PHLEGMASIA CERULEA DOLENCE- RISK FACTORS AND PREVENTION. /CASE REPORT/

Ludmil M. Veltchev[1], Manol A. Kalniev[2], Todor A. Todorov[3],
1 Fellow, Master's Program in Hepatobiliary Pancreatic Surgery, Henri Bismuth Hepatobiliary Institute, 12-14, avenue Paul Vaillant-Couturier, 94804 Villejuif Cedex
2 Department of Anatomy, Cytology and Histology, University of Medicine, Sofia, Bulgaria
3 Department of Pathology, University of Medicine, Sofia, Bulgaria

ABSTRACT

Phlegmasia cerulean dolens is a severe form of deep venous thrombosis characterized by severe venous outflow obstruction, marked limb swelling, pain, bluish discoloration, and even venous gangrene, if the condition is untreated. Etiological factors include malignancy, femoral vein catheterization, heparin-induced thrombocytopenia, anti-phospholipid syndrome, surgery, heart failure, and pregnancy.

In our case, 71 year-old woman, with twenty three years treated diabetes mellitus was accepted for GI imaging study for suspicions of neoplastic process of stomach. On the third day she complained of edema, agonizing pain and cyanosis, many blisters and starting necrosis on the dorsal and lateral surface of right ankle, progressively extended to distal one third of leg. Anticoagulation with intravenous administration of heparin, and fluid resuscitation started immediately.

Key words: venous thrombosis, venous gangrene, anticoagulation, amputation,

INTRODUCTION

More than 600,000 cases of venous thromboembolism are estimated to occur each year in the United States. Pulmonary embolism (PE) complicates approximately 50% of cases of untreated proximal deep venous thrombosis (DVT) and contributes to 10-15% of all hospital deaths. Less frequent manifestations of venous thrombosis include phlegmasia alba dolens, phlegmasia cerulea dolens (PCD), and venous gangrene. All three manifestations result from acute massive venous thrombosis and obstruction of the venous drainage of an extremity. All may occur at any age, but are more common during the fifth and sixth decades of life. Incidence is higher in females than in males. In the 16th century, Fabricius Hildanus first described the clinical syndrome of what is currently called PCD. In 1938, Gregoire made an outstanding description of the condition and used the term PCD to differentiate ischemia-associated massive venous thrombosis from phlegmasia alba dolens, which describes fulminant venous thrombosis without ischemia**.** [1] The exact incidence of these disorders is not well reported. The main causative factor in phlegmasia is massive thrombosis and occlusion of major venous channels with significantly compromised venous outflow. Multiple triggering factors exist. Malignancy is the most common triggering factor and is present in approximately 20-40% of patients with PCD. Other associated risk factors include hypercoagulable syndrome, surgery, trauma, ulcerative colitis, gastroenteritis, heart failure, mitral valve stenosis, vena caval filter insertion, and May-Thurner syndrome (compression of the left iliac vein by the right iliac artery). Pregnancy has often been associated with phlegmasia alba dolens, especially during the third trimester when the uterus is large enough to compress the left common iliac vein against the pelvic rim (i.e., milk leg syndrome). Finally, 10% of patients with phlegmasia have no apparent risk factors. In PCD, the thrombosis extends to collateral veins, resulting in venous congestions with massive fluid sequestration and more significant edema. Without established gangrene, these phases are reversible if proper measures are taken. Of PCD cases, 40-60% also has capillary involvement, which results in irreversible venous gangrene that involves the skin, subcutaneous tissue, or muscle.[2] Under these conditions, the hydrostatic pressure in arterial and venous capillaries exceeds the oncotic pressure, causing fluid sequestration in the interstitium. Venous pressure may increase rapidly, as much as 16- to 17-fold within 6 hours. Fluid sequestration may reach 6-10 L in the affected extremity within days. Circulatory shock, which is present in about one third of patients, and arterial insufficiency, may ensue. In the lower extremities, left-sided involvement is more common by a 3:1 or 4:1 ratio. Involvement of upper extremities occurs in less than 5% of patients with PCD. Manifestations may be gradual or fulminant.

CASE PRESENTATION

A 71-year-old woman was admitted at university hospital for the first time with epigastric pain, nausea , vomiting and anemia syndrome for the last 6 months. Treated at home ferrous medications. Diabetus mellitus was diagnosed and treated with medications from 20 years. On the physical examination middle grade pain at epigastrium and marked edema of lower limbs. Laboratory test showed Hb -82 g/L, Er-2.73, Hct-0.25. Imaging investigations found small gastric polyp without any malignant process confirmed with endoscopic biopsy. On the fifth day of the stay the patient presented cutaneous reactions with rash and itching affected all the skin. 24 hours later she was suddenly onset of sever pain, swelling and cyanosis of right leg. On physical examination patient was found to be shocked, blood pressure was lowest 100/60 mmHg, high pulse rate-112 beats per minutes. A local status showed bluish discoloration of the dorsal and medial surface of the right ankle, and progressively involvement of distal one third of the leg, which become swollen and cyanotic up to the knee. **(Fig.1a, b)** Distal part of leg was cold and pulseless.The femoral pulse was palpable with normal intensity and coolness, but more distant pulse was not felt.

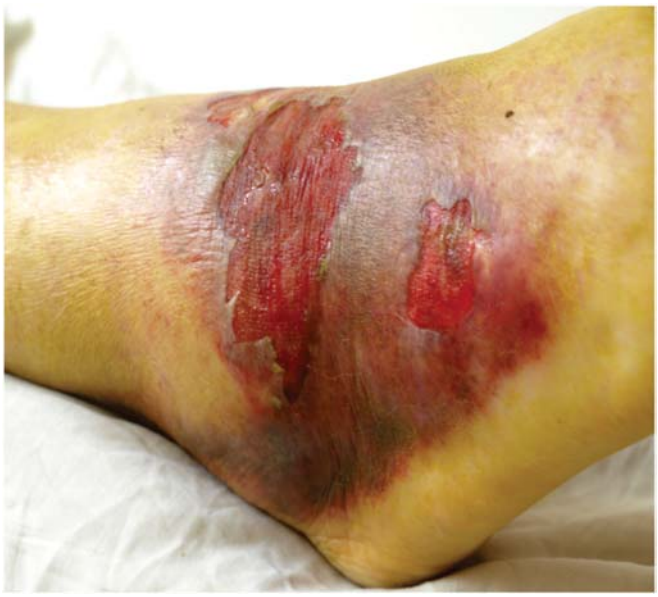

Fig. 1 a

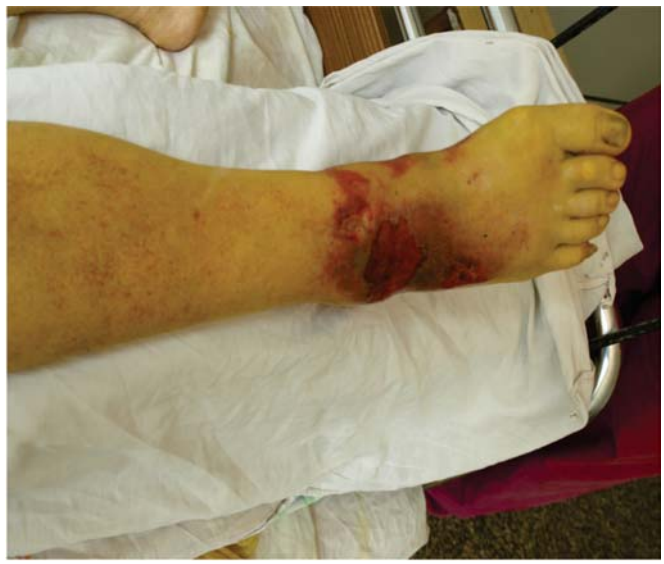

Fig. 1 b

Fig. 1 a, b Case of phlegmasia cerulean dolens of the lower limb

A diagnosis of phlegmasia cerulean dolens was suspected: severe form of deep venous thrombosis which results from extensive thrombotic occlusion of the major and the collateral veins of leg.

Anticoagulation with heparin was initiated: an intravenous bolus of 100 U/kg, followed by a continuous 24 hours infusion of 18 U/h/day with daily monitoring of the activated partial thromboplastin time (aPTT), with a goal range of 2 times the laboratory reference range. Frequently monitor platelet counts to allow the early detection of heparin-induced thrombocytopenia, but there was progressive swelling and cyanosis of the leg. We performed fasciotomy and necrectomy of the superficial tissues. Six days after starting heparin therapy a fall of thrombocyte count was found (16 x 10^{9}/L) and heparin induced thrombocytopenia was suspected. Low molecular weight heparins such as Clexan (Enoxaparine) at doses 1 mg/kg/day in 2 time replaced standard heparin. Despite continued intravenous anticoagulation the clinical findings progressed to venous gangrene and amputation of lower limb was performed. Postoperatively patient was placed on Clexan 0.3 ml sc. At the eight postoperative day patient started rehabilitation program.

DISCUSSION:

Phlegmasia dolens is a rare form of massive venous thrombosis of the lower extremities that is associated with a high degree of morbidity, including venous gangrene, compartment type syndrome, and arterial compromise. [3] The development of a standard treatment for phlegmasia cerulea dolens is ongoing. Intervention is usually required in order to prevent gangrene.[4] For phlegmasia alba dolens and mild nongangrenous forms of phlegmasia cerulea dolens (PCD), conservative medical treatment, such as steep limb elevation, anticoagulation with intravenous administration of heparin, and fluid resuscitation, should be the initial course of therapy.[5] The purpose of rapid heparin anticoagulation is to decrease the risk of proximal clot

propagation or thromboembolism. Heparin does not directly affect limb swelling. The best nonsurgical method to decrease edema is steep leg elevation. Thrombolysis seems to be another attractive alternative in the management of PCD and venous gangrene. In 1970, Paquet was the first to use thrombolysis for the treatment of PDC.[6] Some authors propose catheter-directed thrombolysis directly into the vein with high doses of urokinase or tissue plasminogen activator (t-PA). Other authors support the method of intra-arterial low-dose thrombolysis via the common femoral artery, reasoning 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 cases with venous gangrene. Systemic thrombolysis has also been used.[7]

Surgical thrombectomy performed through a femoral venotomy allows instant decompression of the venous hypertension.

Fasciotomy alone or in conjunction with thrombectomy, or thrombolysis reduces compartmental pressures; however, it significantly increases morbidity because of the prolonged wound healing and the risk of infection.

Concomitant administration of heparin and long-term anticoagulation are mandatory. Regardless, thrombectomy in patients with PCD is associated with a high rate of rethrombosis. Surgical thrombectomy cannot open the small venules that are affected in venous gangrene, and it does not prevent valvular incompetence or postphlebitic syndrome. The incidence of postphlebitic syndrome may be as high as 94% among survivors.

SUMMARY

Phlegmasia cerulea dolens (blue, painful leg) is an uncommon manifestation of deep-vein thrombosis and results from massive thrombosis compromising venous outflow, which causes ischemia. Despite all of the therapeutic modalities described above, phlegmasia cerulea dolens and venous gangrene still remain life-threatening and limb-threatening conditions with overall mortality rates of 20-40%. Pulmonary embolism is responsible for 30% of the deaths reported from PCD. Overall, amputation rates of 12-50% have been reported among survivors.

REFERENCES:

1. Gregoire R. La Phlebite bleue (Phlegmasia Cerulea Dolens). 1938; 48: 1313-15.

2. Lorimer J.W., Semelhago L.C., Barber GG.Venous gangrene of the extremities.Can J Surg. 1994 Oct; 37(5): 379-84. Review.

3. Sarwar S., Narra S., Munir A. Phlegmasia cerulea dolens. Tex Heart Inst J. 2009; 36(1):76-7.

4. Chaer R.A., Dayal R., Lin S.C., Trocciola S., Morrissey N.J., McKinsey J., et al. Multimodal therapy for acute and chronic venous thrombotic and occlusive disease. Vasc Endovascular Surg 2005; 39(5): 375–80

5. Weaver F.A., Meacham P.W., Adkins R.B., Dean R.H. Phlegmasia cerulea dolens: therapeutic considerations. South Med J. 1988 Mar;81(3):306-12. .

6. Paquet K.J., Popov S., Egli H. [Guidelines and results of consequent fibrinolytic therapy in phlegmasia cerulea dolens]. Dtsch Med Wochenschr. Apr 17 1970;95(16):903-4

7. Bird R.L., Hamilton G. Treatment options for phlegmasia cerulea dolens. J Vasc Surg. 1995 Jun; 21(6):998-9.

Corresponding author:
Ludmil Marinov Veltchev, MD PhD
Mobile: +359 876 259 685
E-mail: drlmarinov@yahoo.com