Case Report

Staphylococcus aureus septicemia presenting as disseminated intravascular coagulation - thrombotic thrombocytopenic purpura overlap and thrombus in inferior vena cava, right atrium and right ventricle: a case report

Khwaja Saifullah Zafar*, P. S. Singh, Pulak Raj

Department of Medicine, UPRIMS & R, Saifai, Etawah, Uttar Pradesh, India

ABSTRACT

Staphylococcal sepsis following furunculosis and complicated by suspected deep vein thrombosis and septic inferior vena caval, right atrium, right ventricle emboli accompanied by disseminated intravascular coagulation (DIC) - thrombotic thrombocytopenic overlap in a 65 years old lady is presented. She was managed successfully with antibiotics and anticoagulation. The case is reported for its rarity and brings to light the vivid manifestations of septicemia specially staphylococcal.

Keywords: Disseminated intravascular coagulation (DIC), Staph aureus, Septicemia, Thrombotic thrombocytopenic purpura, Thrombus

INTRODUCTION

Both community-associated and hospital-acquired infection with Staph aureus have increased in the past 20 years. Manifestations of staphylococcal infections usually depend on the type of infection the organism causes. Common types of infections include the following: skin infections(e.g., folliculitis, furuncles, impetigo, wound infections, scalded skin syndrome), soft tissue infections, toxic shock syndrome, purpura fulminans, endocarditis, osteomyelitis, pneumonia, food poisoning, infections related to prosthetic devices and urinary tract infection.

Disseminated Intravascular Coagulation (DIC) is characterized by systemic activation of blood coagulation, which results in generation and deposition of fibrin, leading to microvascular thrombi in various organs and contributing to Multiple Organ Dysfunction Syndrome (MODS).[1]

DIC is estimated to be present in about 1% of hospitalized patients[2] DIC is not itself a specific illness; rather, it is always secondary to an underlying disorder and is associated with a number of clinical conditions, generally involving activation of systemic inflammation and among the list, sepsis and severe infection is of paramount importance.[3] DIC is most commonly observed in severe sepsis and septic shock. Indeed, the development and severity of DIC correlate with mortality in severe sepsis.[4,5]

Venous thrombosis in the lower limb can involve the superficial leg veins, the deep veins of the calf (calf vein thrombosis), the more proximal veins, including popliteal veins, the superficial femoral, common femoral, and iliac veins. Most calf vein thrombi are asymptomatic,[6] but these thrombi can extend proximally and become dangerous. Extension of thrombosis is more likely if the original thrombogenic stimulus persists. Complete spontaneous lysis of large venous thrombi is uncommon,

and even when patients with venous thrombosis are treated with heparin, complete lysis occurs in fewer than 10% of cases.[7] Venous thrombi usually organize slowly and can be complicated by the post-thrombotic syndrome.[8] The residual abnormality can also act as a nidus for recurrent thrombosis.[9]

CASE REPORT

A previously well 65-year-old woman was admitted with 8 weeks of increasing exertional dyspnoea, orthopnoea and leg swelling progressing to generalized anasarca. She had purpura on the right arm, soft palate and tongue. Her pulse was 66 beats per minute, regular without radio-radial and radio-femoral delay and blood pressure was 100/58 mmHg. No history of fever, hemoptysis and chest pain. Raised venous pressure and marked oedema of both legs was noticed. The heart sounds were normal without any murmurs, but there were reduced breath sounds at the left lung base. Tender hepatomegaly and free fluid on abdominal examination was found. Blood tests showed hypoxia, leukocytosis, thrombocytopenia and the features of DIC. Peripheral blood smear shows fragmented RBCs and schistocytes. D-Dimer quantitative assay was strongly positive with value of 3.46 FEU/Ml (Bio. Ref. interval <0.50), Fibrin Degradation Products (FDP) was less than 11 μg/ml (5-10 positive).Renal function test and liver function tests were deranged (Table 1). Urine routine examination and microscopy was normal. Blood culture showed growth of staphylococcus sensitive to linezolid. Total serum protein, albumin and globulin were in normal range. Thyroid function test and fasting lipid profiles were normal. Widal test and microscopy for malarial parasites were negative. Viral markers for HBsAg, HCV and HIV were negative. PT/INR was repeatedly normal. She had a normal sinus rythm, prolonged PR interval, low voltage complexes and right ventricular hypertrophy on ECG. There was cardiomegaly and mediastinal widening on chest X-ray. Spiral CECT thorax showed moderate pericardial effusion, mild right sided and mild to moderate left sided pleural effusion with underlying atelectasis, lobulated thrombus in right suprahepatic, IVC (inferior vena cava),right atrium and right ventricles. USG revealed bilateral pleural effusion and minimal ascites and hepatosplenomegaly without mesenteric lymphadenopathy. Color Doppler of the veins and arteries of lower limb showed reduced flow in femoral and dorsalis pedis arteries and non-compressibility of veins suggestive of deep vein thrombosis. Diagnostic pericardiocentesis findings were unremarkable. Echocardiographic findings were as following: slightly thickened pericardium, mild to moderate pericardial effusion, IVC normal in size and has normal inspiratory collapse, no regional wall motion abnormality, LVEF=50-55%, normal cardiac chamber internal dimensions, normal valvular structure, grade 1 diastolic dysfunction and no intracardiac clot/vegetation seen.

The clinical diagnosis was heart failure with DIC complicated by thrombus in IVC, right atrium and right ventricle and deep vein thrombosis. Septicaemia was a possibility and a septic screen was positive for staphylococcus. She was treated with intravenous diuretics and antibiotics, LMWH (low molecular weight heparin) and was put on tablet warfarin overlapping heparin. By day 7, her clinical state and coagulopathy improved remarkably. Ultrasound studies showed evidence of deep vein thrombosis. She improved slowly and was discharged 5 weeks later. 3 months later, she was well. Her chest X-ray had returned to normal but her ECG remained unchanged. Echocardiography was normal in follow ups.

Table 1: Clinical and biochemical profile of the patient.

Day	BP (mm of Hg)	Hb (gm%)	Total leucocyte count/cumm	Blood urea (mg/dl)	S. creatinine (mg/dl)	Liver function test	INR
1	102/52	13.5	23400	96	2.1	Total bilirubin 4.2 mg/dl, SGOT-94 IU/L, SGPT-158 IU/L	1.38
4	100/60	12.6	22700	127	3.2	Total bilirubin 5.9 mg/dl, SGOT-98 IU/L, SGPT-108 IU/L	1.1
8	86/60	12.8	17000	146	2.6	Total bilirubin 7.2 mg/dl, SGOT-104 IU/L, SGPT-102 IU/L	1.7
15	90/62	14.3	14500	132	2.2	Total bilirubin 6.3 mg/dl, SGOT-101 IU/L, SGPT-158 IU/L	2.1
30	108/62	10.2	10300	62	1.1	Total bilirubin 2.5 mg/dl, SGOT-53 IU/L, SGPT-48 IU/L	1.6

INR-International normalized ratio, SGPT-Serum glutamic pyruvic transaminase, SGOT-Serum glutamic oxaloacetic transaminase
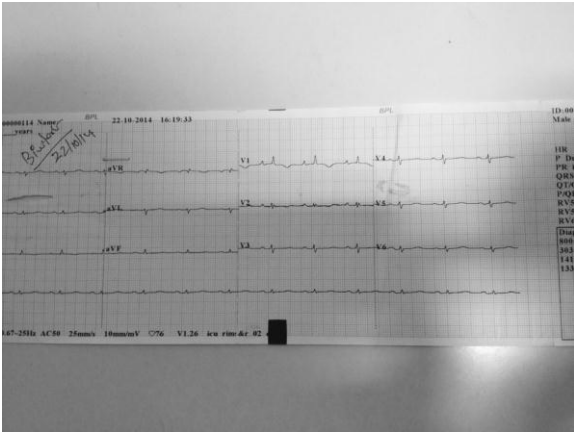
Figure 1: ECG showing low voltage complexes, normal sinus rhythm, PR interval of 0.20 ms and RVH (right ventricular hypertrophy).

Figure 2: CXR-PA view showing cardiomegaly, left sided pleural effusion and upper paratracheal lymph node with prominent bronchovascular markings.

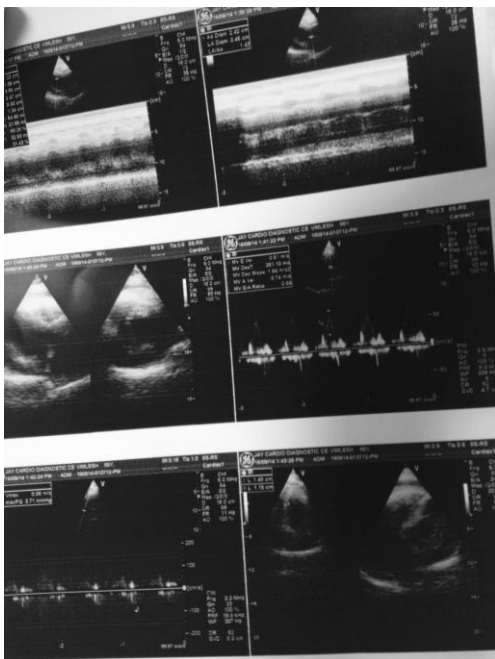
Figure 3: 2D transthoracic echo showing moderate pericardial effusion and no intracardiac clots/vegetations.
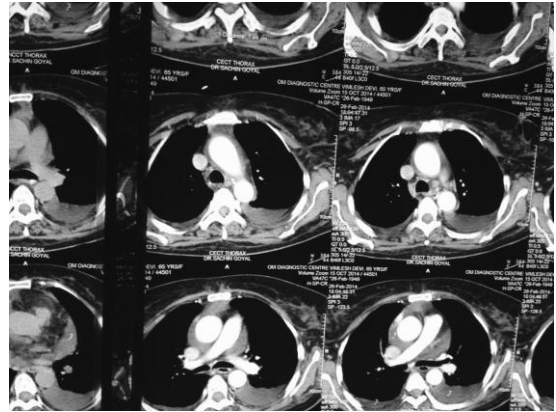

Figure 4: Spiral CECT thorax showed moderate pericardial effusion, mild right sided and mild to moderate left sided pleural effusion with underlying atelectasis, lobulated thrombus in right suprahepatic, IVC (inferior vena cava), right atrium and right ventricles. A left upper paratracheal node is seen measuring 14 mms.

DISCUSSION

This case illustrates a number of unusual clinical features. Right atrial thrombus is uncommon and there is few previous example of it occurring in the presence of DIC. Most reported cases of right atrial thrombi are detected at autopsy. The development of right atrial thrombus may be the consequence of local endothelial damage, the presence of atrial fibrillation or foreign bodies in the right atrium, situations associated with reduced cardiac output, or as a result of embolism from a peripheral venous thrombosis.[10] Our case had reduced flow in peripheral arteries of lower limb and features of deep vein thrombosis. In addition D-Dimer and FDP was significantly raised confirming DIC and accompanying systemic thrombosis. Right atrial thrombi can vary in their clinical presentation. They may be suspected because of difficulty with infusion or withdrawal of blood from a central venous catheter, or because of superior vena cava syndrome, a pulmonary embolism, tricuspid insufficiency, right-sided heart failure, sudden onset of a cardiac murmur, or syncopal episodes.[11-14] The only clinical sign of a thrombotic infection is often fever or sepsis of unknown origin.[15] As in right-sided endocarditis related to the presence of a central venous catheter, the most frequently encountered pathogens in central venous or right atrial septic thrombosis are Staphylococcus and Candida species.[12,16] Similarly in our patients' blood culture was positive for Staphylococcus. In the presence of low cardiac output, the co-existence of DIC, inspite of its auto-anticoagulation, may have the paradoxical effect of enhancing thrombus formation. Thrombus formation in heart failure may also be enhanced by activation of platelets and the coagulation system[17] related to elevation of tumour necrosis factor.[18] Yet right atrial thrombi are rarely reported in spite of many patients having heart failure and a low cardiac

output state. It may be that low cardiac output is insufficient in its own right to result in thrombus formation unless there is a co-existing thrombogenic process. Treatment options for right atrial thrombi include heparin, thrombolytic agents or surgery. The outcomes of these options are similar.[19] Our patient had the pentad of fever, thrombocytopenia, purpura, azotemia, deranged liver function tests and transient neurocognitive impairment thus confirming Thrombotic thrombocytopenic purpura compounded by systemic thrombosis. In most cases involving an infected right atrial thrombus, aggressive treatment is mandatory. Staphylococcus aureus septicemia has been associated with DVT,[20-22] the maximum risk seems to be with osteomyelitis.[22] Staphylococci release alpha toxin and coagulase; the former leads to platelet aggregation and spasm of smooth muscle while the latter promotes clot formation due to interaction with fibrinogen. In some patients, an acute infection related prothrombotic state[20] was evident in the form of antiphospholipid antibodies and elevated factor VIII levels which did not persist on follow up. However, this is not the case in all patients,[21] same to the present patient. Patients with infected DVT can have disseminated staphylococcal infection because DVT acts as a source of septic thromboemboli.[22] This possibility is supported by increased rate of dissemination of thromboemboli to lungs, brain and heart. An ongoing showering of septic emboli to the lungs from the ileo-femoral DVT might have caused the rapid clinical deterioration observed in the patient. In a clinical series, 19% of patients with invasive community acquired Staphylococcus aureus infections and abnormal pulmonary findings had septic pulmonary emboli.[23] Diagnosis of SPE in the present case was based on characteristic CT finding as mentioned previously.[24] Our patient required immediate intervention because of her compromised hemodynamic status. In summary, this is the rarest of rare report of inferior vena caval & right atrial and ventricular thrombus caused by staphylococcal septicemia associated with heart failure and thrombocytopenic thrombotic purpura - DIC overlap, and additionally managed conservatively with a short course of heparin. The formation of right atrial thrombus in situ is likely to be multifactorial.

CONCLUSIONS

Deep vein thrombosis and septic inferior vena caval emboli, right atrial/ventricular thrombus is a life threatening condition resulting from seemingly innocuous folliculitis caused by staphylococcal infection compounded by DIC/TTP. Prompt recognition and institution of antibiotics and anticoagulation could be lifesaving.

ACKNOWLEDGEMENTS

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