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Case Report

A Case of Spontaneous Calf Hematoma with Simultaneous Deep Venous Thrombosis

Jennifer Klein[*] and Sunil Gandhi

[1]Department of Internal Medicine, HCA Healthcare/USF Morsani College of Medicine GME: HCA Florida Citrus Hospital, Inverness, Florida, USA

[*]**Corresponding Author:** Jennifer Klein MD MPH, Department of Internal Medicine, HCA Florida Citrus Hospital, HCA Healthcare/USF Morsani College of Medicine GME Consortium, Inverness, Florida, USA

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Abstract

Patients with active cancer may also have a state of hypercoagulability that increases their risk of venous thromboembolism (VTE). Enoxaparin is a low-molecular weight heparin (LMWH) that is indicated for the prevention and treatment of VTE and is the preferred agent for patients with cancer because of its lower risk of bleeding events and less drug interactions. Bleeding events such as muscular hematomas have been reported with the use of enoxaparin. The risk of hematoma is increased in those with certain risk factors that are frequently present in patients with active malignancy. Coagulation parameters are typically normal in patients with hematoma and there are no accepted criteria to predict which hematomas may become life-threatening. As hematomas present similarly to deep venous thrombosis (DVT), imaging is needed to distinguish them from one another as the treatment for one can worsen the other. Here we present a case of a woman with ovarian cancer and increasing clot burden of chronic diffuse VTE who developed a right calf hematoma while on chronic therapeutic enoxaparin.

Keyword: Case of spontaneous calf hematoma; Simultaneous deep venous thrombosis; Cancer; Chronic therapeutic enoxaparin; Hematoma.

Introduction

Hypercoagulability of malignancy increases the risk of VTE through many proposed mechanisms including the release of pro-coagulant proteins from tumor cells, chemotherapy adverse effect, and hemostasis from compression by the tumor or patient immobility. Enoxaparin, a LMWH, is one of the most commonly prescribed inpatient medications and is indicated for treatment and prophylaxis of VTE [1]. It is preferred over other agents in patients with malignancy due to its lower risk of bleeding and drug interactions, especially with chemotherapy. However, there are still risks of acute bleeding and hematomas have been reported in patients taking enoxaparin [2]. These complications are more common in the elderly, renal

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dysfunction, and extremes of body weight [1]. Patients on enoxaparin may have supratherapeutic coagulation parameters owing to a change in creatinine clearance from the original prescribed dose. In patients with active malignancy, creatinine clearance can be altered over the course of treatment through weight loss or kidney injury due to nephrotoxic chemotherapy agents. However, patients with hematoma typically have therapeutic range International Normalized Ratio (INR) in laboratory studies and it is not common for these patients to have anticoagulation overdose [2]. It can be challenging to distinguish spontaneous hematoma from DVT, even with a thorough history and physical exam. Without imaging studies, patient evaluation results in similar positive findings of history of prior DVT and patients may not report a history of trauma to the area. Physical exam findings of increased calf circumference, erythema, and warmth as well as positive Homan's sign may be present in both etiologies although none of these findings are specific [3]. In patients with a presentation of tender unilateral calf swelling without history of trauma and especially with a history of prior DVT, empiric treatment with heparin may be initiated. With a high suspicion for DVT in the absence of imaging studies, a patient on therapeutic anticoagulation for prior DVT is equally likely to have a spontaneous calf hematoma. D-dimer may be elevated due to the presence of a clot in either case. Because administering or continuing anticoagulation may worsen a hematoma [4], it is important to determine whether there is a hematoma or a DVT. Here we present a case of spontaneous calf hematoma with simultaneous deep venous thrombosis in a patient with active malignancy on chronic anticoagulation with enoxaparin.

Case presentation

A 47-year-old Caucasian female with complaints of right calf pain was found to have deep venous thrombosis by ultrasound study at an urgent care clinic where she was directed to go to the nearest emergency department for further evaluation. In the emergency department, right lower extremity doppler ultrasound revealed thrombi in the common femoral, superficial femoral, popliteal, posterior tibial, peroneal, and anterior tibial veins as well as a superficial thrombus in the greater saphenous vein. Coagulation panel was within normal range with INR 1.1, Prothrombin Time (PT) 10.9 seconds, and activated Partial Thromboplastin Time (aPTT) 26 seconds. Subsequent computed tomography (CT) of the chest revealed bilateral upper and lower lobe pulmonary embolisms. Cancer Antigen-125 (CA-125) level was ordered in the setting of unprovoked venous thromboembolism in a middle-aged woman which returned elevated at 588 and a transvaginal ultrasound confirmed the suspicion of ovarian carcinoma, showing a solid right adnexal mass. The patient was bridged to warfarin and discharged with a therapeutic INR. She sought evaluation of the adnexal mass at a tertiary center where she continued to receive treatment. The patient was diagnosed with ovarian adenocarcinoma and was started on carboplatin and paclitaxel which were changed to doxorubicin after resistance developed. No improvement was seen on doxorubicin so, the patient was commenced on immunotherapy with pembolizumab and adjuvant chemotherapy with paclitaxel. She failed anticoagulation with warfarin, apixaban, dalteparin, and dabigatran with the eventual placement of 4 iliac vein filters, 3 inferior vena cava (IVC) filters, and

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continuation of therapeutic enoxaparin (100mL twice daily). Eleven months after initial presentation, the patient returned to the emergency department with complaints of right lower calf pain, increased swelling, and inability to bear weight on right lower extremity. Right lower extremity ultrasound showed thrombus in the right common femoral vein, right deep femoral vein, and right femoral vein as well as hypoechoic collection in the soft tissues of the right calf. CT scan of right lower extremity confirmed hematoma in the deep posterior muscle compartment of the right calf (Figure 1). Coagulation panel in the emergency room showed PT 11.1 seconds, INR 1.1, and aPTT 30 seconds. The patient reported no trauma to the area. She was admitted for right leg hematoma and her maintenance dose of enoxaparin was held. General surgery was consulted who performed extraction of the hematoma and placed a Jackson Pratt (JP) drain with successful removal on the day of discharge.

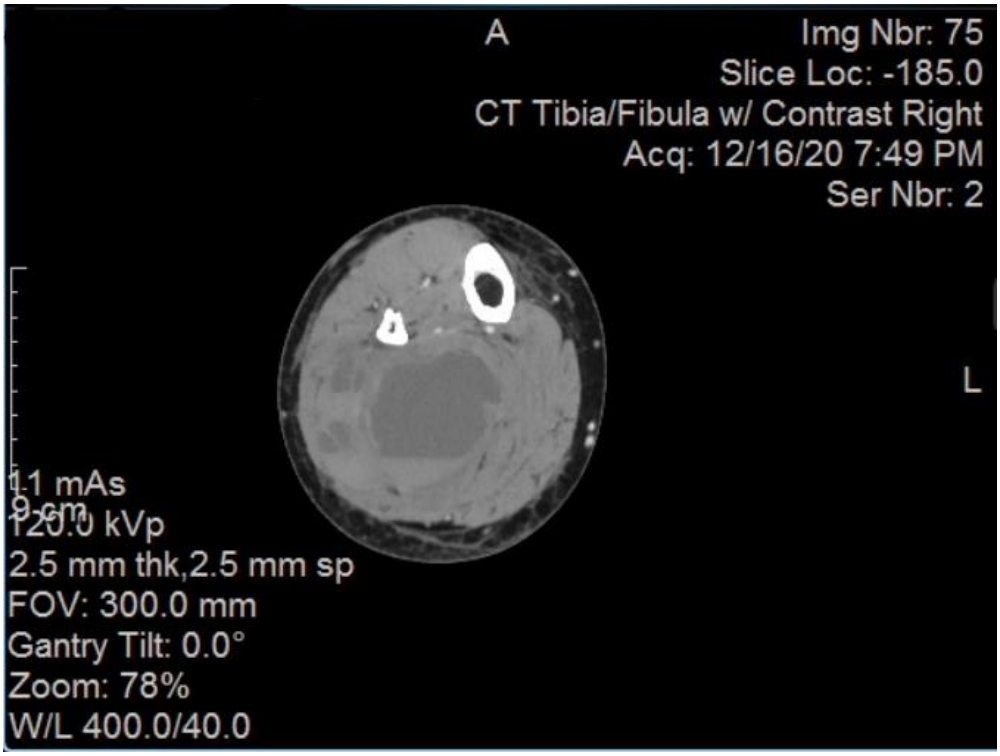

Figure 1: Contrast-enhanced CT of right tibia and fibula shows hematoma in the deep posterior muscle compartment on the same day that right lower extremity ultrasound revealed thrombi in the right common femoral vein, right deep femoral vein, and right femoral vein.

Discussion

In the case described above, the patient had no risk factors for bleeding while receiving enoxaparin including advanced age. Her coagulation panel at the time of presentation with hematoma was within normal range, and therefore, not therapeutic. Additionally, this patient presented with multiple deep vein thrombi that had persisted or worsened despite the long-term use of LMWH with the simultaneous development of a spontaneous muscle hematoma which is maligned with the coagulation parameters for either pathology. This case demonstrates the importance of maintaining a high suspicion of spontaneous muscle hematoma, as in this case continuation of the patient's

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maintenance dose of enoxaparin would have expanded the hematoma. Obtaining imaging to confirm the presence of a hematoma prevented continued bleeding and acute clinical deterioration in this patient. There is no defined criteria that can identify which non-severe spontaneous muscle hematomas will cause sudden deterioration and become life-threatening [2]. The first line for diagnostic imaging of hematoma is unenhanced CT scan which can help guide diagnosis of hematoma and determine its severity. If severe spontaneous muscle hematoma is found, computed tomography angiography (CTA) can be used to identify active bleeding and its origin by visualization of contrast leak in the arterial phase. Management of spontaneous muscle hematoma is often based on strategies employed for traumatic hematoma which can include intravascular volume resuscitation, discontinuing or reversing anticoagulation, and addressing hemostasis disorders if present. In smaller hematomas, a hemostatic plug in the muscle can stop bleeding without any intervention [2].

LMWH-induced hematoma is managed with the administration of protamine sulfate and fresh frozen plasma for reversal of heparin. However, this combination does not always provide a timely reversal or stop bleeding [5]. Daggett et al described a case of a 58-year-old female who was treated with dalteparin for DVT of the upper extremity at the site of a peripherally inserted central catheter (PICC) line that she incurred while hospitalized for bacteremia. The patient had no history of trauma to the area or renal disease and had a normal coagulation panel. She developed bilateral spontaneous calf hematomas due to arterial bleeding of multiple small vessels. The patient was given protamine sulfate, but the hematomas continued to enlarge, and hemoglobin dropped to 5.2g/dL. The patient was given fresh frozen plasma (FFP) with no improvement. After failure of medical management was noted, the patient was sent to the operating room for surgical evacuation which eventually stopped bleeding over the next day [5]. Because we are not able to depend on reversal of bleeding or predict the severity of hematoma, this diagnosis should be considered in patients on anticoagulation with lower-risk medications such as enoxaparin, regardless of coagulation parameters and ambiguous history findings. Our case shows that even with an increasing clot burden and normal coagulation parameters it is possible to have a bleeding event.

Conclusion

Acute unilateral calf swelling can be difficult to diagnose as history and physical examination may not lead to a clear pathology. Determining the time of onset, inciting factors, and associated symptoms can help narrow the differential diagnoses. It is vital to obtain imaging before empiric anticoagulation, especially with no established criteria to predict whether it could become life-threatening. Suspicion of hematoma should be high in patients receiving low-molecular weight heparins for therapeutic anticoagulation or venous thromboembolism prophylaxis.

Patient consent

Written consent for the publication of this case report and accompanying images were obtained from the patient.

HCA healthcare disclaimer

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Conflict of interest

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