsed right atrium and right ventricle.

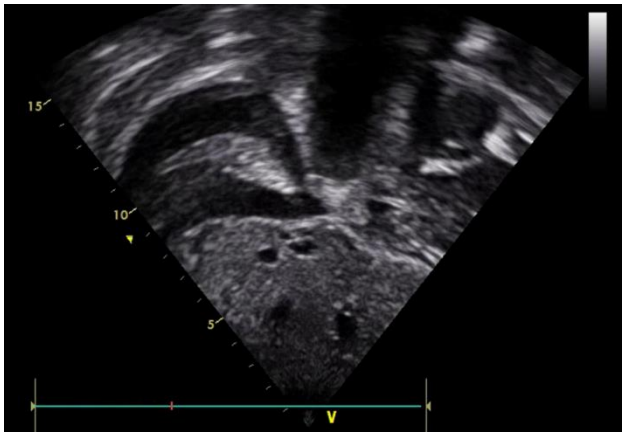

Figure 2: 2D echocardiogram showing subcostal transverse view. The is moderate to severe right sided pleural effusion.

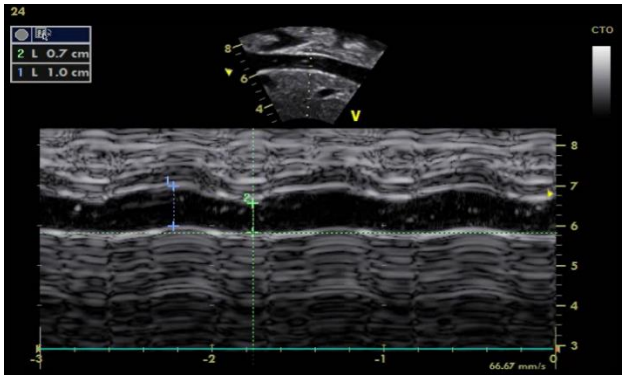

Figure 3: M-mode echocardiogram of inferior vena cava (IVC) showing an IVC partially collapsing with respiration.

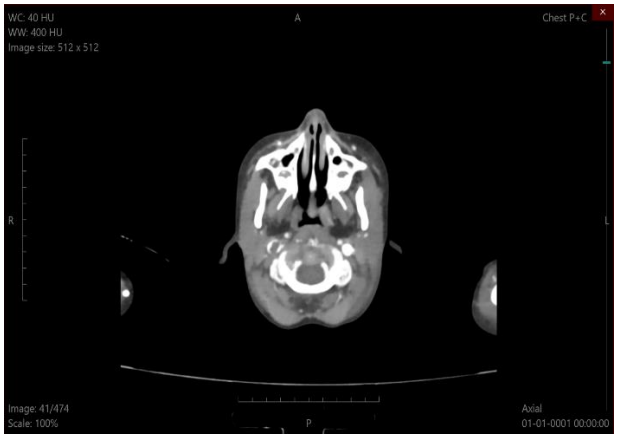

Figure 4: Contrast CT scan of neck vessels showing total occlusion of right IJV by thrombus.

DISCUSSION

In the human body, normally all the procoagulant proteins are balanced by natural anticoagulant proteins that regulate the procoagulant function. The incidence of deficient protein C, protein S, or antithrombin III, which

are natural anticoagulant proteins, are less common than the other known genetic mutations.[3] The cause of SVC syndrome during the childhood is usually due to lymphoproliferative disorders, like Hodgkin's lymphoma, non-Hodgkin's lymphoma, or T-cell acute lymphoblastic leukaemia.[4] Iatrogenic causes, like pacemaker wires, complex cardiac surgeries or use of central venous lines (CVLs) in critically ill children, are responsible for an increasing prevalence of SVC syndrome. The incidence of catheter-induced central venous thromboses is known to range from 0-4.9%.[5] In our case, the SVC syndrome was due to deficiencies of protein C and protein S, which are part of inherited thrombophilia syndromes.

There has not been much attempts of thrombolysis for SVC syndromes in children in the past, except for a few case reports. Tan et al reported thrombolysis with TPA in a 22-month girl with SVC syndrome due to the use of a CVL and/or sepsis. They administered TPA for 2 days. They reported that the clinical features of SVC syndrome disappeared completely within 3 days. There were no complications and radiological investigations showed blood flow through the thrombus occluded vessel after treatment.[6] Comparatively, in our case, clinical improvement was observed by about 2 days of alteplase (TPA) therapy. The optimal dosage for TPA thrombolysis in children is unknown. In paediatric patients where thrombolytic therapy is indicated, the lack of evidence-based medicine forces the practitioners to extrapolate doses from the adult studies. This often results into high rate of major complications. Low-dose TPA is an option, that is effective and safe. In general, an infusion at 0.5 mg/kg/day is given, because at higher doses the risk of complications increases.[6] In our case, we used Alteplase in the usual dose of 0.5 mg/kg/day, and there were no major complications due to the therapy.

CONCLUSION

SVC syndrome is attached to many causes, one being Protein S and C deficiency. However, it can be successfully managed. The reported case suggests that TPA therapy may be an efficient and safe therapeutic regimen in children with severe SVC syndrome, leading to anatomic and clinical restoration of the SVC flow.

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REFERENCES

1. Young G, Albisetti M, Bonduel M, Leonardo B, Chan A, Friedrichs F, et al. Impact of inherited thrombophilia on venous thromboembolism in children: a systematic review and meta-analysis of observational studies. Circulation. 2008;118(13):1373-82.
2. Scott JP, Raffini LJ, Montgomery RR. Hemostasis. Elsevier. 2011.
3. Parish JM, Marschke RF, Dines DE, Lee RE. Etiologic considerations in superior vena cava syndrome. Mayo Clin Proc. 1981;56:407-13.
4. Alexander HR. Vascular access and other specialized tech Nique's of drug delivery. In: De Vita VE, Hellman S, Rosenberg S, editors. Cancer: principles and practice of oncology. Philadelphia: Lippincott, Williams and Wilkins. 1993;556-64.
5. Tan H, Kizilkaya M, Alper F, Becit N, Kürşat H. Thrombolytic therapy with tissue plasminogen activator for superior vena cava thrombosis in an infant with sepsis. Acta Paediatr. 2005;94(2):239-41.
6. Morales M, Comas V, Trujillo M, Dorta J. Treatment of catheter-induced thrombotic superior vena cava syndrome: a single institution's experience. Support Care Cancer. 2000;8:334-8.

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