CASE REPORT

Bleeding heart: a case of spontaneous hemopericardium and tamponade in a hyperthyroid patient on warfarin

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Accepted 27 June 2016

SUMMARY

We describe the case of an 81-year-old female, diagnosed with hyperthyroidism-related atrial fibrillation. Given her CHA2DS2VASc score of 3, she was started on warfarin for stroke prevention. One month later, she was admitted with cardiac tamponade. This tamponade was suspected to be secondary to hemopericardium, based on the elevated international normalized ratio (INR), drop in haemoglobin and the radiodensity (55 HU) of the pericardial effusion on CT. The patient was a Jehovah's witness who therefore initially refused measures for reversing coagulopathy. Given her coagulopathy and absence of imminent haemodynamic compromise, pericardiocentesis was deferred. Unfortunately, 1 day later, the patient deteriorated rapidly. By the time pericardiocentesis was performed and factor VIIa administered, the patient had already started developing multiple organ failure. She developed cardiac arrest and died 3 days after her admission. Only 10 cases of hemopericardium attributable to warfarin have previously been reported. In this report, we review the literature and also describe how hyperthyroidism most likely predisposed our patient to bleeding complications from warfarin.

BACKGROUND

Accumulation of haemorrhagic fluid in the pericardium is called hemopericardium. This can result in cardiac compression, which in turn has the potential to cause tamponade.¹ Spontaneous hemopericardium refers to bleeding into the pericardial sac in the absence of a local pathological lesion.² Anticoagulation is an uncommon cause of spontaneous hemopericardium. There have been 10 previously reported cases of spontaneous hemopericardium in patients on warfarin. We present this case to further expand on this unusual occurrence and also explain the potential role played by our patient's hyperthyroid state.

CASE PRESENTATION

An 81-year-old female with a medical history of osteoarthritis presented to the emergency department with 2 weeks of intermittent palpitations. ECG (figure 1) showed atrial fibrillation with rapid ventricular response along with Q waves in V1–V2, suggesting an old septal infarct. Transthoracic echocardiogram showed an ejection fraction of 70–75%, no regional wall motion abnormalities and mild mitral and tricuspid regurgitation. Laboratory investigations were significant for thyroid

stimulating hormone (TSH) of <0.015 µIU/mL and free thyroxine of 4.85 ng/dL. Her haemoglobin was 10 g/dL with a mean corpuscular volume of 87 fL, ferritin of 377 ng/mL and normal vitamin B12 and folate levels. Her CHA2DS2VASc score of 3 imparted her a 3.2% per year risk of stroke and therefore she was started on warfarin.^{3–4} Prior to discharge, she was also started on metoprolol for rate control and methimazole for hyperthyroidism. One week later, the patient presented to the laboratory for an international normalized ratio (INR) check which was reported as 6.6. The patient's friend, who was listed as the only contact person, was called and informed of this. She was instructed to convey this information to the patient and advise her to discontinue warfarin for the time being. She was also instructed to bring the patient back for a repeat INR check in 3–4 days. It is unclear, however, if this information was relayed to the patient or not.

One month after her initial discharge, the patient presented to the emergency department with 3 weeks of epigastric pain and 1 week of nausea and loss of appetite. She was afebrile with a blood pressure of 145/95 mm Hg; her pulse was irregular at 125 bpm, and respiratory rate and oxygen saturation were normal. Physical examination revealed elevated jugular venous pressure; the rest of the cardiovascular and respiratory examinations were normal. Abdominal examination showed mild epigastric tenderness to palpation.

INVESTIGATIONS

Haemoglobin was 9.1 g/dL (down from 10 g/dL), partial thromboplastin time (PTT) was 99.1 s, and prothrombin time (PT) was 103 s with an INR of 12.7. Thyroid profile was unchanged with a TSH of <0.015 µIU/mL and free thyroxine of 4.49 ng/dL. Basic metabolic profile and the rest of the complete blood count were normal. ECG was also unchanged from the prior admission. Chest X-ray revealed mild cardiomegaly and a left-sided pleural effusion. CT scan revealed a large pericardial effusion and cardiomegaly (figure 2). CT also revealed compression of the right atrium and deviation of the interatrial septum and dilated superior and inferior vena cavae (figure 3). These findings were suggestive of tamponade physiology.^{5–6} Echocardiogram confirmed the CT findings of a large pericardial effusion and tamponade physiology.

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To cite: Sajawal Ali M, Mba BI, Ciftci FD, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-215731

Figure 1 ECG showing atrial fibrillation with rapid ventricular response and Q waves in V1–V2.

DIFFERENTIAL DIAGNOSIS

Given the drop in haemoglobin, elevated INR and large pericardial effusion, the top differential at this point was hemopericardium leading to tamponade. The diagnosis of hemopericardium was also supported by the 55 HU radiodensity of the pericardial effusion on CT.⁷

TREATMENT

The patient was offered fresh frozen plasma (FFP) to reverse coagulopathy; however, she refused since she was a Jehovah's witness. She requested to talk to her religious elders before accepting FFPs and most other agents to reverse coagulopathy. She was therefore administered 10 mg of vitamin K intravenously and started on diltiazem for control of heart rate. Given her coagulopathy and absence of imminent hemodynamic compromise, it was decided to postpone pericardiocentesis until her coagulation profile improved. She was admitted to a telemetry unit for close monitoring.

OUTCOME AND FOLLOW-UP

One day later, the patient was found to be confused and dyspnoeic. She reported worsening abdominal pain. She had a respiratory rate of 26/min, pulse of 130/min, blood pressure of

125/75 and was saturating 89% on room air. She was in respiratory distress and was using accessory respiratory muscles. Repeat laboratory investigations revealed a PT of 120 s, INR of 14.7 and PTT of 167 s. Haemoglobin had dropped to 8.4 g/dL and the white cell count had gone up to 15.9 K/ μ L. She was emergently intubated, soon after which her blood pressure dropped. Intravenous fluids and pressors were started. Emergent pericardiocentesis was performed which produced 400 cc of haemorrhagic fluid. The patient was transferred to the coronary care unit.

At this point, the patient's friend contacted us and informed that their minister had approved the use of recombinant factor VIIa. She was administered factor VIIa, along with a repeat dose of vitamin K intravenously (5 mg). Unfortunately, despite this, the patient's condition continued to deteriorate. Repeat investigations revealed a white cell count of 36.3 K/ μ L and haemoglobin of 7.3 g/dL. The next morning, the patient developed pulseless electrical activity from which she was successfully resuscitated. She was still requiring ventilatory support and an escalating dose of pressors. Later that day, her haemoglobin dropped to 6.0 g/dL and she developed liver and renal failure, with a total bilirubin of 8.3 ng/dL, aspartate aminotransferase of 5421 U/L, alanine aminotransferase of 13 338 U/L and serum creatinine of 4.3 mg/dL. The patient again developed cardiac arrest and could not be revived. She was pronounced dead 3 days after presenting to the emergency department.

DISCUSSION

Hemopericardium has a range of clinical manifestations from being relatively asymptomatic to presenting with cardiac tamponade. Ernest Starling defined tamponade in 1897 as compression of the heart by fluid in the pericardial sac impairing diastolic filling of the ventricles. Recent authors have modified the definition and have defined it as meaning pericardial effusion causing dyspnoea, with the latter being relieved by pericardiocentesis.⁸

Cardiac tamponade is a serious condition which may initially be stable but can rapidly deteriorate into a life-threatening haemodynamic compromise, much like what happened to our patient.⁹ Tamponade occurs when the pericardial pressure exceeds the atrial venous pressure, thereby impeding venous

Figure 2 Large pericardial effusion (red arrows).

Figure 3 (A) Right atrial compression (red arrow). (B) Interatrial septal deviation (red arrow). (C) Dilated superior vena cava (red arrow). (D) Dilated inferior vena cava (red arrow).

return to the heart.¹⁰ Three factors determine the acuity of presentation: volume of fluid in the pericardial sac, rate of accumulation and pericardial compliance.^{11 12} As little as 200–300 mL of rapidly evolving hemopericardium is more likely to be fatal than a slowly evolving 2000 mL hemopericardium.¹⁰ Common symptoms of tamponade include dyspnoea, tachypnoea and fatigue, while common signs are raised jugular venous pressure, hypotension, diminished heart sounds and pulsus paradoxus.¹³

Causes of hemopericardium have evolved over time. While in the 1960s its most common aetiology was dissecting aortic or syphilitic aneurysms, in a series published by Atar *et al*¹⁴ in 1999, iatrogenic trauma, malignancy and myocardial infarction were found to be the foremost aetiologies. In another series published by Swaminathan *et al*¹⁵ in 2007, myocardial infarction and dissecting aortic aneurysm were the top causes. Others have also identified blunt chest trauma as an aetiology.¹⁶

Even though pericardial fluid cultures and cytology could not be obtained in our case given the temporal association with the initiation of anticoagulation, high INR and lack of alternative explanations on history, examination and imaging, the presumed cause of our patient's hemopericardium was warfarin. There are 10 other hemopericardium cases reported in the literature where warfarin was deemed to be the culprit.

Fell *et al* described two cases of hemopericardium in 1965. The first patient was on warfarin for atrial fibrillation and presented with chest pain, vomiting and anorexia. His PT was 94 s with a control of 12.8 s. The diagnosis of hemopericardium was established postmortem. The second patient had been on warfarin since a myocardial infarction and presented with chest pain. His PT was 23.2 s with a control of 11.2 s. He was found to have tamponade and did well after pericardiocentesis.¹⁷ Miler *et al*¹⁸ described a case of tamponade due to hemopericardium in a patient receiving warfarin for deep venous thrombosis prophylaxis. The patient presented with shock; his PT was 53 s with a control of 11 s. He did well after pericardiocentesis.¹⁸ Granot *et al*¹⁹ described a patient who had been on warfarin for deep venous thrombosis treatment. The patient presented with shoulder pain, dyspnoea and abdominal discomfort. His PT was 42 s with a control of 11 s. He was found to have tamponade and did well after pericardiocentesis.¹⁹ Lee *et al*²⁰ described a patient who had been on warfarin for

vertebral-basilar artery insufficiency and presented with abdominal distension. His PT was 30 s (therapeutic range 18–20 s). Hemopericardium was diagnosed and the patient did well after pericardiocentesis.²⁰ Katis *et al*²¹ reported a patient who was being treated for a pulmonary embolus with warfarin. The patient presented with chest pain and dyspnoea. Her INR was 3.51 and she did well after pericardiocentesis.²¹ Hong *et al* described the case of a patient who had been on warfarin since a mitral valve replacement. The patient developed dyspnoea, orthopnoea and was found to have tamponade. His INR was 7.52. The patient recovered after pericardiocentesis.²² Griffins *et al* reported a patient who was taking warfarin for atrial fibrillation and presented with melaena and shock. His INR was >15 and he was found to have hemopericardium postmortem.² Levis *et al* described another patient on warfarin for atrial fibrillation, who presented with hypotension and syncope. His INR was elevated at 6.0. The patient did well after pericardiocentesis.¹¹ Finally, Al-Judi reported a case of tamponade due to hemopericardium in a patient who had been taking warfarin for atrial fibrillation and presented with epigastric pain. Her INR was 16.9. The patient survived after pericardiocentesis.²³

In our case, given the patient's beliefs, we were unable to reverse the coagulopathy quickly enough. Therefore, pericardiocentesis was deemed unsafe on admission, especially given her relative haemodynamic stability early on. Unfortunately, our patient deteriorated rapidly. By the time pericardiocentesis was performed and factor VIIa administered, the cascade of organ hypoperfusion leading to multisystem failure had already set in. The vitamin K administered on admission most likely failed for the same reason.

Looking back at the case, while there is little that could have been done differently by the time the patient was admitted with tamponade, perhaps there should have been further deliberation on the risk benefit ratio of anticoagulation on her previous admission. We calculated our patient's CHA2DS2VASc score which gave her a 3.2% per year risk of stroke. While this is a high enough risk to justify prophylactic anticoagulation in most patients, our patient's bleeding risk was also high. Her HEMORR2HAGES score was 2 (points for age and anaemia), which imparted her a 5.3/100-patient-years risk of major

bleeding.²⁴ The patient's hyperthyroid state was another factor which had earlier inclined us to pursue anticoagulation. However, a closer look at the literature reveals that even though data regarding the relative risk of stroke in hyperthyroidism-related atrial fibrillation were conflicting in the past, two recent studies show that hyperthyroidism is not an independent risk factor for stroke in atrial fibrillation.^{25 26} In fact, hyperthyroidism increases the bleeding risk associated with vitamin K antagonists.²⁷ Thyrotoxicosis decreases the warfarin requirements by speeding up the degradation of coagulation factors.²⁸ Hyperthyroidism also potentiates warfarin mediated hypoprothrombinaemia.²⁹ Non-vitamin K oral anticoagulants can potentially be considered in such cases. Finally, even if the risks and benefits of anticoagulation had otherwise been balanced, our patient's pertinent religious beliefs should have been considered. Having a frank discussion with a Jehovah's witness patient about the potential need for blood products, should bleeding complications arise, might be helpful in making decisions regarding anticoagulation. In retrospect, given our patient's HEMORR2HAGES score, hyperthyroidism and aversion to blood products, anticoagulation should probably have been avoided.

Learning points

- ▶ Spontaneous hemopericardium, with or without tamponade, is an uncommon haemorrhagic complication of warfarin therapy.
- ▶ Cardiac tamponade can present with non-specific symptoms such as abdominal pain; therefore, clinicians should maintain a high index of suspicion in the right setting.
- ▶ CT findings of superior and inferior vena cavae dilation, inter atrial septal deviation and coronary sinus compression are suggestive of tamponade in a patient with pericardial effusion.
- ▶ Bleeding risk prediction models such as HEMORR2HAGES must always be employed before initiation of anticoagulation.
- ▶ Recent literature shows that while hyperthyroidism is not an independent risk factor for stroke in atrial fibrillation, it does significantly increase the bleeding risk with anticoagulation.

Acknowledgements The authors are grateful to all colleagues at the Department of Medicine, John H. Stroger, Jr. Hospital of Cook County.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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