

A rare clinical form of deep vein thrombosis: Phlegmasia alba dolens

Derin ven trombozunun nadir bir klinik formu: Phlegmasia alba dolens

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ABSTRACT

Venous thromboembolism is a frequently seen clinical condition among hematological diseases which may result in death, and it is associated with various risk factors. The most frequent clinical forms of venous thromboembolism are deep vein thrombosis of the lower extremities and pulmonary embolism. Phlegmasia dolens is a rare clinical condition caused by acute deep vein thrombosis which may present in three different clinical forms as phlegmasia alba dolens, phlegmasia cerulea dolens, and venous gangrene. Herein, we report a 66-year-old male patient who was admitted to the emergency department with the complaints of pain, swelling, bullous eruptions, and lividity on his left limb in the previous two days. A thrombus was detected in his common femoral vein with color Doppler ultrasonography. However, it was supposed to be phlegmasia alba dolens, which is a rare form of acute deep vein thrombosis, due to the absence of arterial occlusion. In conclusion, phlegmasia alba dolens, is a rare clinical condition which must be kept in mind by clinicians.

Keywords: Anticoagulant therapy; phlegmasia alba dolens; venous thrombosis.

ÖZ

Venöz tromboemboli; ölümlle sonuçlanabilen, hematolojik hastalıklar arasında sık görülen klinik bir durum olup, çeşitli risk faktörleri ile ilişkilidir. Venöz tromboembolinin en sık görülen klinik formları alt ekstremitelerde derin ven trombozu ve pulmoner embolidir. Phlegmasia dolens, akut derin ven trombozunun neden olduğu nadir bir klinik durum olup, phlegmasia alba dolens, phlegmasia cerulea dolens ve venöz gangren şeklinde üç farklı klinik formda seyredebilir. Bu yazıda, son iki gündür sol bacakta ağrı, şişlik, büllöz döküntü ve morarma şikayetleri ile acil servise başvuran 66 yaşında bir erkek olgu sunuldu. Renkli Doppler ultrasonografide ana femoral vende trombus saptandı. Ancak, arteriyel tıkanıklık olmadığı için akut derin ven trombozunun nadir bir klinik formu olan phlegmasia alba dolens olarak değerlendirildi. Phlegmasia alba dolens, klinisyenler tarafından akıldaki tutulması gereken nadir bir klinik durumdur.

Anahtar sözcükler: Antikoagülan tedavi; phlegmasia alba dolens; venöz tromboz.

Deep vein thrombosis (DVT) is an important cause of mortality and morbidity. In elderly, it has an incidence as high as 1% in the developed countries.^[1] Deep vein thrombosis most frequently arises from the lower extremity and pelvic veins.^[1] Less frequent clinical forms of venous thrombosis are phlegmasia alba dolens, phlegmasia cerulea dolens, and venous gangrene. All those three conditions are caused by acute massive venous thrombosis and obstruction of the venous drainage of the extremity.^[2]

Phlegmasia alba dolens is a condition characterized by limb swelling (edema), tenderness, pain, lividity, and bullous lesions followed by whitening of the limb due to venous stasis caused by femoral vein thrombosis. The collateral vessels are either not affected or affected less extensively than phlegmasia cerulea dolens. Although problematic, the venous return can be partially established. Diagnosis can only be made based on the clinical status of the patient. If the diagnosis is uncertain, Doppler ultrasonography (USG) is as a rapid,

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Figure 1. An image of bullae formations on the left lower extremity.

inexpensive, and non-invasive method for the definite diagnosis. Rapid diagnosis and immediate initiation of treatment are extremely important for preventing amputation, pulmonary embolism, and particularly phlegmasia cerulea dolens and venous gangrene, which have a higher incidence of mortality.^[3,4]

A number of triggering factors play a role in the etiology of phlegmasia dolens. The most common factor is malignancy which is present in 20-40% of patients.^[4] Other risk factors for phlegmasia dolens include immobility, heart failure, venous instrumentation (i.e., placement of central venous catheters and inferior vena cava filters), heparin-induced thrombocytopenia, prothrombin states (i.e., antiphospholipid syndrome), pregnancy, and surgery.^[5]

Subtotal thrombotic venous occlusion called as phlegmasia alba dolens is a milder form of phlegmasia cerulea dolens, and it is characterized by the preservation of the collateral venous system and a whitish rather than cyanotic discoloration in the extremities. Collateral venous systems remain patent; therefore, phlegmasia alba dolens rarely results in death and amputation.^[6] Capillary involvement which results in irreversible venous gangrene involving the skin, subcutaneous tissue, and/or muscle is seen in 40-60% of phlegmasia alba dolens cases.^[7]

Herein, we present a case of phlegmasia alba dolens, which is a rare clinical form of DVT.

CASE REPORT

A 66-year-old male patient was admitted to the emergency department with pain, swelling, bullous eruptions, and lividity on his left foot, extending up to the groin in the previous two days. A thrombus

was detected in the left common femoral vein with color Doppler USG, and the patient was admitted to the intensive care unit for the treatment. A written informed consent was obtained from the patient.

The patient had a history of diabetes mellitus, hypertension, and smoking. There was no history of trauma, fever, cough, dyspnea, or loss of weight or appetite. He had a history of diabetes mellitus, hypertension, and smoking. On arrival, his arterial blood gas analysis and 12-lead electrocardiogram

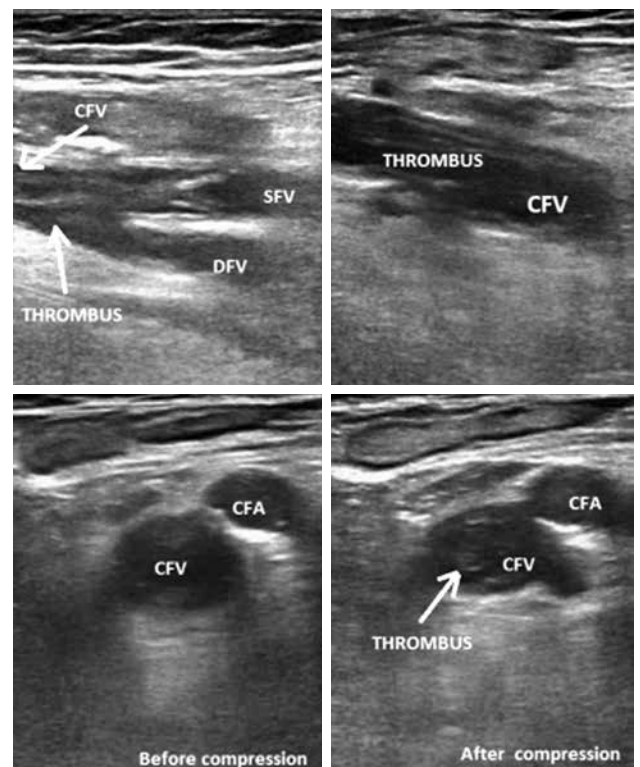


Figure 2. Thrombus in the common femoral vein on venous color Doppler ultrasonography. CFV: Common femoral vein; SFV: Superficial femoral vein; DFV: Deep femoral vein; CFA: Common femoral artery.

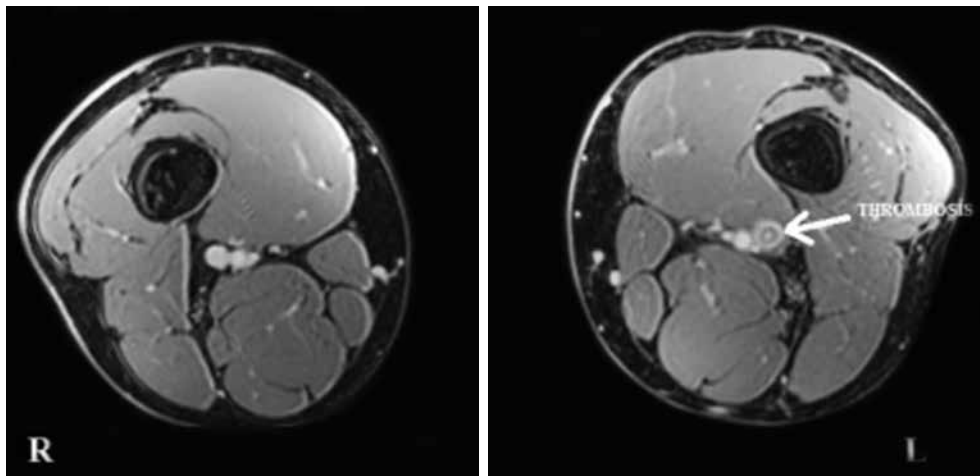


Figure 3. Thrombus in the left femoral vein on magnetic resonance imaging.

findings were normal. His blood pressure was 140/90 mmHg, pulse rate was 80 bpm, respiratory rate was 16 breaths per min, and axillary temperature was 37.8°C. On his physical examination, swelling of the left limb from the foot to the groin, tenderness, lividity, and multiple bullous lesions with diameters of 1 to 3 cm were evident (Figure 1). The Homans' sign was positive on the left side. Left femoral, popliteal, and dorsalis pedis and tibialis anterior arterial pulses were weak on palpation. The examination findings of other systems were normal. The international normalized ratio was 1.1 (reference: 0.8-1.2). Other laboratory findings were as follows: leucocyte count 22,800/mm³, platelets 234,000/mm³, hematocrit 45.6%, hemoglobin 14.9 mg/dL, glucose 443 mg/dL, total cholesterol 130 mg/dL, triglyceride 152 mg/dL, high-density lipoprotein (HDL)-cholesterol 36 mg/dL, low-density lipoprotein (LDL)-cholesterol 80 mg/dL, lipoprotein (a) 28.3 mg/dL (normal range: <30 mg/dL); C-reactive protein 74.3 mg/dL (normal range: 0-0.8 mg/dL), homocystein 7.46 μmol/L (normal range: <15 μmol/L), serum fibrinogen 255 mg/dL (normal range: 200-400 mg/dL), anti-cardiolipin antibodies immunoglobulin (Ig)G 5.7 GPL/mL (normal range: <23) and IgM 4.8 GPL/L (normal range: <11), protein C 77% (normal range: 70-130%), protein S 80% (normal range: 65-130%), factor V 92% (normal range: 70-120%), antithrombin III 110% (normal range: 75-125%), and D-dimer 80 ng/dL (normal range: <500 ng/dL). The tumor marker levels were as follows: alpha fetoprotein 1.37 ng/dL (normal range: <9), CA-125 18.5 U/mL (normal range: <35), CA-15-3 2.3 U/mL (normal range: <30), CA-19-9

8.94 U/mL (normal range: <37), carcinoembryonic antigen 2.23 ng/mL (normal range: <5), and prostate-specific antigen 3.7 ng/dL (normal range: <4.5). All other tests including complete blood count, electrolytes, renal and hepatic functions were in normal limits. Anteroposterior chest X-ray, abdominal USG, and echocardiography were normal.

On venous color Doppler USG, there was an image resembling a hypoechoic thrombus which allowed a very low flow in the lumens of left common, superficial and deep femoral, and popliteal veins (Figure 2). The patient with the clinical presentation of phlegmasia cerulea dolens (there was cyanosis on the left limb initially) was diagnosed with phlegmasia alba dolens, since the arterial color Doppler USG performed later revealed no arterial occlusion. There was a filling defect on magnetic resonance imaging (MRI),



Figure 4. Healing bullous lesions on the left lower extremity on Day 10 of anticoagulant treatment.

the lumen of the left femoral vein was completely obliterated, and this appearance was suggestive of a thrombus (Figure 3). The patient was administered intravenous heparin with a bolus dose of 5,000 IU initially, followed by an infusion of 1,000 IU per hour. Activated partial thromboplastin time was checked every six hours within the first 24 hours of therapy, and it was adjusted to stay 1.5 to 2.5 times of the normal value. Oral anticoagulant (warfarin) was started on the second day of therapy with a dose of 5 mg per day. As recommended by the dermatology clinic, topical antibiotherapy was administered for the skin lesions of phlegmasia alba dolens. The left limb was elevated. No complications related to heparin treatment were seen. The blood platelet count was followed closely. Heparin was discontinued on the fourth day of treatment, since edema, swelling, and skin lesions began to resolve. The patient was taken to the ward following adjustment of the warfarin dose. On the ninth day of oral anticoagulation therapy, limb discoloration and bullous skin lesions completely resolved. His skin lesions completely resolved without conversion to phlegmasia cerulea dolens or venous gangrene (Figure 4), and he was discharged on the 14th day of treatment with warfarin.

DISCUSSION

Deep vein thrombosis is frequently defined as the obstruction of venous blood flow caused by a thrombus in the deep lower extremity veins. Although there have been improvements in the medical and surgical treatment of DVT in recent years, DVT is still a serious problem causing pulmonary embolism, venous gangrene, chronic venous insufficiency, and post-thrombotic syndrome.^[8]

Phlegmasia dolens is a rare clinic condition of massive venous thrombosis of the lower extremities. It may present in three different clinic forms as phlegmasia alba dolens, phlegmasia cerulea dolens, and venous gangrene. Each of them may cause morbidity. Phlegmasia dolens may occur at any age; however, it is seen more frequent in the fifth and sixth decades of life.^[5,6] It is also more common in females.^[5,6] As in our case, it was reported that left limb involvement was more frequent.^[2,9,10]

Phlegmasia alba dolens is characterized by massive thrombosis of deep and superficial venous systems of the extremity involved; however, there is no obstruction in the venous collateral vessels.

Therefore, extremity amputation and mortality are rare. In addition, complications such as venous gangrene, arterial occlusion, and hypovolemic shock may occur in phlegmasia cerulea dolens, since venous collaterals are also obstructed.^[9]

Signs of phlegmasia dolens may emerge slowly or fast. Arterial pulses are usually absent or very weak. Symptoms of phlegmasia alba dolens include severe pain, pallor, and edema. Cyanosis is less frequent. On the other hand, pain, cyanosis, and motor and sensory deficits are noticeable in phlegmasia cerulea dolens. Bullae filled with serous fluid in the affected lower extremity within a few days may be seen in both clinical situations. The pallor (whitening) in the lower extremity affected by phlegmasia alba dolens was initially thought to be caused by arterial vasospasm; however, it was shown later that subcutaneous edema without venous congestion was the reason. If treatment is not started early, phlegmasia alba dolens rapidly progresses to phlegmasia cerulea dolens and venous gangrene, which have worse prognoses.^[6] Venous gangrene following the development of ischemic obstruction has been reported in 40-60% of phlegmasia dolens cases.^[7] Similarly, there were multiple bullous lesions in the various sizes on the popliteal, medial infrapopliteal and anterior sides of the left limb as well as total cyanosis in our case. In addition, there was no venous gangrene or compartment syndrome in the left limb at the time of admission; however, the pulses on the left leg were weak.

The etiological factors in phlegmasia dolens include coagulation disorders, Factor V Leiden mutation, G20210A prothrombin gene mutation, Protein C, S, and antithrombin deficiencies, cancer, use of oral contraceptives, trauma, surgical interventions, hypercoagulability syndrome, heart failure, immobility, heparin-induced thrombocytopenia, pregnancy, antiphospholipid syndrome, catheter placement into the femoral vein, mitral stenosis, ulcerative colitis, gastroenteritis, placement of vena cava filters, May-Turner syndrome (obstruction of the left iliac vein by the right iliac artery and the vertebral body at the back). No etiological factors may be found in 10% of the patients with phlegmasia dolens.^[3,8,11] Similarly, no etiological factors can be detected in the laboratory investigations or physical examination in our case.

Diagnosis of phlegmasia dolens is made clinically. However, the diagnosis should be confirmed by venous system Doppler USG. Intense thrombus is

visualized in the deep and superficial venous system of the affected extremity by Doppler USG. Inability of the vein lumen to be compressed is pathognomonic for venous thrombus.^[4] However, if the extent of thrombus is to be determined, computed tomographic angiography and magnetic resonance venography may be used.^[3] In our case, the diagnosis was based on clinical presentation, venous color Doppler USG and MRI.

Although randomized trials and guidelines for treatment are not clearly documented, treatment options for DVT include conservative management with systemic heparin or low-molecular-weight heparin versus more invasive treatment with systemic or local thrombolysis, percutaneous thrombosuction or other thrombus removal techniques, percutaneous transluminal angioplasty with or without stenting, surgical thrombectomy with or without fasciotomy, or a combination of these. Recently, conservative therapy such as limb elevation, administration of intravenous heparin, thrombolytics and fluid replacement are suggested as the initial therapy for phlegmasia alba dolens and mild forms of phlegmasia cerulea dolens without gangrene. If the anticoagulant therapy fails, percutaneous intervention or surgical thrombectomy is advised.^[12] In the present case, limb elevation, fluid replacement, heparin infusion, and oral anticoagulants were used for the treatment. Percutaneous intervention or surgical thrombectomy were considered unnecessary, since there were no compartment syndrome or venous gangrene at the time of admission.

In conclusion, phlegmasia cerulea dolens and phlegmasia alba dolens are rare clinical conditions with a poor prognosis due to high morbidity and mortality rates, if the diagnosis of DVT cannot be made early. Rapid diagnosis and immediate initiation of treatment are of utmost importance to prevent gangrene, amputation, pulmonary embolism, and death. Although the primary treatment rationally should be aimed at prohibiting further thrombus formation by the use of heparin or low-molecular-weight heparin, in case of arterial insufficiency and venous gangrene, thrombolysis or even mechanical thrombus removal may be needed; however, optimal treatment strategy is well-established.

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