Case report

Venous thromboembolism in the setting of IVC calcification managed with pharmacomechanical thrombectomy and anticoagulation: A case report✩✩✩

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ABSTRACT

In this paper, we describe a case of an otherwise healthy 51 year old Caucasian male who presented with extensive venous thrombosis and a large retroperitoneal hepatoma without active bleeding. On imaging he was found to have focal calcification in the juxta-renal IVC and extensive thrombosis of the iliofemoral and femoropopliteal veins as well as the infrarenal IVC. Despite treating the patient with pharmacomechanical thrombectomy and anticoagulation, he passed away likely due to a new pulmonary embolism. According to the literature available to us, IVC calcification is a rare finding in adults and has been associated with an increased incidence of recurrent deep vein thrombosis and pulmonary embolism. While long term anticoagulation has been recommended for patients with recurrent venous thromboembolism (VTE), there is no expert consensus or societal guidelines for the treatment VTE in the setting of IVC calcification, specifically, regarding pharmacomechanical Vs. surgical thrombectomy [1]. Furthermore, no recommendations currently exist regarding whether expectant management Vs. prophylactic anticoagulation is appropriate. In conclusion, disease specific management guidelines by professional medical societies may be needed regarding the utility and appropriateness of pharmacomechanical thrombectomy Vs. surgical thrombectomy for symptomatic cases as well as expectant management Vs. prophylactic anticoagulation for asymptomatic cases in the setting of IVC calcification.

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Introduction

We present a case of inferior vena caval (IVC) calcification associated venous thromboembolism (VTE) managed with pharmacomechanical thrombectomy and systemic anticoagulation in the setting of retroperitoneal hematoma with poor outcome. To our knowledge, this is the first case report of IVC calcification associated VTE managed with pharmacomechanical thrombectomy. This case report has not been published anywhere else.

Case presentation

Institutional review board approval was not required for this report and informed consent was obtained. A 51-year-old otherwise healthy Caucasian male with no significant family history presented to our hospital with abdominal pain and discoloration of bilateral lower extremities. The patient denied lower extremity pain, numbness or tingling and had intact lower extremity pulses. Subsequent CT angiogram (CTA) of the chest, abdomen and pelvis demonstrated a left retroperitoneal hematoma without active bleeding and without aortic pathology. Extensive thrombosis of the bilateral iliofemoral, and femoropopliteal veins was noted along with thrombosis of the infrarenal IVC. A bullet shaped focus of calcification was evident in the juxta renal IVC (Fig. 1). The bilateral common iliac and external iliac veins were dilated with thrombus. Findings were confirmed with Duplex venous ultrasound which showed acute total obstruction of the deep venous system of the lower extremities. The retroperitoneal hematoma was thought to be sequela of venous hypertension, and anticoagulation with heparin drip was initiated. However, given the existing bleed, the PTT was left subtherapeutic between 30 and 40 seconds and the patient was taken for pharmacomechanical thrombectomy the next day.

Venogram through bilateral popliteal vein access confirmed findings consistent with prior CT. In addition, the suprarenal infrahepatic IVC was noted to be small in caliber presumably due to lack of antegrade venous flow. IVC filter placement was initially considered but not performed due to concern for lack of complete filter expansion given the small caliber of the suprarenal IVC. A total of 3 days of pharmacomechanical thrombectomy was performed. The first day, mechanical thrombectomy of the infra renal IVC, as well as bilateral iliofemoral and femoropopliteal veins was performed using balloon clot maceration with 10 and 12 mm compliant balloons then using the Inari clot retriever device

Fig. 1 – CT abdomen/pelvis in the venous phase is shown: (A) axial image at the level of the abdomen small caliber suprarenal IVC. (B) axial image of the pelvis shows thrombosed and dilated bilateral external iliac veins (C&D) coronal and sagittal images with curved multiplanar reconstruction show a bullet shaped focus of IVC calcification in the juxta renal IVC (arrows) with caval thrombus below this calcification. A left retroperitoneal hematoma is evident (*). Again, note the small caliber suprarenal IVC on the sagittal image (D)
(Inari medical, Irvine, CA) with mild improvement in clot burden. Thrombolysis with Alteplase was performed overnight via 5 F infusion catheters (Cragg McNamara valved infusion catheter; ev3, Irvine, CA) through each popliteal vein access at 20 cc/hr for 24 hours. The second day, additional mechanical thrombectomy of the aforementioned lower extremity veins and infrarenal IVC was performed using a 12 mm high pressure balloon, AngioJet Ultra thrombectomy system (Medrad, Minneapolis, MN), and Cleaner XT device (Argon medical device, Plano, Texas) with moderate improvement in clot burden. Thrombolysis was resumed after the mechanical thrombectomy using 5 F infusion catheters via each popliteal vein access with Alteplase running at 40 cc/hr for another 24 hours. Of note, cavogram during the second day showed moderate stenosis of the IVC at the level of calcification which was resistant to balloon angioplasty. The third day, final mechanical thrombectomy was performed this time via bilateral common femoral vein access, using a 14 mm high pressure balloon and Cleaner device. At the end of the procedure, brisk flow within the bilateral femoropopliteal veins was restored without significant clot burden. Mild to moderate clot burden within the bilateral iliac veins was noted again with brisk flow. Brisk flow was also noted through the IVC; however, persistent moderate stenosis was noted at the level of the IVC calcification (Figs. 2 and 3). Thrombolysis was terminated and the popliteal and common femoral sheaths were removed, and the patient was left on Heparin drip with PTTs between 30 and 40 seconds. The patient was started on therapeutic enoxaparin on day 2 of pharmacomechanical thrombectomy and was completely transitioned to enoxaparin within the next three days.

Two days after the completion of pharmacomechanical thrombectomy, the patient was noted to have new onset dyspnea and increasing oxygen requirements. CTA of the chest, abdomen, and pelvis was subsequently obtained. CTA chest showed a central thrombus within the right main pulmonary artery and PE involving multiple bilateral segmental and subsegmental pulmonary arteries (Fig. 4 A). Transthoracic echocardiogram obtained the next day showed no evidence of right heart strain. CTA abdomen and pelvis showed complete re-thrombosis of the bilateral lower extremity veins and IVC (with clot extending now to the infrahepatic IVC) with stable left retroperitoneal hematoma without active hemorrhage (Figs. 4 B and D). A duplex venous ultrasound of the bilateral lower extremities obtained the next day confirmed these findings. In addition, a duplex venous ultrasound of the bilateral upper extremities obtained a day after the CT showed acute thrombosis of the right cephalic vein with otherwise patent veins throughout. Hematology consult was obtained who determined the re-thrombosis did not represent a failure of enoxaparin given patient received only three doses, and the patient was re-started on Heparin drip while the enoxaparin was continued. Work up for thrombophilia including Factor V Leiden, and prothrombin mutations, as well as antiphospholipid antibody were obtained with negative results. A heparin induced thrombocytopenia (HIT) enzyme linked immunosorbent assay (ELISA) obtained when the re-thrombosis of the lower extremity veins was discovered was initially negative.

On the second day of Heparin drip re-initiation, and two days after the initial negative HIT ELISA, the patient was noted to have a drop in his platelets from 175 to 83 K/mm³.

Fig. 2 – Post pharmacomechanical thrombectomy venogram (images were stitched together) shows mild to moderate residual clot burden within the bilateral common iliac veins with antegrade flow all the way to the cava. Persistent moderate stenosis was noted at the level of the IVC calcification (arrow)
A repeat HIT ELISA was obtained which was strongly positive. Subsequently, all heparin and heparin related products were stopped, and a serotonin release assay was obtained for confirmation of HIT. The patient was switched to apixaban (ELIQUIS; Bristol-Myers Squibb, New York, NY). The patient continued to do better over the next few days with mild improvements in oxygen requirements.

Two days after apixaban was started, the patient was found down in the lavatory with agonal breathing and later became unresponsive with no palpable pulse or cardiac activity. A CODE BLUE was called immediately, and CPR was initiated according to ACLS protocol. Two separate doses of 50 mg of Alteplase were administered given high suspicion for a large PE, the first dose being administered 20 minutes into the code. For most of the code the patient remained in pulseless electrical activity. The code was continued for another 20 minutes, however, return of spontaneous circulation could not be restored. After discussing the implications of prolonged code activity on cerebral perfusion with patient’s family, decision was made to terminate CPR. The patient passed away shortly thereafter.

**Discussion**

The proposed pathophysiology of IVC calcification associated VTE is disturbance of blood flow caused by the calcification creating conditions that promote Virchow’s triad [2]. There is
currently no expert consensus or professional medical society guidelines in the management of IVC calcification associated VTE likely due to the rarity of this condition. The American College of Chest Physicians recommends long term anticoagulation for patients with recurrent VTE regardless of etiology, however, to our knowledge no recommendations exist regarding pharmacomechanical vs. surgical thrombectomy. In our case, pharmacomechanical thrombectomy was utilized in the setting of retroperitoneal hematoma, and the IVC calcification was not factored in our decision to perform the intervention. In retrospect, however, we question the utility of pharmacomechanical thrombectomy in the setting of IVC calcification associated VTE. While thrombectomy as in this case can result in a significant decrease in clot burden and symptomatic relief in the short term, these benefits may not be long lasting since the primary purported cause of the thrombosis remains undiagnosed. In our case, the moderate residual stenosis at the level of the IVC calcification after the intervention may have been a significant factor leading to the venous re-thrombosis if it resulted in continued non-laminar blood flow in the IVC. Following the same line of reasoning, we question whether surgical thrombectomy of the caval calcification could have been considered in this patient for definitive management of this condition.

Yet another potential contributing factor for the re-thrombosis in our case was the positive HIT. The patient initially tested negative for HIT based on the first ELISA which was obtained when the re-thrombosis was discovered, and he was resumed on heparin drip the next day. He then developed thrombocytopenia two days afterwards and repeat HIT ELISA was strongly positive. Serotonin Assay test which came back after the patient passed away was also positive, confirming HIT positivity. Despite the negative initial HIT ELISA test obtained when the re-thrombosis was discovered, it is possible that the first round of unfractionated heparin may have still contributed to intervention failure specially since an unprovoked right cephalic vein thrombus was also noted at the same time.

As this case report demonstrates, it is also important to remember that mechanical thrombectomy carries a significant risk for PE. IVC filter placement can be a lifesaving intervention that can decrease incidence of PE when mechanical thrombectomy is being considered. In our case, a filter was not placed given the small caliber supra-renal IVC, and with the reasoning that such a small caliber IVC would serve as an auto filter preventing large emboli from entering the pulmonary circulation. This case report shows however that clinically significant PE may occur even in the setting of small caliber IVC as the cause of death in this case was most likely PE induced cardiac arrest. The larger point remains the risk-benefit profile of pharmacomechanical thrombectomy for management of IVC calcification induced VTE, especially when IVC filter cannot be placed.

Determining the strength of the association between IVC calcification and VTE remains an important but unresolved matter. While IVC calcification is primarily noted in the pediatric age group, it is only rarely seen in adults [3,4]. There are only a handful of case reports in the literature describing
IVC calcification in adults, some reporting no symptoms while others reporting significant VTEs. The strength of the association has been difficult to determine given the rarity of this condition. As a result, we don’t have enough evidence to recommend expectant management Vs. prophylactic anticoagulation in asymptomatic patients with IVC calcification.

**Conclusion**

Our case report demonstrates IVC calcification is an exceedingly rare finding in adults that has been linked with VTEs. The theorized mechanism of hypercoagulability is the disturbance of blood flow caused by the calcification creating conditions that promote Virchow’s triad. However, the strength of this association remains uncertain. IVC calcification remains an important finding that needs to be reported by radiologists when seen on imaging and an important factor to consider during workup of unprovoked DVT. There is no expert consensus or societal guidelines in the management of VTEs in the setting of this rare condition. Long term anticoagulation has so far been the mainstay of treatment, however, disease specific management guidelines by professional medical societies may be needed regarding the utility and appropriateness of pharmacomechanical thrombectomy Vs. surgical thrombectomy for symptomatic cases as well as expectant management Vs. prophylactic anticoagulation for asymptomatic cases in the setting of IVC calcification.

**Ethics human rights**

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

**Author contribution**

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

**Availability of data and material**

Not applicable.

**Patient consent**

The authors declare that this report does not contain any personal information that could lead to the identification of the patient. Informed consent was obtained from the patient and his son before the death of the patient.

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