Simultaneous Arterial and Venous Ultrasound-Assisted Thrombolysis for Phlegmasia Cerulea Dolens

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Phlegmasia cerulea dolens is a rare condition in which an extensive deep venous thrombus can partially or completely occlude venous outflow from the affected extremity. Clinical presentation is typically characterized by extremity edema, cyanosis, and pain. This condition is associated with a high rate of extremity amputation and mortality. Although numerous therapies have been described, there is no generalized treatment consensus and less invasive forms of therapy continue to evolve. We report a case of phlegmasia cerulea dolens in a patient who presented with concomitant arterial and venous thrombosis of the affected extremity. The patient’s condition was successfully treated using combined ultrasound-assisted intra-arterial and intravenous catheter-directed thrombolysis.

CASE REPORT

A 69-year-old woman with a medical history significant for coronary artery disease with coronary artery bypass grafting, congestive heart failure, chronic kidney disease, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, and Parkinson’s dementia presented with an acutely ischemic and edematous left leg to a referring institution. The patient had no history of lower extremity arterial occlusive symptoms or venous disease. Ultrasound of the left lower extremity demonstrated arterial and venous thrombosis. The patient was started on intravenous heparin and transferred to our institution. On arrival, physical examination was significant for a markedly cyanotic, edematous left lower extremity with absent distal arterial signals (Fig. 1A).

The patient was emergently taken to the interventional suite and percutaneous access was first obtained from the right common femoral artery. A 6-F sheath was placed and angiography revealed normal bilateral external/internal iliac arteries, left common femoral artery, and left profunda femoris. The left superficial femoral artery (SFA) occluded (Fig. 2B) with reconstitution of the below-the-knee popliteal artery and a single vessel runoff through the anterior tibial artery to the level of the foot. After the thrombotic occlusion in the SFA was traversed, we substituted the existing Quick-Cross...
(Spectranetics Corporation, Colorado Springs, CO) catheter for a 40-cm EKOS (EKOS Corporation, Bothell, WA) infusion catheter and initiated alteplase (Genentech Inc, South San Francisco, CA) infusion at a rate of 0.5 mg/hr through this catheter. The patient was then placed prone and ultrasound-guided access of the popliteal vein was obtained. A 6-F sheath was placed in this vessel and a venogram demonstrated total occlusion of the popliteal, femoral, and iliac veins (Fig. 2D). A 50-cm EKOS infusion catheter was then advanced from the popliteal vein into the proximal inferior vena cava and alteplase was infused at a rate of 0.5 mg/hr for a total of 1.0 mg/hr through both arterial and venous catheters.

Heparin was continued at 250 U/hr through both of the 6-F sheaths (500 U/hr total).

After approximately 24 hours of thrombolytic therapy, the patient demonstrated a significant clinical improvement in the discoloration of her left lower extremity. At this time, the patient’s fibrinogen level acutely dropped to <60 mg/dL; therefore, thrombolytic therapy was discontinued and she returned to the interventional suite. Repeat imaging demonstrated complete thrombus resolution within the left SFA and popliteal arteries with single vessel runoff to the anterior tibial artery. Some irregularity was appreciated at the level of the proximal SFA and this was successfully balloon-angioplastied with no residual

**Fig. 1.** Lower extremities (A) at time of presentation, (B) 2 days postintervention, and (C) 7 days postintervention.

**Fig. 2.** Thrombolytic therapy. (A) Arterial and venous catheters. Superficial femoral artery (B) before and (C) after ultrasound-assisted thrombolytic therapy and balloon angioplasty. Superficial femoral vein (D) before and (E) after ultrasound-assisted thrombolytic therapy.
stenosis (Fig. 2C). The right common femoral artery puncture site was then closed using a Perclose ProGlide device (Abbott Laboratories, Redwood City, CA). Venogram through the proximal venous sheath demonstrated thrombus resolution up to the external iliac vein but persistent occlusion of the left common iliac vein (Fig. 3B). Percutaneous mechanical thrombectomy was then performed with the use of the AngioJet Ultra DVX Thrombectomy System (Medrad International/POSSIS, Minneapolis, MN) to remove the residual thrombus. The culprit lesion in the left common iliac vein was then treated with balloon angioplasty and deployment of a 14 × 60 mm self-expandable S.M.A.R.T. Control stent (Cordis Endovascular, Miami Lakes, FL; Fig. 3A, B).

The patient was closely monitored in the intensive care unit with frequent lower extremity neurovascular assessments, and compression stockings were initiated on postoperative day 4. A hypercoagulable workup initiated at the time of presentation was negative, and there was no evidence of underlying malignancy on subsequent computed tomographic imaging. By postintervention day 7, the patient’s lower extremity symptoms had completely resolved (Fig. 1C). The patient was transitioned over to oral warfarin therapy when clinically stable with plans for lifelong anticoagulation.

**DISCUSSION**

Extremity gangrene secondary to a venous etiology was first described by Hildanus in the 16th century and the term PCD was first used by Gregoire in 1938. PCD is the result of extensive iliofemoral DVT which causes partial or complete venous outflow occlusion. In severe cases, this venous occlusion is complete resulting in compromised arterial inflow and ischemia leading to venous gangrene. The mechanism of arterial ischemia is believed to be secondary to the collapse of small arteries as a consequence of increased interstitial tissue pressure from tissue edema. The disease is recognized clinically with a classic triad of swelling, cyanosis, and severe pain in the affected extremities. PCD has a gender predilection of 4:3, with women being more affected than men, the left leg more often affected than the right, and is more commonly seen in the elderly population and in hypercoagulable states such as malignancy, and the postpartum or postoperative period. Alternatively, if no obvious cause is found, a thorough workup should be done to evaluate for an intrinsic hypercoagulable disorder. In our patient, the etiology for the DVT seemed to be secondary to May-Thurner syndrome, as was observed on our completion venogram (Fig. 3A), in addition to her relative immobility caused by mild dementia. The extent of the DVT, and resulting increased venous and tissue pressures, may further have contributed to the arterial occlusion because the patient had previous records documenting a palpable dorsalis pedis pulse before this limb-threatening event.

Treatment of PCD is initially aimed at clot stabilization followed by definitive treatment with clot removal. Many therapeutic modalities have been described with no generalized consensus. Systemic approaches with heparin, vasodilators, sympatholytics, sympathectomy, dextran, and thrombolytic therapy have been used.
Additionally, surgical interventions have included vein ligation, open surgical thrombectomy, reconstruction of flow by creation of arteriovenous fistulas, fasciotomy, and amputation. Modern endovascular techniques use catheter-directed thrombolysis to accelerate clot and symptom resolution. Additional adjunctive procedures often incorporated to rapidly decrease the clot burden include ultrasound-assisted thrombolysis and percutaneous mechanical thrombectomy. In our case, we used both ultrasound-assisted thrombolysis and percutaneous mechanical thrombectomy to facilitate clot breakdown/removal to minimize the patient’s limb ischemia time. We elected not to use percutaneous mechanical thrombectomy as an initial mode of therapy because of concern about the patient’s presenting renal dysfunction and the risk of complete renal failure associated with hemoglobinuria.

Previous endovascular reports and techniques described in the previously published data have largely focused on catheter-directed infusion of thrombolitics to the venous system. Wlodarczyk et al. reported success with performing intra-arterial infusion thrombolysis on a limited case series of patients presenting with PCD. Although all patients in this reported series had favorable outcomes, it is unknown whether this approach has any clinical advantages over a more conventional intravenous approach. Our report constitutes the first use of a combination of ultrasound-assisted intra-arterial and intravenous catheter-directed thrombolysis for concomitant arterial and venous thrombosis in a patient presenting with PCD. In patients with complex thrombotic presentations and no contraindication to thrombolytic therapy, this approach may be favorable in facilitating rapid thrombosis resolution.

REFERENCES