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Original Article

Spontaneous Hemopericardium with Dabigatran Etexilate

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ABSTRACT

A 66-year-old male who presented to ED with chest pain associated with shortness of breath. At presentation, he was found to be in atrial fibrillation (A-fib) with rapid ventricular rate (RVR). A-fib converted spontaneously to normal sinus rhythm (NSR). However, he remained tachycardic, hypotensive and dyspneic. A stat chest computed tomography scan (CT) was performed and showed large pericardial effusion with Hounsfield units of 12 in the anterior pocket and 21 in the posterior pocket. A beside echocardiography was performed, and was consistent with cardiac tamponade. Pt was taken emergently to cardiac catheterization lab for pericardiocentesis. 500 cc of hemorrhagic pericardial fluid was aspirated, and hemodynamics improved immediately. Approximately 2 weeks prior to the admission, the patient had been started on dabigatran etexilate (Pradaxa) for newly diagnosed non-valvular paroxysmal atrial fibrillation.

Key words: Atrial fibrillation, Pardaxa, Oral anticoagulant, Hemopericardium, Dabigatran Etexilate.

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BACKGROUND

A 66-year-old Caucasian male presented to ED after having chest pain associated with shortness of breath (SOB). At presentation, he was found to be in A-fib with RVR. On admission, A-fib spontaneously converted to normal sinus rhythm. However, he remained tachycardic, hypotensive and dyspneic.

Approximately 2 weeks prior to the admission, the patient had been started on dabigatran etexilate (Pradaxa) 150 mg orally twice/day for the treatment of newly diagnosed, nonvalvular paroxysmal atrial fibrillation. His other medications consisted of cetirizine, metoprolol, simvastatin, omeprazole, calcium carbonate, and a multivitamin. The patient's serum creatinine concentration at that time was 1 mg/dl, with an estimated creatinine clearance of 78 ml/minute (using the Cockcroft-Gault equation). His other medical history includes hypertension, alcohol and tobacco dependence, diabetes, chronic back pain, carotid artery disease, infrarenal abdominal aortic aneurysm, and coronary artery disease.

The patient was in his usual state of health till the day prior to the admission when he experienced fatigue and dizziness. He noticed his systolic BP was in low 80's. Later in the day he experienced SOB, chest pressure and palpitations. Of note, patient denied any injury or falls in recent weeks prior to and after his last visit to ER.

On arrival to the emergency department, the patient was afebrile. Vital signs included HR of 120 beats/min, RR of 30 breaths/min, oxygen saturation of 99% and BP of 90/60 mm/Hg. Lungs were clear to auscultation. Cardiac exam revealed tachycardia with very distant heart sounds. Other physical exam was unremarkable. Pertinent laboratory findings on admission were serum hemoglobin 9.5g/dl (11.6–15.2 g/dl), creatinine 1.7 mg/dl (estimated creatinine clearance 45 ml/minute), prothrombin time 23.8 seconds (9.5–13.1 sec), international normalized ratio (INR) 1.8 (0.9–1.1), and activated partial thromboplastin time (aPTT) 55 seconds (24–35). Levels of troponin, creatine kinase, white blood cell count, platelet count, serum bicarbonate, and blood urea nitrogen were normal. New changes in lab findings in comparison to the previous admission were elevated creatinine and hemoglobin drop from 12.5g/l to 9.5g/l. First EKG showed A-fib with RVR

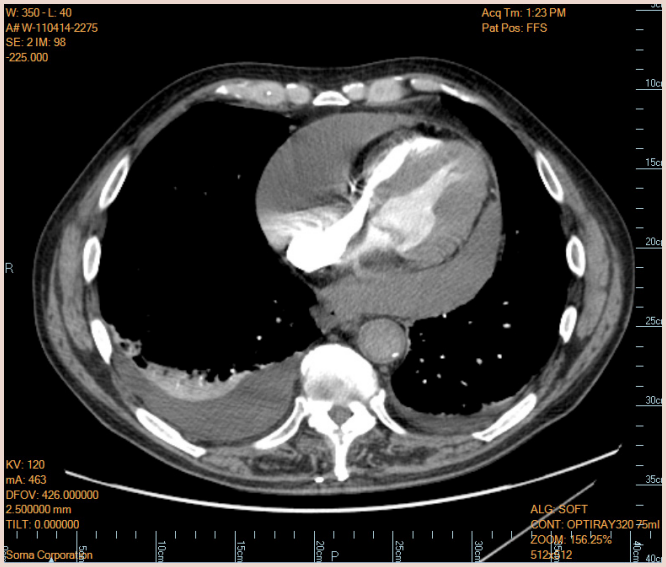

Figure 1: Chest CT, large circumferential pericardial effusion (white arrows).

with non-specific ST-T changes however patient's rhythm spontaneously converted to NSR.

In the ED, because of respiratory distress, a contrast computed tomographic scan was obtained (Figure 1), which showed a large pericardial effusion (right fluid pocket measures 4.9 cm and the posterior pocket measures 4.2 cm. The pericardial fluid has Hounsfield units of 12 in the anterior pocket and 21 in the posterior pocket.). There was no structural abnormality or great vessels abnormality. An emergent echocardiography (Figure 2) was performed and showed severe early diastolic right atrial and right ventricular collapse, which was consistent with tamponade. Patient was urgently taken to cardiac catheterization lab for pericardiocentesis. 500 cc of hemorrhagic pericardial fluid was aspirated. Fluid

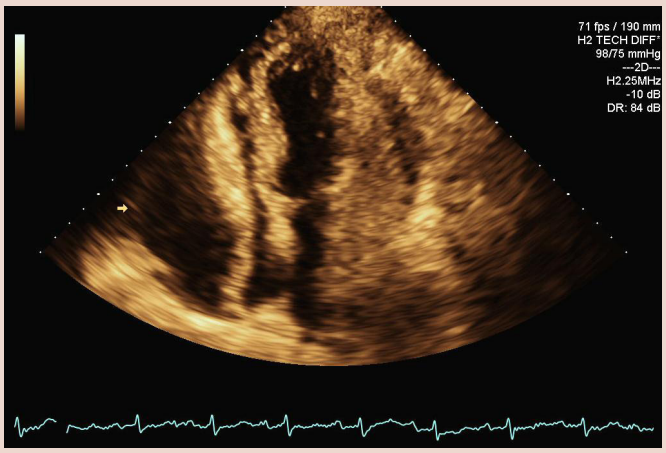

Figure 2: Echo at time of presentation (pericardial effusion yellow arrow, Right atrial collapse white arrow).

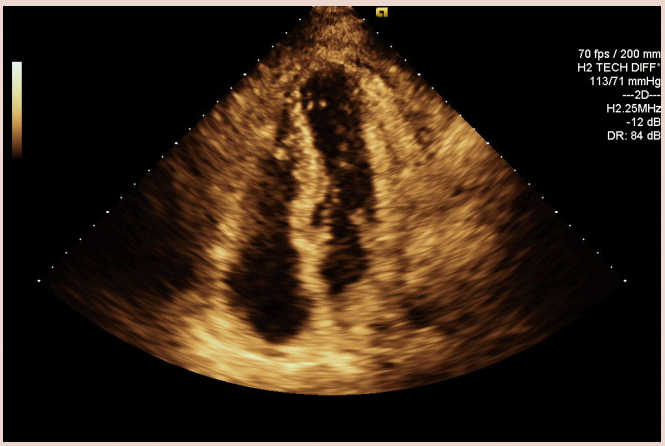

Figure 2: Echo after pericardiocentesis

was sent for cytology and diagnostic workup for further evaluation. Hemodynamics improved immediately, with increase in SBP to 140s and decrease in HR to 70's.

Dabigatran etexilate was discontinued because of concern for hemopericardium. After pericardiocentesis, the patient remained hemodynamically stable without progression of effusion; therefore, no attempt was made to reverse anticoagulation. Cytological examination of the pericardial fluid revealed no malignant cells and was described as fresh blood. Chemical analysis showed a glucose level of 34 mg/dl, protein 4.6 g/dl, lactate dehydrogenase 300 u/l, red blood cell count greater than 0.1 x 10^6/mm^3, and white blood cell count 5.2 x 10^3/ mm^3 (neutrophils 66%, lymphocytes 19%, monocytes 9%, eosinophils 5%, and basophils 1%).

Transthoracic echocardiography was performed on hospital day-3 that showed minimal residual pericardial effusion (Figure 3). Gram stain, bacterial culture, mycobacterial culture, AFB stain, adenosine deam nase and fungal culture were negative. Also immuno-histochem cal staining for B72.3, BerEP4, PSA, PSAP, TTF-1 and Napsin showed no evidence of metastatic carcinoma.

DISCUSSION

Hemopericardium has been reported in patients with malignancy, post percutaneous interventional procedures, post-pericardiotomy syndrome, post-myocardial infarction thrombolysis, aortic dissection, infection and trauma.[1] Our case did not have any of the aforementioned etiologies.

There are few case reports of non-traumatic hemopericaridum in setting of warfarin therapy.[2,3] Most of these cases, which were reported so far, had supra-therapeutic anticoagulation.[4,5] In the RE-LY trial risk of hemopericardium was 0.03% (3 case reports on dabigatran etexilate150 mg BID)[6]. So far, to the best of our knowledge, only 5 cases of hemopericardium related to dabigatran etexilateuse (150 mg BID) were reported in medical litretures.[7-9] Some of the case reports suggested that dabigatran may cause serious bleeding events, particularly in the setting of acute renal failure.[10] According to the pharmaceutical company and the FDA-approval, there is no need for dosage adjustment in CrCl >30 mL/minute. In most case reports, patients had decreased GFR however the GFR cut off for dabigatran use is 30 mL/minute which was not applicable to our case. Of note, our patient had acute kidney injury (AKI) on presentation, which was most likely secondary to decreased cardiac output and subsequent reduced renal blood flow. AKI resolved after redundant resolution of tamponade and restoration of normal hemodynamic function.[11] The other possible factor(s) that would increase the risk of hemopericardium with dabigatran use could be pericarditis or pericardial effusion.[12,13] In our case, there was no such a history or physical finding before initiation of the dabigatran therapy. As there was no echocardiography before initiation of therapy, we could not completely exclude this possibility.

Aside from acute complication of hemopericardium and tamponade, constrictive pericardium has been reported in patient with hemopericardium as well.[14] Managing life threatening bleeding in patients receiving dabigatran etexilate is challenging since there is no specific antidote at present or any proven anticoagulation reversal agent for it. There is an antibody based antidote for Pradaxa in the development phase.[15]

CONCLUSION

Our case report adds to the previous reports of hemopericardium associated with dabigatran etexilate (Pradaxa). We believe that in our case the initiation of dabigatran etexilate led to the spontaneous development of hemopericardium and tamponade. We also propose that if there is a high clinical suspicion of ongoing pericardial processes, a screening echocardiography may be judicial before initiating an anticoagulant therapy. More importantly, complaint of increasing short of breath or hypotension in patient on therapeutic anticoagulation should raise concerns regarding hemopericardium and cardiac tamponade. This case with other case reports highlight concerns regarding the newer oral anticoagulants and their association with development of hemopericardium. Further studies will be needed to clearly identify the risk factors that potentiate the risk of hemopericadium in patient who are on the new oral anticoagulants.

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