# Giant Coronary Artery Aneurysm in a Severe Hemophilia A with Acute Coronary Syndrome: A Case Report and Brief Literature Review

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## ABSTRACT

The management of acute coronary syndromes (ACSs) among adult patients with severe hemophilia A remains a clinical challenge, due to the use of anti-platelet, anti-thrombotic agents and/or revascularization procedures in them. We report here a case of severe hemophilia A presented with acute non-ST elevation myocardial infarction (NSTEMI), with incidental finding of coronary artery aneurysms (CAA), requiring an open-heart surgery. He successfully underwent a combined coronary artery bypass grafting (CABG) and closure of right coronary artery giant aneurysm with factor VIII (FVIII) replacement therapy, without bleeding complications nor requiring blood product transfusion. His FVIII activity level was maintained above 100% during the operation and 72 hours post-operatively. Thereafter, the FVIII coverage was reduced to maintain a trough level above 50% for another 1-week before switching back to his prophylactic dose. No inhibitor was detected. He was put on dual anti-platelets for 6 months, in which was reduced to single anti-platelet until today with no occurrence of chest pain. This case highlighted the occurrence of NSTEMI as a consequence of underlying CAA and its management challenge during the open-heart surgery.

## INTRODUCTION

With significant increased in life expectancy of hemophilia patients, cardiovascular disease risks also have become increasingly common in them as they age. The management of acute coronary syndromes (ACSs) among adult patients with severe hemophilia A and hemophilia B is challenging, as the exposure to antithrombotic agents and/or revascularization procedures may confer an enhanced risk of bleeding in this group of patients. Management of this group of patients is mainly based on experience from case reports and/or opinion of the experts. There is also limited information on the dosage and duration of factor replacement therapy in hemophilia patients undergoing cardiac surgery. We report herein a case of severe hemophilia A presented with acute non-ST elevation myocardial infarction (NSTEMI), with incidental finding of coronary artery aneurysms (CAA), requiring an open-heart surgery.

## CASE REPORT

A 43-year-old engineer, a non-smoker with underlying severe hemophilia A complicated with bilateral chronic arthropathy, who is on prophylaxis of factor VIII (FVIII) replacement 1500IU weekly, presented with acute severe chest pain 4 hours post-infusion of his FVIII. An electrocardiogram (ECG) revealed sinus bradycardia with transient ST-segment elevation at leads I, V5 and V6 that resolved on repeated ECG. Troponin T was increased at 0.030 ng/mL (normal < 0.014 ng/mL). He received a stat dose of 300mg aspirin. He underwent a coronary angiography via radial approach the next day, preceded by a dose of 2000IU of FVIII and 300mg of clopidogrel. Angiography revealed multiple CAA with slow flow in the left anterior descending artery (LAD), left circumflex and right coronary artery, with total occlusion of the left circumflex and mild disease of the LAD. A giant aneurysm was found in the right coronary artery, measuring 41.7 mm in diameter with a length of 48.1 mm **(Figures 1-2)**.

**Figure 1:** 3D reconstruction of CT angiography.

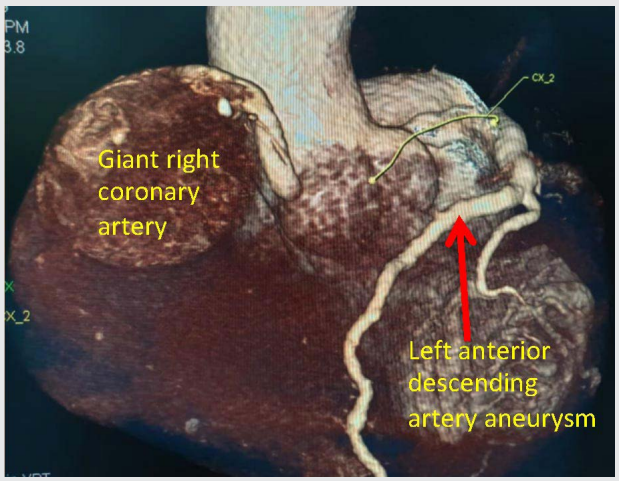
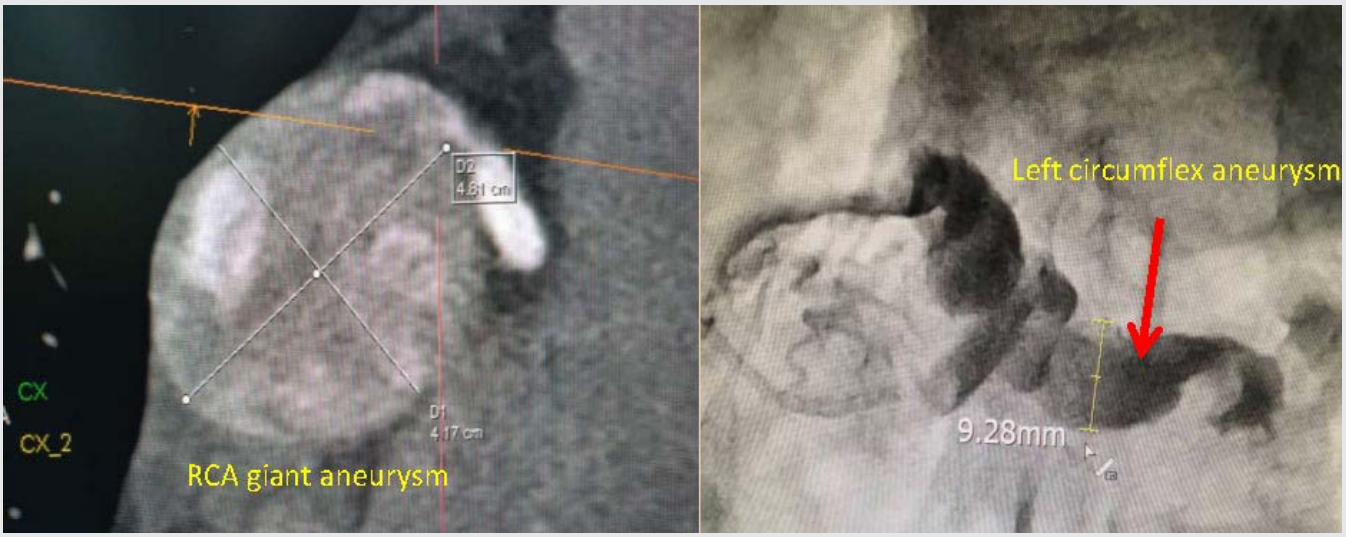


**Figure 2:** Images from CT angiography.



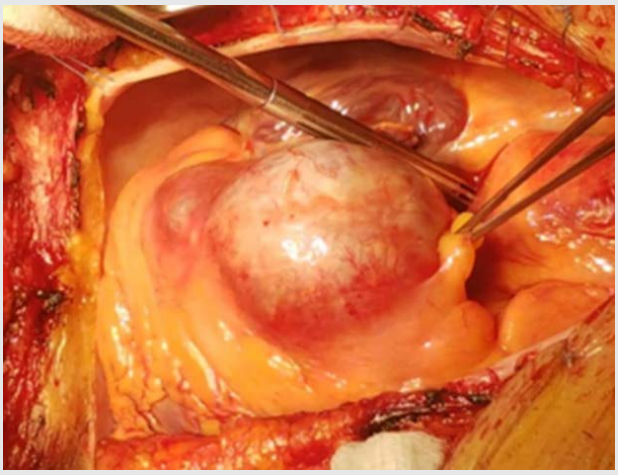

Laboratory investigations showed total cholesterol of 7.2 mmol/L (normal <5.2 mmol/L) with low-density lipoprotein of 5.4 mmol/L (normal <2.6 mmol/L). Blood glucose was normal. He has no history of hypertension. In view of the angiography findings, he was continued on dual antiplatelet therapy (aspirin and clopidogrel) and was referred to cardiothoracic surgeon for surgical intervention. Patient eventually underwent 4 vessels coronary artery bypass grafting (CABG) and closure of right coronary artery giant aneurysm **(Figure 3)** with factor VIII coverage to secure haemostasis.

He received an initial dose of 50iu/kg bolus just before induction followed by 25iu/kg intra-operatively 4H post initial bolus and followed by another bolus of 25iu/kg 4 hours later. He was then maintained at a dose of 25iu/kg 8 hourly. An experience hematologist joined the team in the operation theatre to oversee the management of factor infusions. Factor levels were checked daily and screening for inhibitor was performed, which was negative. His FVIII level was maintained above 100% during the operation and 72 hours post-operatively. Thereafter, the coverage was reduced to maintain a trough level above 50% for another week before switching back to his prophylactic dose.

The patient did not experience any significant bleeding complications during the surgery or post operatively. There was no blood transfusion required. The giant right coronary artery aneurysmal wall that was sent for histopathology study and cultures did not reveal any features suggestive of infection or Kawasaki Disease.

During the following days of hospitalization, no chest pain or bleeding episodes were observed. He was put on double antiplatelet for 6 months post operatively and was then reduced to aspirin until today. He continues to take prophylactic FVIII replacement 3x/week, has preserved left ventricular function of 60% and has been free from angina since his last episode of NSTEMI.

**Figure 3:** Intraoperative photo of giant aneurysm of right coronary artery.



## DISCUSSION

To our best knowledge, this is the first case report describing a patient with severe hemophilia A and NSTEMI who needs a combined procedure of CABG and closure of an underlying giant coronary aneurysm. Severe hemophilia A is defined when factor VIII level < 1%. This case also highlights the occurrence of NSTEMI as a consequence of underlying CAA and its management challenge during the open-heart surgery. CAA is defined as artery dilation more than 1.5 times the diameter of normal adjacent segments or the diameter of the largest coronary artery.[1] Giant coronary aneurysm refers to an aneurysm with a diameter > 20 mm.[1] CAA is typically diagnosed incidentally during coronary angiography.[2] CAA is associated

with thrombus formation due to abnormal laminar flow, as well as abnormal platelet and endothelial-derived pathophysiologic factors within the CAA. Once formed, mural thrombus may potentiate the deposition of additional thrombus within aneurysmal segments.[2]

Besides the underlying CAA and hypercholesterolemia as risk factors of thrombosis in this case, we also looked at the possibility of a treatment-related event. Acute coronary events have been found to be associated with hemophilia treatment. Studies have discovered that replacement of deficient factors especially in large amounts of concentrates to achieve high levels as those required for major surgery (level of 80-100%) have the highest thrombotic risk.[3] There were reports of thrombotic cases occurring during or shortly after supernormal factor concentrates infusion.[4] However, there is no report of similar thrombosis events associated with the usual prophylactic dose of factor infusions.

Cardiac surgery is associated with significant coagulation abnormalities leading to an increased intra- and post-operative bleeding risk, secondary to heparinization, surgical trauma, extracorporeal circulation, hypothermia, and increased fibrinolysis.[5] Hence cardiac surgery on hemophilia patients poses an extreme hemostatic challenge. Unfortunately, there is lack of guidelines available on how best to strategize the treatment plan. Moreover, a standardized hemostatic treatment protocol will seem to be an unlikely solution, based on the small number of hemophilia patients needing cardiac surgery, and the difference in disease severity.

P Lin *et al* [6] did a retrospective analysis of published literatures on perioperative management of hemophilia A patients undergoing cardiac surgery. Analysis of fifty articles showed that among 72 patients, 25 (35%) were severe hemophilia A. Factor VIII concentrates were given to ensure normalization of perioperative coagulation function. Although an eventful clinical outcome was achieved in the majority of cases, 20% of patients developed complications with different severities. The analysis concluded that a thorough factor replacement with careful monitoring of factor levels is the key to an optimal outcome.

In another retrospective survey done on 10 patients with hemophilia by Shalabi A *et al*,[7] the authors suggested factor level to be maintained above 80% at the end of surgery until 48-hour post-operatively. Thereafter, factor level to be maintained above 50%. All their patients received antifibrinolytics intraoperatively, but not postoperatively except in cases of bleeding despite optimal factor replacement. During the immediate post-operative period, the authors preferred to use continuous infusion of factor VIII than bolus factor replacement, as it reduced total factor use, improved safety with stable factor VIII activity, and guarded against a lack of deep troughs below the hemostatic range.

Current literature is sparse regarding the use of long-term anti-thrombotic or anti-platelet treatment in hemophilia patients after cardiac surgery. However, several case studies reported safe anti-thrombotic and anti-platelet treatment in hemophilia patients, on the condition that there is adequate replacement therapy.[8] Low-dose aspirin is generally well tolerated in hemophilia patients and can be used as prophylaxis for life.

The management strategies of CAA include medical therapy, surgery and percutaneous coronary intervention (PCI). To date, there is no consensus on the optimal treatment of CAA because the natural history and long-term outcomes of CAA remain unclear. Previous studies have reported good short- and long-term outcomes for CABG performed in patients with CAA.[9, 10] In a study by Khubber S *et al* [11] that looked into outcomes of CAA following medical, PCI and surgery found that CABG was associated with a lower rate of major cardiovascular and cerebrovascular events over a period of 10 years, compared to medical management, but no significant difference was noted between PCI and CABG. A CABG was performed on this case as he also presented with significant coronary arteries occlusion, in which the management was aimed towards both revascularization and repair of CAA.

## CONCLUSION

Cardiac surgery in patients with severe hemophilia is a challenging execution. A perioperative management strategy with a multidisciplinary approach, a thorough factor replacement protocol and careful monitoring of factor levels can facilitate an optimal outcome for severe hemophilia patients undergoing cardiac interventions.

**Keywords**
Hemophilia A; NSTEMI; coronary artery aneurysms; cardiac surgery; factor VIII

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**Informed Consent**
Informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Conflict Interests Disclosure**
No conflict of interests to be declared.

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