Phlegmasia cerulean dolens: complication of femoral vein catheterization

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Abstract There are three less frequent manifestations of acute massive venous thrombosis and obstruction of the venous drainage of an extremity. They are phlegmasia alba dolens, phlegmasia cerulean dolens (PCD), and venous gangrene. The term PCD differentiates ischemia-associated massive venous thrombosis from phlegmasia alba dolens, which describes fulminant venous thrombosis without ischemia. We present a 55-year-old hypertensive, who presented with pedal oedema and breathlessness at rest. About a month prior to this admission, she suffered dislocation of left patella. She was treated with a plaster cast and immobilization for 3 weeks. Her serum creatinine was 8.8 mg/dL. She was initiated on haemodialysis via two single-lumen catheters placed in left femoral vein. The femoral vein catheters were removed after third session of haemodialysis. On fourth day, the patient complained pain and blue discolouration of left toes. On examination, the left lower limb was swollen, discoloured, and cold with blebs up to upper one-third of left leg. The left dorsalis pedis and posterior tibial arteries were not palpable. A Doppler of veins of lower limb revealed, thrombosis of deep, and superficial venous system of left lower limb. As there was no response to anticoagulation below, knee amputation was performed.

Keywords Phlegmasia cerulean dolens · Femoral vein · Seldinger technique · Heparin · Fondaparinux

Introduction

There are three less frequent manifestations of acute massive venous thrombosis and obstruction of the venous drainage of an extremity. They are phlegmasia alba dolens, phlegmasia cerulean dolens (PCD), and venous gangrene. The term PCD differentiates ischemia-associated massive venous thrombosis from phlegmasia alba dolens, which describes fulminant venous thrombosis without ischemia [1]. The main causative factor in phlegmasia is massive thrombosis and occlusion of major venous channels with significantly compromised venous outflow. In PCD, the thrombosis extends to collateral veins, resulting in venous congestion with massive fluid sequestration and more significant oedema. Of PCD patients, 40–60 % also has capillary involvement, which results in irreversible venous gangrene that involves the skin, subcutaneous tissue, or muscle [2].

In these circumstances, the hydrostatic pressure in arterial and venous capillaries exceeds the oncotic pressure, causing fluid sequestration in the interstitium. Venous pressure may increase to 16-fold to 17-fold within 6 h [3]. Fluid sequestration may reach 6–10 L in the affected extremity within days [4]. Circulatory shock, which is present in about one-third of patients, and arterial insufficiency, may evolve.

Case report

A 55-year-old lady, non-diabetic, hypertensive for the past 15 years has presented with pedal oedema and breathlessness at rest (New York Heart Association Functional Classification Class IV). There was no history of oliguria, dysuria, and haematuria. She had no complaints of chest

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pain, palpitation, and syncope. About a month prior to this admission, she fell down and was diagnosed dislocation of left patella. She was treated with a plaster cast and immobilization for 3 weeks. Blood pressure was 180/100 mmHg. Pulse was 90 bpm. She had crackles in bilateral infrascapular, interscapular, and infraaxillary areas. There was left ventricular third heart sound. Investigations revealed serum creatinine 8.8 mg/dL, blood urea 150 mg/dL, serum sodium 138 mEq/L, serum potassium 6.5 mEq/L, haemoglobin 8.5 g/dL, platelet count 1.8 lakhs per mm^3 , serum bicarbonate 9.4 mmol/L, and on ultrasound abdomen: right kidney 7.8×3.5 cm, left kidney 8.0×3.8 cm. She was diagnosed chronic kidney disease stage 5 probably secondary-to-hypertension. It is our institute's protocol to initiate haemodialysis through femoral veins in all patients. She was initiated on haemodialysis via two single-lumen catheters (14 GA and 13.3 cm, Shinecath, St. Stone Medical Devices Pvt. Ltd., India) placed in left femoral vein. The catheters were placed using the Seldinger technique. After three sessions of haemodialysis of 1-, 2-, and 3-h duration on three consecutive days, an untunnelled internal jugular catheter was placed on right side. The first of these haemodialysis was without anticoagulation. It was to avoid bleeding if the femoral artery was accidentally hit during the procedure of femoral vein cannulation. The remaining two sessions were with tight heparin prescription. The femoral vein catheters were removed after the third session of haemodialysis. On fourth day, the patient complained pain and blue discoloration of left toes. On examination, the left lower limb was swollen, discoloured, and cold up to ankle joint. The left dorsalis pedis and posterior tibial arteries were not palpable. Within next 12 h, the signs extended to upper one-third of left leg and there were blebs (Fig. 1). A Doppler of veins of lower limb revealed, thrombosis of left common, external iliac, femoral, popliteal, anterior, and posterior tibial veins. There was thrombosis of superficial venous system of left lower limb. The arterial system of the left lower limb did not show arterio-occlusive disease. The D-dimer was high. It was 2.5 $\mu\text{g/mL}$ (reference range

Fig. 1 Left leg, cyanosed with blebs

0.5 $\mu\text{g/mL}$) (Fig. 2). Patient did not complain pleuritic chest pain, new onset breathlessness, or haemoptysis. An echocardiography did not reveal right ventricular enlargement or right ventricular dysfunction. Table 1 shows all investigations. Elevation of the left lower limb was done.

Fig. 2 Investigations

Table 1 Investigations

Parameter	Day 0	Day 4	Day 5	Day 8	Day 11	Day 15
Serum creatinine (mg/dL)	8.8	6.5	6.4	6.7	6.8	6.5
Haemoglobin (g/dL)	8.5	8.1	8.0	7.5	7.8	7.0
Platelet count (lakhs per mm ³)	1.8	1.65	1.64	0.25	0.23	0.48
Prothrombin time (s)	15.2	13.9	13.8	15.2	120	124
INR	1.3	1.19	1.1	1.4	2.5	2.6
aPTT (s)	34.8	34.8	35	44	40.3	41
D-dimer (μg/mL)			2.5	2.7		

Patient had 3 of 6 “Ps” associated with compartment syndrome—pain out of proportion to the physical findings, paresthesia, pallor, paralysis, pulselessness, and poikilothermia. The fasciotomy of multiple compartments was done. She was initiated on unfractionated heparin and antibiotics. Heparin was given as an initial bolus of 80 U/kg, followed by a maintenance infusion of 18 U/kg per hour until aPTT was 1.5 times the normal. On the third day of treatment with heparin, the platelet count reduced to 25,000 per mm³. It was replaced with fondaparinux (7.5 mg subcutaneous once daily). The treatment with fondaparinux was overlapped with acitrom (acencoumarol) 2 mg per day. The dose was modified to maintain international normalized ratio at 2.5. On third day after initiation of therapy, there was hypotension. She required inotropes. A team of cardiologists and cardiovascular surgeons opined that she might not be fit for inferior vena cava filter placement and surgical thrombectomy owing to hypotension. After 2 weeks of treatment, there was partial recanalization of left common, external iliac, and femoral veins, but the swelling of muscle and pain in left leg have worsened. The number of blebs increased and limb became cold and blue. Below knee, amputation of left lower limb was performed. It is our institute’s protocol to encourage patients for the peritoneal dialysis. During second week, a Tenckhoff peritoneal dialysis catheter was placed, and she was initiated on the peritoneal dialysis after 10 days. Patient was discharged after 4 weeks. At discharge, there was partial recanalization of left common, external iliac, and femoral veins.

Discussion

The aetiology of PCD and venous gangrene include malignancy, in 20–40 % of patients and primary hypercoagulable state, such as deficiencies of antithrombin III, proteins C or S, or plasminogen. Lupus anticoagulant maybe detected. It may also occur following surgery or after trauma and postpartum. Prolonged immobility is a precipitating factor. It has been reported in patients with ulcerative colitis, pneumonitis and gastroenteritis, severe

mitral stenosis with heart failure, after insertion of a vena cava filter, and following intravenous drug abuse. In approximately 10 % of patients, no cause is found [5]. In this patient, investigations revealed no hypercoagulable state, and lupus anticoagulant was absent.

The highest incidence is between fifth and sixth decades of age, and women are more affected than men. Left lower limb is more affected than right because of overlying of right iliac artery on left iliac vein. Swelling, pain, and cyanosis are the triad of clinical features that characterize PCD. Swelling develops rapidly. It is tense, firm, and massive. It may cause formation of cutaneous blebs and bullae. It may extend onto abdomen. Pain affects whole limb, constant feature, bursting quality, and difficult to treat. Cyanosis spreads from distal to proximal involving whole limb [5, 6].

Heparin helps in preventing proximal propagation of thrombosis. Heparin may act as a hapten, and thus be targeted by the immune system. In type 2, heparin-induced thrombocytopenia (HIT), the immune system forms antibodies against heparin when it is bound to a protein called platelet factor 4 (PF4). These antibodies are usually of the IgG class and their development usually takes about 5 days. Unlike other forms of thrombocytopenia, HIT is generally not marked by bleeding; instead, venous thromboembolism and arterial thrombosis may occur. In our patient, the thrombosis of left lower limb veins was diagnosed before the initiation of heparin. Fondaparinux is used to anti-coagulate patients with established HIT, as it has no affinity to PF-4 [7]. We have not contemplated to use novel oral anticoagulants, dabigatran (direct thrombin inhibitors), and apixaban and rivaroxaban (factor Xa inhibitors) for these drugs were not approved for patients in stage 5 chronic kidney disease [8].

The options to treat the thrombosis include thrombolysis and surgical thrombectomy. Catheter-directed thrombolysis directly injects high doses of urokinase or tissue plasminogen activator (t-PA) into the vein. Intra-arterial low-dose thrombolysis via the common femoral artery may also be tried. The reasoning is that the arterial route delivers the thrombolytic agent to the arterial capillaries and subsequently to the venules. The intra-arterial approach seems to

be more effective in the cases with venous gangrene. Systemic thrombolysis has also been used [6]. Surgical thrombectomy performed through a femoral venotomy allows instant decompression of the venous hypertension. The high rates of rethrombosis are common. As in surgical thrombectomy or catheter-directed deep venous thrombolysis, there is a risk of pulmonary embolism; an inferior vena cava filter placement provides effective prophylaxis for embolism. Currently, thrombolysis and thrombectomy are generally reserved for treatment following the failure of anticoagulation or impending venous gangrene. The mortality rate of PCD is between 20 and 40 % [5]. Pulmonary embolism is responsible for 30 % of the deaths reported from PCD. Overall, amputation rates of 12–50 % have been reported among survivors [6].

PCD and venous gangrene are rare conditions. Nephrologists encounter them only a few times in a career. In our patient, the effect of immobilization appears to be compounded by the femoral vein catheterization resulting in PCD. The major pitfall in our management of this patient was failure to perform a Doppler of left lower limb venous system prior to left femoral vein catheter placement when there was history of immobilization of lower limb.

Compliance with ethical standards

Conflict of interest None.

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