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Case Study

Abdominal Aortic Aneurysm with Persistent and Rebound Coagulopathy Despite Aggressive Corrective Treatment: A Case Report

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Abstract

Abdominal aortic aneurysm (AAA) is not uncommon to cause coagulopathy. Warfarin use in patients presented with ruptured AAA can further complicate the preparation for surgical intervention and affect prognosis. We reported a case of impending rupture AAA that progressed to contained leak AAA in a warfarin user, with persistent elevated and rebound international normalized ratio (INR) despite aggressive correction with fresh frozen plasma (FFP) and three-factor prothrombin complex concentrate (3F-PCC). Persistent and rebound coagulopathy is possible in AAA. Corrective treatment with FFP or 3F-PCC alone does not always guarantee the successful reversal of coagulopathy in AAA. Some cases, especially those that failed the initial corrective treatment, require more aggressive reversal with co-administration of vitamin K. This case described coagulopathy in AAA, anticoagulation reversal agents used and emphasized the importance of rigorous coagulation profile monitoring in managing AAA.

Keywords:- Abdominal Aortic Aneurysm, Coagulopathy, Three-Factor Prothrombin Complex Concentrate, Fresh Frozen Plasma

Introduction

Abdominal aortic aneurysm (AAA) is not uncommon to cause coagulopathy. In patients presenting with ruptured AAA, the incidence of significant coagulopathy and disseminated intravascular coagulation (DIC) are 6% and 2.4%, respectively (Kordzadeh *et al.*, 2016). Patients on warfarin presented with AAA can further complicate the coagulopathy management in preoperative preparation. This case report describes tenacious coagulopathy despite aggressive pre-surgical haemostatic treatment in a ruptured infrarenal AAA patient on warfarin therapy for underlying mitral valve replacement (MVR). This case report was registered under the Malaysian Medical Research and Ethics Committee, Ministry of Health Malaysia (NMRR ID-22-00525-CZP).

Case Study

A 57-year-old man was referred to Hospital Kuala Lumpur for impending rupture of mycotic infrarenal AAA. He had underlying prosthetic MVR, ischemic heart disease (history of stenting and coronary artery bypass graft), hypertension, diabetes, dyslipidemia and cholelithiasis. Due to the AAA, he is on lifelong warfarin with a target international normalized ratio (INR) of 2–3.

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This patient presented to a district hospital with abdominal pain and intermittent fever for three days. His vital signs were stable. His initial INR was 3.29. CTA abdomen findings (Fig. 1) suggested infrarenal AAA with impending rupture (8.5 x 7.5 x 13.3 cm); left iliac fossa artery contained contrast leak in left iliopsoas muscle and surrounded by perivascular soft tissues suggestive of pseudoaneurysm; right common iliac artery fusiform aneurysm (Figure 1). His blood culture grew Salmonella non-tophi. He was given four units of fresh frozen plasma (FFP) before being transferred to our centre.

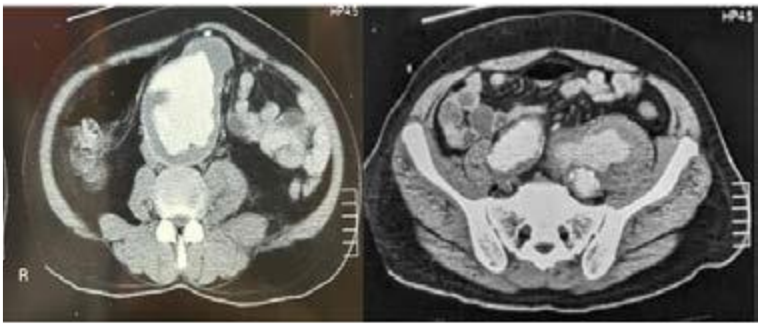

Figure 1: Patient's CT abdomen

On arrival at our centre, the patient's vital signs were stable, except having a temperature of 38oC. Coagulation profile on day-2 showed PT, 31.6s, INR, 2.73; and aPTT, 70.2s. Given the need to reverse the anticoagulation effects of warfarin for surgical intervention, the patient was given another six units of FFP. However, the patient developed urticaria over the abdomen area and pruritus after the FFP transfusion, and he was given IV hydrocortisone and chlorpheniramine. His INR remained elevated post-FFP (PT, 25s; INR, 2.18; and aPTT, 59s). Subsequently, 975 units (15 units/kg) of 3F-PCC was given to this patient after a total of 10 units of FFP (> 20 ml/kg) was given within the last 24 hours.

Following the administration of 3F-PCC, the INR showed an unexpected increment from 2.18 to 2.85. Given the urgency for surgery and despite previous transfusion reaction, the patient was given another six units of FFP plus 10mg of IV vitamin K1, after which the INR was successfully reduced to <1.5 (INR 1.28). The patient underwent an open aneurysmectomy and inlay graft repair on day-4. Intraoperatively, he was transfused with 3 pints packed cells, 4 units of FFP and 6 units of cryoprecipitate due to massive blood loss (estimated 3.7L).

Post-surgery and without any anticoagulant, he continued to show labile INR ranging from 1.6 to 2.54. On day-7, the patient's INR dropped to < 2 (Fig. 2) and in view that he has MVR, he was restarted on warfarin and subcutaneous fondaparinux for three days as bridging therapy. The patient was transferred back to the district hospital to continue care. No adverse drug reaction or thromboembolism event was observed during hospitalization. His liver function test was normal throughout the hospitalization.

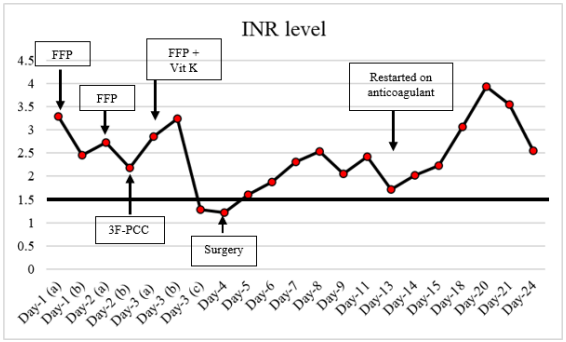

Figure 2: The patient's INR levels throughout the hospitalization

Discussion

Patients with mechanical heart valves (MHV) have a higher risk of thromboembolic events and require long-term anticoagulation with warfarin. Perioperative management in valve replacement patients is challenging as the rapid reversal of anticoagulation exposes the patient to a high risk of valve thrombosis and thromboembolism.

Contained leak and free intraperitoneal rupture are the two types of ruptured AAA. The ruptured AAA is known as a contained leak or retroperitoneal leak if the blood leaks into the retroperitoneal and gets 'contained' by the tissues. A free intraperitoneal AAA rupture is when the rupture is into the peritoneal cavity, and there are no tissues to 'contain' the escape of blood from the aorta (Gawenda & Brunkwall, 2012). Ruptured AAA is an emergency condition with up to 50% mortality requiring surgical intervention to control haemorrhage (Hoornweg *et al.,* 2008). However, differentiation of impending or contained rupture from frank rupture of AAA is vital in selecting proper treatment. Patients with AAA may benefit from preoperative assessment and management before the urgent surgery .

Reported coagulopathy and DIC in AAA are not uncommon. The presence of coagulopathy in patients with ruptured AAA presented during admission to the emergency department has been associated with management failure and higher mortality (Davies *et al.,* 2005). Significant coagulopathy was defined as APTT >40s and/or INR >1.5 and/or platelet count <100x10/L (Greuters *et al.,* 2011). DIC, also known as consumptive coagulopathy, is characterized by systemic activation of the coagulation cascade, which results in the generation and deposition of fibrin and thus the formation of microvascular thrombi in various organs. Consumption of clotting factors and platelets together with derangement in the fibrinolytic system in DIC will eventually lead to life-threatening bleeding (Papageorgiou *et al.,* 2018).

In non-ruptured AAA, endothelial disruption occurs from either dissection or atheromatous plaque rupture. Exposed collagen and tissue factor activate the coagulation cascade, leading to clotting factor consumption. Upon rupture, the activated coagulation system further intensifies. Loss of aortic wall integrity exposes the collagen and subendothelial matrix, resulting in additional thrombin formation (Kordzadeh *et al.,* 2016 & Skagius *et al.,* 2008). It had been proposed that four criteria for DIC associated with AAA, i.e. the presence of acquired chronic bleeding disease with laboratory evidence of consumptive coagulopathy, reversal of coagulopathy post aneurysm repair, and the maintenance of the normal coagulation for at least three months. In this case, the patient did not meet these criteria and resolution of coagulopathy post-repair was not apparent as warfarin therapy was reinitiated on day-6 postoperatively. Furthermore, the platelet levels for this patient were always within the normal range.

A normal coagulation profile is a prerequisite in perioperative management for AAA repair. The selection of the coagulation reversal agents(s) is crucial, especially for valve replacement patients on warfarin therapy, to ensure effective coagulation reversal with minimal risk of thromboembolism. The option of reversal agents for warfarin includes FFP, PCC and vitamin K1. FFP is the fluid portion of the whole blood frozen within eight hours. FFP contains all coagulation factors and is commonly used to correct coagulopathy. Administration of 10–20 ml/kg of body weight can increase coagulation factors by 20–30% to sufficiently correct haemostasis. However, PCC is the preferred reversal agent for anticoagulation if the patient is on warfarin, a vitamin K antagonist. PCC contains only vitamin K-dependent factors. There are two types of PCC available in the market, i.e. 3F-PCC and 4F-PCC. 3F-PCC contains coagulation factors II, IX and X, whereas 4F-PCC contains all the vitamin K-dependent factors II, VII, IX and X. 3F-PCC is the only PCC available in our facility for the reversal of anticoagulation effects of warfarin in patients who require emergency procedure and life-threatening or clinically significant bleeding. 3F-PCC has several advantages over FFP, i.e. rapid reconstitution, small volume, rapid infusion, fast onset of action within 15 minutes, no requirement to check blood group compatibility, minimal risk of viral transmission and transfusion-associated adverse reactions such as circulatory overload and acute lung injury (Tran *et al.,* 2013).

Vitamin K1 is another common drug used in correcting coagulopathy. The onset of IV vitamin K1 in producing coagulation factors is as early as 1 hour, with peak effects for INR normalization at 12–24

hours. A large dose of vitamin K1 (>5mg) can cause warfarin resistance for up to a week due to accumulation in the liver, which can bypass vitamin K epoxide reductase.

Failure to promptly correct the coagulopathy preoperatively had delayed the surgical intervention in this case. We postulated that the coagulopathy was due to both warfarin and coagulation cascade activation triggered by AAA as a total of 10 units (>30mls/kg) FFP given during the first 24 hours could not achieve INR <1.5 as expected. Furthermore, the patient's INR level was unexpectedly rebound from 2.18 to 3.24 after administration of 3F-PCC. Warfarin was withheld for more than 48 hours, and there was no significant warfarin-related drug-drug or drug-disease interaction. Thus, we postulated that the ongoing coagulation process consumed the coagulation factors continuously, although the patient did not fulfil the DIC criteria. The rebound INR post-3F-PCC may suggest the progression of AAA from impending rupture to contained leak at that point as AAA rupture can intensify the activated coagulation. On the fourth corrective treatment, the FFP and Vitamin K combination reduced INR to <1.5 and maintained it for about 24 hours. We did not give Vitamin K early, considering the high thromboembolism risk and the risk of warfarin resistance. In this case, the vitamin K effectively prevented INR from an early rebound and did not cause warfarin resistance. Postoperatively, we observed continuous coagulation activation where INR spontaneously increased to 1.6 within 24 hours and raised to 2.5 by day-5. The INR reduction on day-6 post-operationmight suggest the recovery of the coagulation system.

Conclusion

Corrective haemostatic treatment with FFP or 3F-PCC alone does not always guarantee the successful reversal of coagulopathy in AAA. Some cases, especially those that failed the initial corrective treatment, require more aggressive reversal with co-administration of vitamin K. Rigorous pre-and postoperative monitoring of coagulation profile is needed in managing AAA.

Conflict of Interest

The authors declare that they have no competing interests.

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