



Hemorrhagic Cardiac Tamponade Apixaban - Induced: A Case Report

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Received date: 07 June 2021; Accepted date: 10 June 2021; Published date: 12 June 2021

Citation: Badawaki H, Awada B, Mokdad R, Tekriti Z, Chaddad R (2021). Hemorrhagic Cardiac Tamponade Apixaban - Induced: A Case Report. SunText Rev Cardiovasc Sci 1(1): 103.

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Abstract

Direct oral anticoagulants (DOACs) are used for many conditions where anticoagulation is needed such as non-valvular atrial fibrillation, deep vein thrombosis (DVT) and pulmonary embolism (PE). Apixaban is a direct oral anticoagulant (DOAC) that works by factor Xa inhibition. This agent is associated with a lower risk of bleeding compared with vitamin K antagonists such as warfarin. Hemopericardium is a lifethreatening bleeding event that is rarely caused by anticoagulants. We describe the case of an 84-year old male patient who was diagnosed with nonvalvular atrial fibrillation and treated with apixaban, and presented with severe anemia and hypotension with no apparent bleeding sources. Further diagnostic testing with CT scan and transthoracic echocardiography showed cardiac tamponade treated urgently by pericardiocentesis.

Keywords: Non valvular atrial fibrillation; Apixaban; Hemopericardium

Introduction

Inhibitors of factor Xa in the coagulation cascade such as apixaban become more popular as one of the DOACs due to its rapid absorption and multiple medical uses [1]. This novel agent is preferable over warfarin mainly for its decreased risk of bleeding events as well as better facility in follow up with lake to dosing adjustments according to international normalized ratio (INR) [2]. Despite all apixaban's benefits, it can still causes major and non-major hemorrhage complications that may need medical and interventional therapy for stabilization [3]. Hemorrhagic cardiac tamponade (HCT) is a serious life-threatening condition happening in many medical circumstances such as trauma, cardiac surgery, acute myocardial infarction, aortic dissection and malignancy. To note that anticoagulation related HCT is rarely reported in literature as principal cause of bleed in the absence of precipitating factors [4]. In this report, we present a case of hemopericardium complicated by tamponade and kidney injury in an elderly with chronic atrial fibrillation. Patient developed acute blood loss with hemodynamic instability in the context of use of apixaban 5mg twice daily.

Case Presentation

An 84 year old elderly patient with known to have atrial fibrillation on apixaban presented with palor, dyspnea and lethargy. Vital signs upon presentation showed blood pressure 80/50 mmHg, heart rate 45 beats/min, temperature 36.8 °C and oxygen saturation 80%. He was in moderate respiratory distress with jugular venous distension, lungs were clear to auscultation, distant and muffled heart sounds. A chest radiograph revealed a significant cardiomegaly and bilateral minimal pleural effusions, which were not demonstrated in his previous chest films. Laboratory tests showed severe anemia with 4 units drop in hemoglobin (compared to his baseline hemoglobin one week ago) associated with acute kidney injury and electrolytes disturbance. The laboratory and imaging findings (Tables 1,2).

Medical history is negative for any melena, rectorrhagia or hematemesis. Stabilization with face mask oxygen, IV hydration and transfusion immediately started. An urgent TTE showed a large circumferential pericardial effusion measuring 2.5 cm and evidence of tamponade physiology. The mitral inflow dopplers

showed evidence of more than 25% respiratory variation. The late diastolic collapse of the right atrium and early diastolic collapse of the right ventricular free wall was seen.

Table 1: Laboratory results.

	Day 0	Day 5	Day 10
Hemoglobin	6.8	8.9	10.4
Hematocrit	23	27.2	32.4
Creatinine	3.51	2.17	0.85
Sodium	173	153	142
Potassium	4.55	3.81	3.75

Table 2: Pericardial fluid analysis.

RBC	LDH	PROTEIN	ALBUMIN
3552000	295 IU/L	49.3 g/L	25.4 g/L

Plethora of the IVC was also noted. Urgent pericardiocentesis was performed with drainage of 2600 ml of bloody fluid. Patient's hemodynamics improved immediately after drainage of the large pericardial effusion along with amelioration of his anemia, renal failure and electrolytes disturbances. Further Computed tomography scan findings supported the diagnosis of hemopericardium, with no evidence of kidney obstruction, active gastro-intestinal bleeding or malignancy. Flow cytometry, histopathology, immune staining, and cultures were negative for malignancy or infection. Patient was discharged after ten days with return to his baseline (Figures 1,2).

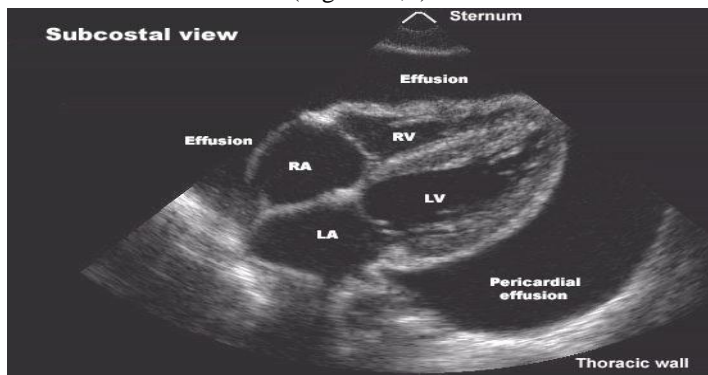


Figure 1: Echocardiography showed large circumferential pericardial effusion.

Discussion

Among randomized controlled trials, only five trials have reported pericardial hemorrhage with DOACs (incidence 0.05%) [5]. In the setting of pericarditis the use of anticoagulation mainly heparin has been documented to produce hemorrhagic cardiac

tamponade [6]. Only a few reports exist concerning hemopericardium in patients treated with VKAs [4]. Identified in a systematic review 26 cases of hemorrhagic tamponade with mean age of 70 years and male predominance of 73% taking DOAC. This life threatening complication was seen mainly with rivaroxaban use (46%) followed by dabigatran and apixaban with 37% and 19% successively [7].

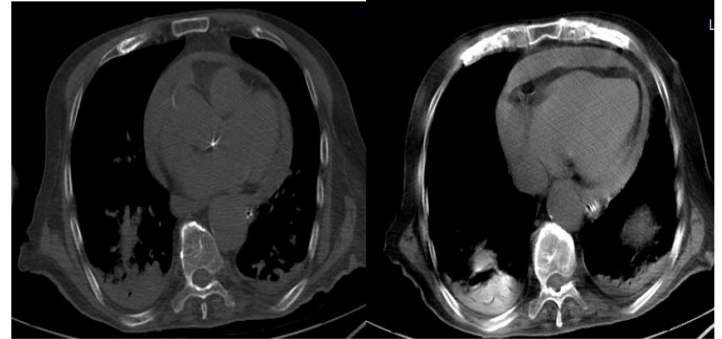


Figure 2: CT scan Chest showed a large circumferential pericardial effusion.

The highest incidence of hemorrhagic cardiac tamponade in rivaroxaban group may be due to being the most commonly used DOAC at the time of the reported cases [8]. Multiple risk factors were noted in the reported cases including old age, male gender, hypertension, and drug interactions, elevated INR and elevated Cr. The patient in our case was free of major risk factors that may increase the risk of bleed with the use of DOAC; he had normal creatinine before being started on apixaban, not taking any medications that can interact with this DOAC increasing its level in the blood and not taking any NSAID or antiplatelets that can increase the bleeding risk. The first case report of hemopericardium secondary to apixaban treatment of atrial fibrillation after 6 weeks of therapy. In this study, the hemorrhagic pericarditis with apixaban may be explained by the drug interaction with venlafaxine or the decreased GFR which cause an increase in the apixaban blood levels. Malignancy is a major cause of hemopericardium as previously reported [9,10]. It accounts for 65% of the primary etiology of patients presenting with cardiac tamponade requiring urgent drainage in a 10 years prospective survey in a single-center, and it may be the first and only manifestation of non-cardiac primary neoplasm, which is not the case in our patient; the pericardial fluid cytology was free of malignant cells. In a reported case the reversal of bleeding in hemopericardium in patients taking dabigatran has been successful with the antidote idarucisumab [11]. For the other DOAC therapies andexanet alfa is an agent shown to rapidly reverse the anticoagulant effects of direct and indirect (enoxaparin and fondaparinux) factor Xa inhibitors; this agent reverse the effects of rivaroxaban and apixaban and could offer a solution for the patients presenting with such life-threatening complication

like our patient, although no phase three clinical trials or head-to-head trials with usual care are currently available [12,13]. Our case report adds to the growing evidence for the major bleeding complications with the use of DOACs especially for the life threatening hemorrhagic cardiac tamponade that require a high clinical suspicion in any patient presenting with signs of shortness of breath or chest pain or any other manifestation of pericardial effusion shortly after starting on any DOAC therapy.

Conclusion

This article aims to alert clinicians to this rare but increasingly reported side effect of apixaban. A high index of clinical suspicion is needed for recognition and diagnosis of spontaneous hemopericardium. Caution should be observed especially in elderly patients with declining renal function. With increasing use of apixaban and other novel anticoagulants and the recent approval of a new reversal agent, more research are needed to develop monitoring laboratory parameters to determine and monitor their therapeutic range.

References

1. Bristol-myers Squibb Company. Prescribing Information. 2018.
2. Touma L, Filion KB, Atallah R, Eberg M, Eisenberg MJ. A meta-analysis of randomized controlled trials of the risk of bleeding with apixaban versus vitamin K antagonists. *Am J Cardiol.* 2015; 115: 533-541.
3. Eisho S, Nouran M, Salem, Janet L, Hoffman, John M, et al. Major bleeding with apixaban in atrial fibrillation, patient characteristics, management, and outcomes. *Hospital Practice.* 2018; 46: 165-169.
4. Sigawy C, Apter S, Vine J, Grossman E. Spontaneous Hemopericardium in a patient receiving apixaban therapy: First Case Report. *Pharmacotherapy.* 2015; 35: 115-117.
5. Singh A, Verma V, Chaudhary R. Direct oral anticoagulants associated hemopericardium. *Am College cardiol.* 2021.
6. Xu B, MacIsaac A. Life-threatening haemorrhagic pericarditis associated with rivaroxaban. *Int J Cardiol.* 2014; 174: 75-76.
7. Asad ZUA, Ijaz SH, Chaudhary AMD, Khan SU, Pakala A. Hemorrhagic cardiac tamponade associated with apixaban: a case report and systematic review of literature. *Cardiovasc Revasc Med.* 2019; 20:15-20.
8. Loo SY, Aniello SD, Huiart L, Renoux C. Trends in the prescription of novel oral anticoagulants in UK primary care. *Br J Clin Pharmacol.* 2017; 83: 2096-2106.
9. Cinelli M, Uddin A, Duka I, Soomro A, Tamburrino F, Ghavami F, et al. Spontaneous hemorrhagic pericardial and pleural effusion in a patient receiving Apixaban. *Cardiol Res.* 2019; 10: 249-252.
10. Cornily JC, Pennec PY, Castellant P, Bezon E, Gal GL, Gilard M, et al. Cardiac tamponade in medical patients: a 10-year follow-up survey. *Cardiol.* 2008; 111: 197-201.
11. Hsi DH, Krishnamurthy M, Ryan GF, Luo P, Woodlock TJ. Successful management of hemopericardium and cardiac tamponade secondary to occult malignancy and anticoagulation. *Exp Clin Cardiol.* 2010; 15: 33-35.
12. Song S, Cook J, Goulbourne C, Meade M, Saliccioli, Lazar J, et al. First reported case report of hemopericardium related to dabigatran use reversed by new antidote Idarucizumab. *Case Rep Cardiol.* 2017; 6458636.
13. Andexxa-an antidote for apixaban and rivaroxaban. *JAMA.* 2018; 320: 399-400.