Clinical Case Studies and Reports

Case Report ISSN: 2631-5416

A Case of Eliquis associated Spontaneous Pericardial Effusion in absence of underlying malignancy

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Abstract

The patient presented with shortness of breath and tachypnea; an inpatient workup revealed pericardial effusion. He underwent a pericardial window with the resolution of the effusion. He was on Eliquis for atrial fibrillation and stent placement. Without any inciting event or pathology, we suspect the findings are a result of his anticoagulation medication.

History of Presentation

a 78-year-old male with a history of A Fib, CAD, and CHF was admitted for tachypnea and shortness of breath. He experienced 1 week of progressive shortness of breath. The patient stated he was discharged from another hospital 8 days prior after a 4-day inpatient stay due to similar symptoms. Per the patient, he was given Lasix during his stay for suspected CHF exacerbation and was transitioned from Plavix to Eliquis. He was discharged with stable vitals. Upon returning home, symptoms continued to worsen, and respiratory status declined.According to the patient, he had chairs placed around the house as he could not walk more than a few feet without becoming dyspneic. He was seen by his cardiologist this morning at which point he was sent to our facility for further evaluation and workup.

Upon arrival at the ED, the patient was hypotensive, and labs revealed leukocytosis. His troponin was negative with elevated PT and INR. On physical examination, he was pale and diaphoretic. Wheezes were auscultated bilaterally with decreased breath sounds at the lung bases and 1+ pitting lower extremity edema. Additional findings of right-sided abdominal distention and abdominal purpura due to a known hernia.

Past Medical History

The patient had a past medical history of gout, abdominal hernia, and hypertension. Pertinent cardiac history included CHF with an EF of 55%, ECHO unavailable, and a recent diagnosis of atrial fibrillation on Eliquis. He has a CAD stent placement in March 2022. Operative report unavailable.

Differential Diagnosis

Based on the patient's presentation and past medical history, the differential diagnosis included septic shock, CHF exacerbation, shock liver, abdominal hernia incarceration, and pericardial tamponade.

Investigations

On initial CBC, the patient had left-shift leukocytosis and thrombocytosis. Supratherapeutic PT and INR at 53.5 and 4.36 respectively. BUN and Creatinine were suggestive of AKI. AST 1644, ALT 1200, and Bilirubin total of 1.7, but hepatitis and HIV panel were negative. The patient was COVID-negative. Furthermore, in the initial presentation BNP of 488, lactic acid of 5.1, and procalcitonin of 0.20. Chest x-ray showed massive enlargement of the cardiac silhouette. Hepatomegaly and cholelithiasis with thickened gallbladder were seen on Liver Ultrasound. CT chest-abdomen-pelvis showed a large complex pericardial effusion with impingement on the right ventricle with trace pleural effusion R>L. ECHO confirmed LVEF of 65% and large pericardial effusion, without findings indicative of tamponade.

Pericardial fluid was removed and sent for further evaluation. The fluid was red and turbid with an RBC > 4,000,000; the light's criteria were positive indicating exudative fluid. Cytology was negative for malignancy. Uremic pericarditis was unlikely as creatinine was 1.0 in January of the same year. Pericardial fluid was acid-fast negative, with no bacterial growth at the end of 7 days, and no fungal growth at the end of 28 days. ADA was elevated in the pleural fluid.

Management

After reviewing the findings and confirming results with ECHO, cardiology and cardiovascular surgery were consulted. The patient underwent a pericardial window with a biopsy. Approximately 1100CC serosanguinous fluid was evacuated leading to a rise in systolic blood pressure. The fluid was sent to the lab for further studies. A pericardial drain and chest tube were placed to optimize fluid removal; both were removed before the patient was discharged. Eliquis was held throughout his stay as it was the suspected cause of the pericardial effusion.

Discussion

Anticoagulation is linked to many complications associated with uncontrolled bleeding. Previous studies have shown the risk of spontaneous bleeding with warfarin and DOAC. More recently there have been several cases correlating Eliquis with Pericardial effusion.

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Received: February 05, 2023; **Accepted:** February 20, 2023; **Published:** February 25, 2023

Pathogenesis is not yet fully known and there are no current studies for which we can link the two events as our study was a diagnosis of exclusion. We hope that as more cases are present the underlying correlation can be better understood.

Over the last decade, DOACs have been rising in popularity due to studies showing that they are at least as safe and effective as vitamin K antagonists as seen by both the ARISTOTLE trial and AMPLIFY trial.

Eliquis is FDA-approved for non-valvular a fib, prevention of VTE after total knee and total hip replacement, treatment of DVT and PE, and prevention of recurrent DVT and PE [1].

Off-label indications for Eliquis are the treatment of HIT, prevention, and treatment of cancer association DVT, prevention of VTE and hospitalized acutely ill medical patients, and prevention of VTE after PCI with nonvascular afib [1].

When compared to warfarin, DOACs have shown to be easier to dose in the outpatient setting and have required less follow-up with labs.

However, with the quick rise in their popularity, the medical community does not have as much long-term research on DOACs as we have on warfarin. What we do know is that Eliquis can cause bleeding that can be severe. That risk is increased if the patient is on aspirin, NSAIDs, warfarin, heparin, SSRIs, or SNRIs [2]. Spinal or epidural blood clots can form in patients who have medicine injected into the spinal or epidural area [2] It has been documented that those that should not take Eliquis are patient with artificial heart valves, diagnosis of APS [2].

A 2017 study looked at spontaneous bleeding on Eliquis [3]. It showed that any type of hemorrhage was reported in 18% of cases in the US, 31% in Australia, and 26% in Canada [3]. However concomitant use of medicine for potential bleeding risk increased spontaneous adverse events of bleeding up to 47.6% in Canada, 65.5% in Australia, and 49.4% in the US [3].

The most commonly reported hemorrhage was G.I. hemorrhage. Other forms of bleeding that were studied included CVA hemorrhage, vascular hemorrhage, DVT, myocardial infarction, CVA thrombosis, all hemorrhage, and death [3].

We have not seen many cases of hemopericardium caused by Eliquis. The first documented case was in 2015 with previous knowledge of hemopericardium in patients taking dabigatran and rivaroxaban [4]. The case in 2015 featuring apixaban reported spontaneous pericardium occurred 6 weeks after initiation [4].

In our most recent case, pericardial bleeds within 7 days of initiation [5,6].

Limitations

There are limitations to our analysis. As the etiology of the patients, hemopericardium was a diagnosis of exclusion. Infectious causes, autoimmune disease, trauma, post-MI, malignancy, mediastinal radiation, renal failure with uremia, drugs, and aortic dissection extending into the pericardium were all ruled out. We do not know if the patient was taking any concomitant medications that increased his risk for a spontaneous adverse event.

More research needs to be done to fully understand the risk factors of starting patients on Eliquis.

Follow-Up

The patient was discharged 7 days post pericardial window in stable conditions. He was given instructions to follow up an outpatient with cardiology. The patient has since been lost to outpatient follow-up.

Conclusions

In the absence of other underlying causes and comorbidities, we concluded that the recent change from Plavix to Eliquis led to the development of this patient's pericardial effusion. A literature review uncovered similar case reports that supported this theory. This case highlights an uncommon risk associated with Eliquis.

Learning Objectives

To discuss the risk of developing pericardial effusion while on Eliquis in patients without any underlying malignancies.

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