CLINICAL VIGNETTE

Acquired Factor VIII Inhibitor in an Elderly Patient

Elaine Parker, MD

Case

An 83-year-old male was brought in by his caregiver complaining of severe right hip and leg pain. His past medical history of chronic kidney disease stage IV, atrial fibrillation previously on apixaban, dilated cardiomyopathy EF 20%, coronary artery disease, severe aortic stenosis and prior CVA. The patient lived independently but had several friends who provided some assistance with transportation to appointments. The patient reported onset of severe right hip and leg pain 3 days prior to presentation. The pain was in the proximal right leg rated 8/10 severity with no radiation. He reported no exacerbating or alleviating factors and denied any recent trauma or falls. He had been taken off apixaban during a prior admission but had impaired memory and was unclear whether he was still taking this medication. He was unable to complete medication reconciliation. He denied any spontaneous mucosal bleeding. He had been recommended for a higher level of care during his last hospital admission and he reported only sporadic supervision of medications. He had no prior history of spontaneous deep muscle or retroperitoneal bleeds or mucosal or intracranial bleeds.

On exam, the patient had diffuse ecchymosies on his right thigh and was intermittently confused on exam. Imaging ruled out acute fracture in his right hip. His hemoglobin typically 8-9 g/dL dropped to 6.3 g/dL. His activated partial thromboplastin time was very prolonged at >90. On admission, additional imaging documented a 7cm retroperitoneal bleed and 9cm right iliacus hematoma. He was treated with 4 units packed red blood cells, FFP and Kcentra. A mixing study did not correct his PTT. A Bethesda assay found only 1% factor VIII activity. Apixaban level was undetectable. Lupus anticoagulant testing was negative. He was diagnosed with a Factor VIII inhibitor and hematology recommended prednisone and cyclophosphamide treatment. He did not respond to this treatment and had subsequent hospitalizations for spontaneous bleeding events and was later treated with Rituximab.

Discussion

An acquired inhibitor against factor VIII is called acquired hemophilia A. This autoantibody disrupts the function of clotting factor activity that leads to a bleeding disorder. It is rare, with incidence of 1 case per million/year.[1] Acquired hemophilia A typically affects the elderly between 68 and 80 years old. It also affects younger patients who are post-partum. Patients with acquired hemophilia A, have a mortality rate between 7.9%-22%.[1] This condition can occur in association with rheumatoid arthritis and systemic lupus erythematosus, malignancy and secondary to drugs.[2] The development of Factor VIII inhibitors has been associated with solid tumors such as prostate and lung adenocarcinomas. Penicillin, phenytoin and interferon have also been associated with Factor VIII inhibitor.[2]

The type of bleeding with acquired hemophilia A differs from congenital hemophilia A. Congenital hemophilia A typically manifests as hemarthrosis, whereas acquired hemophilia A may present with hemorrhage into muscle and mucous membranes. Bleeding is frequently severe and may be a medical emergency. A typical presentation is an elderly patient who presents with a large hematoma or ecchymosis in the setting of no or minimal trauma.[3] Gastrointestinal and retroperitoneal bleeding is common. The diagnosis of acquired hemophilia A is established with a prolonged activated partial thromboplastin time (aPTT) which cannot be corrected with mixing study/inhibitor screen and a reduced FVIII activity. Prothrombin time is normal (PT). It is recommended to rule out antiphospholipid antibody syndrome.[4]

Treatment of acquired FVIII inhibitors involves management of the acute bleeding event and removing the inhibitor with immunosuppression. The decision regarding which immunosuppressant medication is based upon the severity of bleeding and the titer of the inhibitor.[5] Long term treatment of acquired Factor VIII inhibitor involves immunosuppression with prednisone, cyclophosphamide or rituximab. Steroids (+/-use of cyclophosphamide) are first line while rituximab therapy is second line in treatment of an acquired factor VIII inhibitor. There are no large randomized controlled trials that address the treatment of Factor VIII inhibitors, thus treatment is based upon expert clinical opinion. Infections related to the immunosuppression are a major risk in this largely elderly population.[6]

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