CASE REPORT

Pharmaco-mechanical Thrombectomy for Recurrent and Multiple Deep Vein Thrombosis in Puerperium

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INTRODUCTION

Pregnancy is a prothrombotic condition. Increased viscosity of blood, prolonged venous stasis and vascular endothelial damage all predispose to venous thrombosis.[1] Women with protein C and protein S deficiency, factor V Leiden, Lupus anticoagulant, anticardiolipin antibodies and β_2-glycoprotein increase the risk of thrombosis. The more proximal the DVT, the greater are the symptoms.[2] Iliofemoral DVT is an under diagnosed condition with a high morbidity and a not inconsiderable risk of amputation. Affected patients may present with a phlegmasia cerulean dolens (PCD) which heralds impending gangrene. Subsequently we have described a case of recurrent multiple postpartum deep vein thrombosis managed by pharmaco-mechanical thrombectomy.

CASE REPORT

A 28 years old primigravid attended our institution as an emergency at 30 weeks gestation by her dates with reduced fetal movements. She was unbooked but had been seen by her general practitioner in another country where she was commenced on antihypertensive medication (alpha-methyldopa 250 mg bd) at 24 weeks gestation. On arrival at the hospital she complained of vaginal discharge for one day and reduced fetal movements for three days.

In her clinical history she reported prior treatment in her native country with steroids for Systemic Lupus Erythematosis. She informed the team that she was A Rh-positive and had no significant surgical, family or personal history of concern. On arrival her blood pressure was normal. There was no proteinuria on dipstick examination. She denied headache, blurring of vision or epigastric pain. The fundal height measured 26 cm. Ultrasound examination suggested an Intrauterine Fetal Demise and induction of labor was planned for the next day.

The next day she was induced with misoprostol and subsequently delivered a still born male infant weighing 900 gm with an intact perineum. The placenta on gross examination was unhealthy and malodorous. A placental swab was taken and the placenta was sent for histopathology. Postdelivery the alpha-melthyldopa was withdrawn as the patient was normotensive. Day 2 postdelivery, the patient was discharged home on oral coamoxyclav.

Four days postdelivery, the patient was referred back to the hospital by a public health nurse as the patient was complaining of chills, a generalized body ache and had an elevated temperature of 38.4°C. On admission she was started on intravenous flucloxacillin and metronidazole as the placental swab had grown *Staphylococcus aureus* which was sensitive to flucloxacillin. Six days after the delivery the antibiotic regime was changed to coamoxyclav in view of continuing pyrexia. The following day her left leg appeared mottled on clinical examination and her left calf was found to be 2.5 cm greater in diameter than her right calf. The clinical diagnosis of deep vein thrombosis was suggested and tinzaparin sodium was commenced at the dose of 175 IU/kg.

Day 9 postdelivery the blood cultures were found to have no growth but the patient's pyrexia was now 38.8°C. An ultrasound doppler of the left lower suggested there was no acute deep vein thrombosis in the left lower limb and hence the tinzaparin sodium dose was changed from the therapeutic dose to the prophylactic dose 3500 IU s/c OD. The patient continued to be pyrexial and was subsequently commenced on intravenous Cefotaxime and Metronidazole after consulting the microbiologist. Thirteen days postdelivery the patient complained of left hip and groin pain and was recommenced on a therapeutic dose of tinzaparin sodium. After three days of therapy the left thigh measured 56 cm with the right thigh

measuring 48 cm in circumference. A venogram of the left leg veins was subsequently performed which revealed an abrupt termination of the left common femoral vein with opacification in the mid thigh with extensive collateralization. No proximal flow in the left common femoral or left iliac vein was identified. A diagnosis of left common iliac vein, external iliac vein, common femoral vein and sapheno-femoral vein thrombosis was made. Figures 1 and 2 illustrate the absence of flow in the left femoral vein and sapheno-femoral vein respectively.

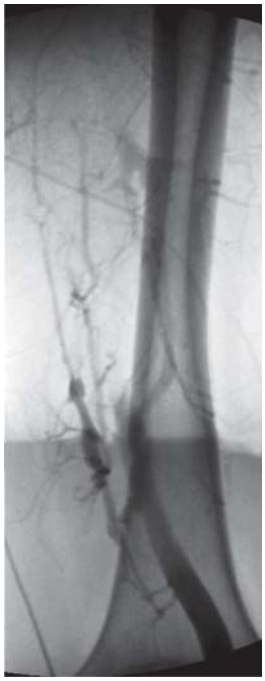

Fig. 1: Left femoral vein thrombosis

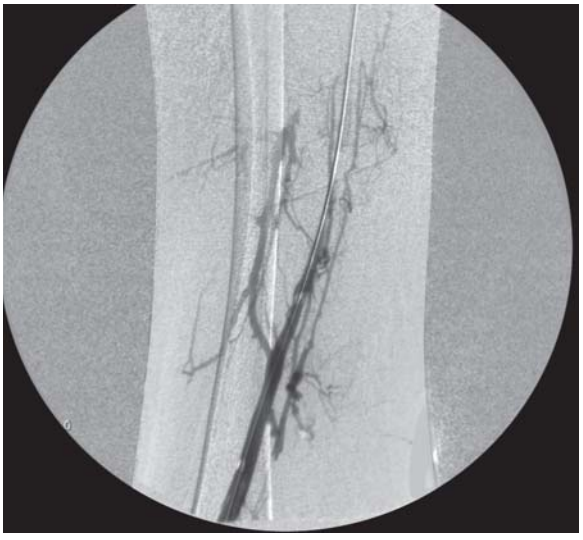

Fig. 2: No flow seen in the left sapheno-femoral vein

A pharmaco-mechanical thrombectomy was contemplated whereby a mixture of the thrombolytic agent, Tissue Plasminogen Activator (tPA), blending device, and a suction device is used to chemically destroy, physically macerate the thrombus followed by aspiration the clot. There is minimal systemic passage of tPA and hence essentially no increased risk of hemorrhage. The ipsilateral popliteal vein was punctured under ultrasound guidance and venography was performed. The thrombosed segment was identified and the Bacchus Trellis® device was utilized to isolate the treatment area by inflating balloons on either side of the clot. Three milligrams of Tissue Plasminogen Activator was added to 6 ml of normal saline. The wire was then oscillated at the rate of 4000 rpm for a period of 5 minutes. The clot was then aspirated as depicted in Figure 3. A balloon angioplasty was performed and a self expanding stent was inserted.

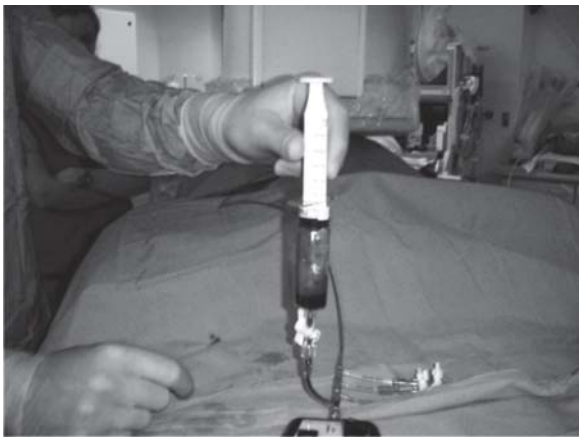

Fig. 3: Aspiration of the clot

The pharmaco-mechanical thrombectomy was successful with a satisfactory result. Post-trellis the left common iliac vein was found to be open, as was the left sapheno femoral vein as is seen in Figures 4 and 5 respectively. A diagnosis of an acute on chronic DVT was reached. Initially the patients left leg improved dramatically and an ultrasound on day 3 postop showed no remaining thrombus. However, clinically the patient was slower to settle, with persistent temperatures, and on day 11 she complained of leg stiffness. Two weeks postprocedure a Doppler ultrasound of her left leg then showed that essentially the entire venous system of the left leg had rethrombosed.

Sixteen days postdelivery it was observed that the patient had developed small bilateral popliteal abscesses measuring up to 1 cm. One week later a CT scan revealed that the supra-renal inferior vena-cava and renal veins appeared patent but the infrarenal inferior vena-cava was thrombosed. The previously inserted stent that extended down through the left iliac veins to the proximal left superficial femoral vein was

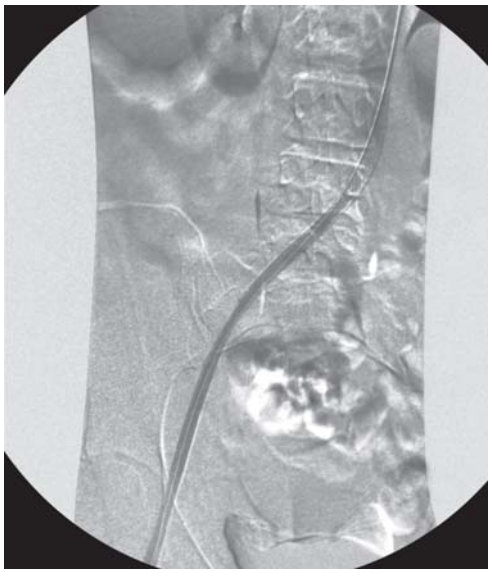

Fig. 4: Patent left iliac vein post-trellis

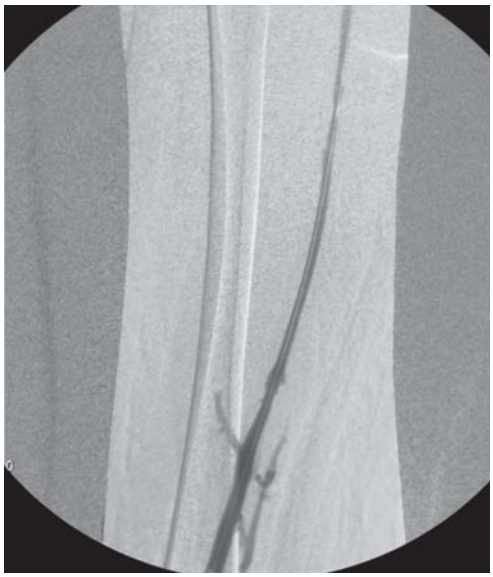

Fig. 5: Post-trellis left sapheno-femoral vein open

occluded. The right common iliac vein also appeared thrombosed and a number of collateral veins were noted on the anterior abdominal wall. Repeat bilateral and inferior vena-caval pharmaco-mechanical thrombectomy was successfully carried out and an IVC filter placed. Figure 6 depicts an Inferior vena-cava filter with the top Trellis® balloon just below it. Postprocedure both the left and right iliac veins were patent as depicted in Figures 7 and 8 respectively.

Repeat ultrasonography two weeks following the bilateral venous thrombectomy revealed a patent IVC and right sided deep venous system but repeat thrombosis of the left leg deep veins once more despite full anticoagulation and mobilization. Rather surprisingly the left leg was not especially symptomatic-in keeping with what was probably initially acute on chronic (although no prior history—the presence of collaterals strongly suggests chronicity).

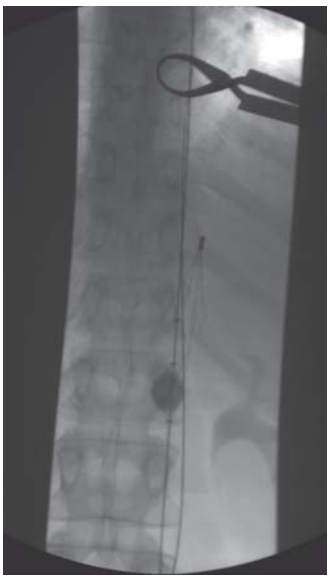

Fig. 6: IVC filter with top trellis balloon just below it

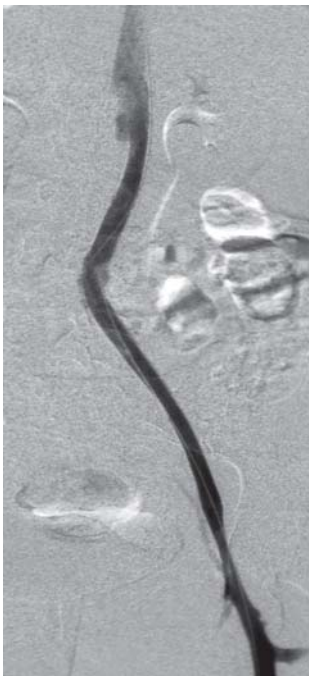

Fig. 7: Left iliac vein stented and patent

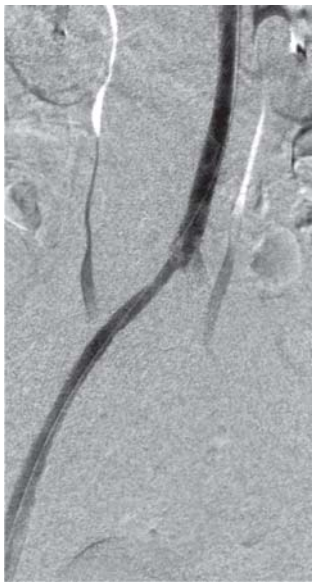

Fig. 8: Right iliac vein poststenting seen to be patent

DISCUSSION

The current gold standard for care in a case of deep vein thrombosis is anticoagulation. Most physicians are unaware that neither warfarin nor heparin actually reduce the clot size[3] and anticoagulants have not been proven efficacious or safe in VTE,[4] merely decreasing the risk of proximal propagation and/or pulmonary embolus. Using standard anticoagulation, the clinical symptoms of deep vein thrombosis are to an extent ignored, relying on bed rest and elevation of the affected limb, together with the development of collaterals to reduce limb swelling. Symptoms of pain, edema, skin changes, and/or ulceration can affect upwards of 70% of individuals to some degree. Studies have determined that early intervention of thrombus removal may help prevent post-thrombotic syndrome in a significant number of patients.[5]

The primary aim of any aggressive method of deep vein thrombosis treatment is thrombus removal. This can be accomplished in several ways. Until quite recently *systemic* thrombolysis was the standard therapy for a variety of acute thrombotic conditions including acute myocardial infarction and pulmonary embolus. It offers little to affected limbs however as the active agent (e.g. streptokinase, tPA) bypasses the thrombosed segment, in addition there is a markedly increased risk of hemorrhage.

Catheter directed thrombolysis (CDT) first came to the fore in the mid 1990s[8] and was shown to offer significant advantages in terms of thrombus removal and symptom resolution, while maintaining a low risk profile. It is however time consuming, requires multiple blood draws, and generally an ICU bed. Newer methods of thrombus removal involve a combination of chemical lysis and mechanical fragmentation: the so-called pharmaco-mechanical thrombectomy (PMT).[9] Surgical thrombectomy is an alternative to CDT (Catheter-Directed Thrombectomy) or PMT, but is rarely performed nowadays has largely been replaced by endovascular methods. Table 1 illustrates the advantages and disadvantages of various thrombolytic techniques.

Following confirmation of the thrombosis by means of an ultrasound, an ascending venogram is performed typically from the ipsilateral popliteal vein. This is punctured using ultrasound guidance to avoid the artery. A standard wire and catheter technique is used to maneuver past the area of obstruction. In this patient the Trellis® device (Bacchus Vascular, CA, USA) was used to affect pharmaco-mechanical thrombectomy. This is essentially an over-the-wire propeller like device with balloons at either end of the rotating propeller/wire segment to prevent migration of the thrombus as it is macerated. Tissue plasminogen activator (tPA, Genentech, South San Francisco, CA, USA) is sprayed through holes in the device to eat into the thrombus while the wire rotates with the balloons inflated. What is left of the thrombus is then aspirated and the next segment treated. In this manner, little if any of the tPA ever has the potential to

Table 1: Various thrombolytic techniques: A comparison

No.	*Thrombolysis technique*	*Advantages*	*Disadvantages*
1.	Systemic thrombolysis	Used for arterial thrombosis.[6]	Very large doses of enzyme to generate large amounts of circulating plasmin.[7] Hemorrage Avoid in pregnancy
2.	Catheter directed thrombolysis	Targeted thrombus directly to high (undiluted) concentrations of thrombolytic enzyme and converts clot-bound plasminogen to plasmin at the very site where it is most needed and where it is relatively protected from neutralization by antiplasmin[7]	Longer stay then pharmaco-mechanical thrombectomy. Minor bleeding and hematomas[7] Multiple venepuncture
3.	Trellis® device	No bleeding complications[11] Day case procedure[9] Walk the patient to the ward[9]	Expertise in the procedure required.

pass into the systemic circulation. The clot disintegrates and is subsequently aspirated. The half life of tPA is < 5 minutes; hence, by the time the balloons are deflated the tPA has been deactivated. As a result, the systemic side effects are minimal with little or no risk of hemorrhage. Usually an underlying stenosis is unmasked by treatment and stent placement is required.

Traditional anticoagulation therapy, although effective by preventing further clot formation, lack the advantage of rapid clot removal that thrombectomy offers. Percutaneous mechanical thrombectomy (PMT) is a minimally invasive procedure that results in rapid clot removal however when thrombolytic agents are used in combination, there is a risk of increased hemorrhage due to release of the thrombolytic agent into the systemic circulation.[9] With pharmaco-mechanical thrombectomy, the thrombolytic agent is confined to the region of interest in the vessel with little or no chance of agent entering into the systemic circulation. Ilio-femoral DVT is under-diagnosed, as we have become overtly dependent on ultrasound. If clinical concerns persist, a CT venogram is a much more appropriate investigation. The patient undoubtedly had a DVT on day 7 postadmission but there was a significant delay until a venogram was performed.

Technically, with hindsight, it may have been less than desirable to proceed with PMT while the patient was actively septic. The combination of severe sepsis, dehydration, and an underlying procoagulant condition (SLE) caused the patient to rethrombose, not only in the previously stented area but also the IVC which is the first time this has ever occurred to a patient treated in this fashion in nearly 1000 cases treated in this fashion.[10] Undoubtedly, our patient had a prior undiagnosed DVT which led to marked collateral formation, another risk factor for DVT and this eventually decreases long term patency. In any event at the time of first Trellis® the patient had few other options. While the development of bilateral popliteal blisters (despite no puncture of the right sided popliteal vein prior to this) heralds impending venous gangrene, it also was a sign of rapidly rising venous pressure in the leg in this circumstance.

CONCLUSION

Pharmaco-mechanical thrombectomy is an effective tool to reduce clot size, to re-establish flow in an acute deep vein thrombosis with the benefit of avoiding treatment in an intensive care unit and enables the patient to mobilize back to the ward.

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