

Introduction

- Acquired hemophilia A (also known as an acquired factor VIII inhibitor) is a rare disease that occurs when autoantibodies directed against factor VIII are formed and interfere with its coagulant properties.
- Although rare, this is the most common acquired disease affecting clotting factors, occurring at approximately 1 person per million each year.^[1, 2]
- The etiology of this condition is not entirely known, and an identifiable cause is not elucidated in most cases.
- 40-50% of cases are associated with the post-partum period, underlying malignancy, drug administration or autoimmune disorders.^[3]
- There is also some data in the literature suggesting an association between cancer surgery and factor VIII auto-antibody formation.^[4]
- To our knowledge, there is no known association with the use of FOLFIRINOX therapy specifically.
- Reports of hemophilia A in patients with pancreatic cancer have been previously described.^[5]
- Here, we report a 76-year-old male with pancreatic cancer, status post Whipple procedure and cytotoxic chemotherapy with FOLFIRINOX who was found to have an acquired factor VIII inhibitor.

Case Description

A 76-year-old male with a past medical history of pancreatic cancer (status post Whipple procedure and FOLFIRINOX), peptic ulcer disease with upper gastrointestinal bleeding, type II diabetes and coronary artery disease presented to the hospital after a fall at home. On arrival to the emergency department, he was dyspneic and reported generalized weakness. Vital signs were within normal limits. Physical exam was notable for a large ecchymosis overlying his right hip. Initial lab testing revealed a hemoglobin of 6.2 g/dL. Activated partial thromboplastin time (aPTT) was prolonged at 95 s. Prothrombin time (PT) and international normalized ratio (INR) were normal at 11.1 s and 1.00 respectively. Trauma workup including CT imaging of the chest, abdomen, pelvis, head and c-spine did not reveal any fractures and there were no masses or enlarged lymph nodes seen.

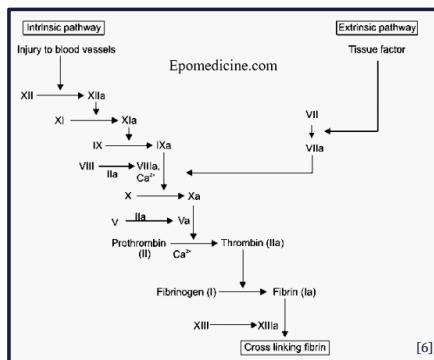
Clinical Course

He was transfused packed red blood cells and gastroenterology was consulted for workup of suspected upper GI bleed. CT angiogram of the abdomen did not reveal any source of bleeding. The following day he was noted to have worsening of his right hip ecchymosis and new development of ecchymosis over his left arm. He was also noted to have conjunctival hemorrhage of his right eye. CT imaging of the head, chest, abdomen, pelvis, left upper extremity and left lower extremity without contrast were performed and showed possible hemorrhage of the left chest, left axilla and left lateral body wall. Trauma surgery was consulted, no acute intervention was performed.

Hematology was consulted and a mixing study was performed that revealed an acquired factor VIII inhibitor. Factor VIII activity was <1% and factor VIII antibody titer was 12.2 Bethesda units (BU). His aPTT only partially corrected with initial mix, and then significantly prolonged again on incubated mix, consistent with the presence of an inhibitor.

He was started on prednisone (1mg/kg daily) as well as NovoSeven (coagulation factor VIIa, recombinant) as a bypassing therapy. He also received 2 doses of rituximab. Repeat factor VIII activity was again <1% and factor VIII antibody titer increased to 20.8 BU. He then developed worsening left upper extremity swelling. Given concern for bleeding, therapy with recombinant factor VIIa was switched to factor VIII inhibitor bypassing activity (FEIBA), a prothrombin complex concentrate.

After receiving a total of 11 units of packed red blood cells and the therapies listed above, his bleeding stopped, and hemoglobin remained stable around 8.0 g/dL. He was discharged with prednisone 1mg/kg daily. He was instructed to have complete blood count, factor VIII assay and factor VIII antibody titer checked weekly and to follow up with hematology to complete doses 3 and 4 of rituximab. Repeat testing 3 months after discharge revealed normalized factor VIII activity >150%.



Discussion

- Acquired hemophilia A is a rare disorder that portends significant morbidity and mortality. 80% of patients develop severe or life-threatening bleeding, with mortality from hemorrhage ranging from 7.9 to 22%.^[3]
- Most patients are diagnosed after they develop bleeding into the skin or muscles, hematuria, hematemesis, melena or prolonged post-partum or post-operative bleeding. Rarely, patients are diagnosed before symptoms arise after aPTT is incidentally found to be prolonged on routine testing.^[3]
- In our patient it is unclear what led to the development of autoantibodies against factor VIII. He has a history of pancreatic cancer that was treated with surgery and chemotherapy. He does not have a history of autoimmune disorders. His surgery took place roughly seven months prior to diagnosis of acquired hemophilia A. His last chemotherapy session occurred roughly two months prior to his presentation.
- From our literature search it does not appear that FOLFIRINOX therapy has been associated with acquired inhibitors to factor VIII. In fact, there is a report of a 70-year-old woman with carcinoma of the pancreas and an acquired factor VIII inhibitor who was observed to have disappearance of her anti-factor VIII antibody after initiating chemotherapy with fluorouracil and lomustine.^[7]
- This case illustrates the importance of recognizing this disease entity when patients present with bruising or bleeding and an isolated elevation of the aPTT. This patient was able to achieve complete response through prompt recognition and involvement of the hematology team.

References

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