

Phlegmasia Cerulea Dolens of the Upper Extremity: A Fatal Complication after Coronary Artery Bypass Grafting- Case Report and Review of the Literature

J. Vahedian MD and A. Sadeghpour MD

Abstract

Phlegmasia cerulea dolens (PCD) is the term describing the painful venous congestion that results from near-total venous occlusion of a limb. Acute symptomatic upper extremity deep vein thrombosis (DVT) is estimated to account for only 2-4% of all DVTs. Upper extremity DVT leading to PCD occurs in an estimated 2-5% of these cases. Progression of PCD to venous gangrene is extremely rare with only a handful of cases reported in the literature. Only a few of the cited cases document significant tissue loss. This report describes a 56-year-old female who developed upper extremity DVT complicated by PCD, which led to venous gangrene and hemorrhagic cerebral stroke and death two weeks after coronary artery bypass graft (CABG) (*Iranian Heart Journal 2007; 8 (4): 63-68*).

Key words: upper extremity ■ deep vein thrombosis ■ phlegmasia cerulea dolens ■ venous gangrene ■ CABG ■ subclavian vein thrombosis

Upper extremity deep vein thrombosis (DVT) was postulated by Paget in 1875 as a cause of arm edema in two cases and termed gouty phlebitis. Nine years later, Von Schroeder independently reported a similar case. The term Paget-Schroeder syndrome was introduced by Hughes in 1949 in a report tabulating 320 such cases.¹⁻³ Upper extremity DVT accounts for 1-2% of all venous thrombosis.⁴⁻⁶ Effort thrombosis accounts for only a minority of upper extremity DVTs.⁷ Factors which predispose to DVT include immobility, cardiac disease, hypercoagulable states, a history of DVT, malignancy, estrogen use, orthopedic procedures, and with increasing frequency, the use of central venous catheters.

A grave complication of DVT is phlegmasia cerulea dolens (PCD), which may lead to venous gangrene and limb loss and even death. PCD is estimated to complicate lower extremity DVT in 2-10% of cases, but is seldom associated with upper extremity DVT.⁷⁻¹⁰

PCD is characterized by the classic triad of cyanosis, edema and pain. This report describes a 56-year-old female who developed upper extremity DVT complicated by PCD, which led to venous gangrene and hemorrhagic cerebral stroke and death two weeks after coronary artery bypass graft surgery (CABG).

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From the Dept. of Cardiovascular Surgery, Shaheed Rajaei Cardiovascular Medical Center, Mellat Park, Vali Asr Ave, Tehran, Iran.

Correspondence to: J. Vahedian MD, Dept. of Cardiovascular Surgery, Shaheed Rajaei Cardiovascular Medical Center, Mellat Park, Vali Asr Ave, Tehran, Iran
Tel: 02123922589

Case Report

A 56-year-old right handed female underwent uncomplicated coronary artery bypass grafting (CABG), utilizing the left internal mammary artery, left radial artery, and greater saphenous vein for conduits. The patient was discharged on postoperative day six on clopidogrel 75mg three times daily as an antiplatelet regimen. At the time of operation, a central venous catheter placed through the right internal jugular vein and right radial artery line was utilized for hemodynamic monitoring.

She was readmitted after 10 days following a three-day history of left upper extremity pain and swelling and cyanosis. The patient had no history of DVT.

Physical examination at time of admission was significant for severe left upper extremity edema with cyanotic discoloration. Axillary, brachial, and ulnar artery pulses were palpable normally. Arterial Doppler wave forms were triphasic at the left brachial and ulnar arteries. Color flow venous duplex examination showed acute thrombus in the left brachial, basilic, and cephalic veins extending into the axillary vein. The affected limb was elevated and intravenous heparin was initiated with a bolus of 10,000 units followed by an infusion of 1000 units/hr. The patient's platelet count on admission was 158,000/mm²; and 118,000/mm² and 120,000/mm² on the following two days, respectively. Fibrinolytic therapy was contraindicated due to the history of cardiac surgery. On hospital day two, the patient's limb had become more edematous, painful and cyanotic. On hospital day three, a left forearm compartment syndrome was clinically apparent as the patient had further deterioration in her sensation and motor examination and decreasing ulnar artery pulse. Compartment pressures were not directly measured because of her anticoagulated state. Heparin was held, and left forearm fasciotomies were performed (Figs. 1, 2). Following fasciotomies, the patient's hand improved slightly with

decreased edema, increased sensation and improved color. On hospital day four, the patient became unconscious and developed right-sided paraplegia. Brain CT scan revealed a hemorrhagic area in the left cortex (Fig. 2). The patient's condition deteriorated and she died on hospital day six due to intracranial hemorrhage. Her affected extremity was gangrenous.



Fig. 1.



Fig. 2.

Discussion

The prevalence of upper extremity DVT is rare. As was mentioned earlier, it accounts for 1-2% of all venous thromboses.⁴⁻⁶ As the use of central venous lines and pacemaker wires has increased, their role in the etiology of upper extremity DVT has become prominent.¹¹⁻¹⁴ Mustafa in a retrospective study in a community teaching hospital reported 60% prevalence of central venous access lines in the upper extremity DVT patients.⁹ Recognized causes of upper extremity DVT include surgery, trauma, childbirth, hypercoagulable states, malignancy, heart disease, infection, prolonged immobility, infusion of hypertonic solutions, septic phlebitis, anatomic abnormalities, a previous history of DVT, estrogen use and central venous access

catheters.¹⁵⁻¹⁸ In one analysis of 58 patients with upper extremity DVT, a defined hypercoagulable state, a previous history of lower extremity DVT or venous access was associated ($p<0.05$) with the development of upper extremity DVT.¹⁹ Other reviews estimated 29-30% of upper extremity DVT to be secondary to central venous access catheters.^{16,17} The risk of thrombosis increases with the length of time the catheter is left in place and does not appear to be related to the material of the catheter.⁷ Upper extremity DVT in the past had been considered to be benign and self-limited. More recent data have suggested that this is not the case.¹⁹⁻²¹ The literature shows a 7-9% incidence of symptomatic pulmonary embolism in patients with upper extremity DVT.^{20, 22, 23} Upper extremity DVT often presents as unilateral upper extremity swelling, especially of the forearm, with or without distended superficial veins.^{7, 24, 25} There does not appear to be any gender or right/left predisposition.^{15, 26} A high index of suspicion should be maintained if any of the predisposing causes are suggested by history or physical finding. Evaluation for suspected upper extremity DVT includes contrast venography, duplex ultrasonography (DUS), computed tomography (CT), and magnetic resonance imaging (MRI). The best screening test is DUS. It offers a noninvasive modality with high specificity and sensitivity. One review found the sensitivity of DUS to be as high as 100% and the specificity to be at 93% when compared with contrast venography.¹⁹ The main disadvantage of DUS is technician dependency. CT can detect subclavian vein thrombus but has not been sufficiently studied. MRI is very specific but has a low sensitivity (80% for complete occlusion and 0% for partially occluded thrombus) and therefore is not a reliable screening examination.²⁷ Magnetic resonance venography (MRV) has the potential to be used as a stand-alone test for DVT but requires further evaluation.²⁸ Venography is very sensitive and specific but remains

invasive and is associated with more significant costs.

PCD causes a clinical triad of pain, edema and cyanosis. Pulses may not be palpable if there is sufficient edema. Normal arterial signals may be obtained by DUS in the early stages of the syndrome.²⁶ PCD is estimated to complicate lower extremity DVT in 2-10% of cases¹⁵ and is seldom found in upper extremity DVT. In fact, only 2-5% of upper extremity DVT is estimated to progress to PCD and ultimately less than 1% to venous gangrene.^{7,15} In distinction to lower extremity DVT, upper extremity DVT is thought to begin centrally and propagate distally. Prior to the onset of irreversible ischemic changes, the extremity may become cyanotic, with subsequent bullae formation. The skin and subcutaneous tissue is preferentially involved and later followed by myonecrosis and neuritis.²⁶ The extent of tissue loss below the epidermis is notably less in patients with venous gangrene compared to those with acute arterial occlusion associated with comparable skin changes.

The differences between uncomplicated upper extremity DVT and PCD must be clear in order to understand the disease processes and the need for rapid intervention. Thrombus of upper extremity DVT is usually proximally located, and forearm compartment pressures are estimated to be 15-30 mmHg. PCD is rare and is the result of DVT progression. It is associated with extensive thrombosis and severely increased compartment pressures (50-60 mmHg). Additionally, shock, venous gangrene, amputation and even death may ensue.²⁹ Review of the 16 reported cases of upper extremity DVT leading to PCD showed that 38% were associated with hematological abnormalities (HIT, cryoglobulinemia, DIC, and polycythemia vera) and 62% of these patients developed upper extremity DVT during a severe systemic illness. Finally, 50% of patients with upper extremity DVT complicated by PCD progressed to venous gangrene with tissue loss.²⁶

Management of uncomplicated upper extremity DVT is usually non-operative and includes anticoagulation and extremity elevation. Management of upper extremity DVT complicated by PCD is less well standardized and includes anticoagulation with elevation, fibrinolytics, thrombectomy, correction of a predisposing anatomic defect, fasciotomy, SVC filter placement and amputation. Documented experience using these modalities is extremely limited with this rare clinical entity. Definitive conclusions regarding the relative merits of each intervention cannot be made. Anticoagulation and extremity elevation is often efficacious. In 1982, non-operative therapy was decided as the first line of treatment for PCDs. Patel and Paidas concluded that non-operative therapy appears to be effective in preventing limb loss and avoiding the risks of thrombectomy and thrombolysis in critically ill patients.²⁹ If thrombectomy is utilized, it should be attempted within 5 days of PCD and prior to diffuse small venule thrombosis.⁸ Once venous gangrene is present, the complication rates associated with treatment regimens of anticoagulation alone or combined with thrombectomy dramatically increase.³⁰ It has been speculated that fibrinolytics may be more effective in upper extremity DVT versus lower extremity DVT, possibly because there are more venous collaterals in the shoulder and a smaller volume of thrombus.¹⁵ Fasciotomy should be performed when compartment pressures exceed 30 mmHg. In summary, treatment guidelines are controversial due to the rarity of this entity and resultant lack of substantial outcome data.

The risk of pulmonary emboli in patients with upper extremity DVT is reported to be 19-36%.^{19,23,24,26,27} Anticoagulation with heparin is thought to maintain venous collaterals and decrease thrombus propagation. Duration of anticoagulation is not well defined. Some authors suggest 3-6 months. One retrospective review of 95 patients found that there were decreased long-term sequelae if patients were

anticoagulated for more than 3 months. In this study, late morbidity was associated with 40% of patients who had upper extremity DVT. These late sequelae include swelling and fatigue of the extremity, pain, SVC syndromes, loss of central venous access, venous gangrene, limb loss, pulmonary emboli, and death.⁷

Conclusions

No large studies regarding outcomes of upper extremity DVT complicated by PCD have been reported due to the rarity of this clinical syndrome. Yet, some general treatment guidelines can be summarized. Extremity elevation and heparinization, once upper extremity DVT is confirmed, are necessary. A thorough search for either an anatomic abnormality or a hypercoagulable state should be commenced following diagnosis. Pharmacologic and/or operative intervention should be accompanied by careful clinical monitoring. Early fasciotomy must be performed if PCD is complicated by compartment syndrome to limit myonecrosis. Warfarin therapy should be continued for at least 3-6 months. Diagnosis can be straightforward but must be made early in the course of the process for treatment to be effective. Treatment has historically produced only modest results, and patients continue to suffer a high morbidity and mortality. PCD represents a devastating complication of upper extremity DVT. Early, aggressive restoration of adequate cardiac output and thrombectomy and/or thrombolytic therapy, if no contraindication exists, may provide the best chance for tissue salvage and survival in this group of patients.

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