Management of Ruptured Sinus of Valsalva for Device Closure in a Patient with Haemophilia

Abstract

The association of Hemophilia A and ruptured aneurysm of sinus of valsalva (RSOV) has never been reported to the best of our knowledge. We report the case of a 29-year-old male patient with Hemophilia type A who presented with a RSOV into right atrium (RA). The patient underwent device closure off the RSOV and received Factor VIII infusions to decrease blood loss. The peri-procedural management is being presented in this case report.

Keywords: *Anesthesia, device closure, factor VIII, hemophilia A, ruptured aneurysm of sinus of Valsalva*

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Introduction

Rupture of an aneurysm of sinus of Valsalva (RSOV) is an uncommon disease most commonly congenital in origin. The aneurysm involves the right coronary sinus in majority of cases followed by the left coronary sinus. The occurrence of RSOV in a patient with hemophilia A is rare and not described in literature to the best of our knowledge. We report a rare case of RSOV in a patient with hemophilia A, who was managed successfully using an occluder device in the catheterization laboratory (cath lab).

Case Report

A 29-year-old male patient weighing 57 kg who was diagnosed to have hemophilia type A since 13 years of age and was on intermittent blood and factor VIII (FVIII) transfusions presented with complaints of chest pain, breathlessness, and palpitations since 4 months which suddenly increased to Grade IV dyspnea since 15 days before admission.

On examination, he had elevated jugular venous distension, wide pulse pressure, epigastric pulsations, and a continuous murmur best heard over left sternal border. His electrocardiography (ECG) showed left ventricular hypertrophy with tall P-wave in lead II and a bifid P wave in lead V. Cardiac computed tomography angiography was performed wherein the aortic annulus was 25 mm, sinus - 37 mm, ascending aorta - 24 mm, and the noncoronary sinus showed a focal dilation (15 mm × 12 mm) protruding into the right atrium suggestive of RSOV of noncoronary sinus.

Laboratory investigations revealed hemoglobin of 14 g/dl and platelet count 2 lakhs/cumm. His coagulation profile including prothrombin time and activated partial thromboplastin time was within normal limits except for FVIII level, for which FVIII assay was done, which was 1% of normal. His disseminated intravascular coagulation profile (platelet counts, fibrin degradation products, etc.) was repeated after injecting 3000 units of FVIII and his FVIII level increased to 100% of normal.

A hematology consultation was sought, and the patient was planned for device closure of the RSOV under general anesthesia in catheterization laboratory by cardiologist, especially in view of Hemophilia type A to avoid risks associated with surgical repair of the RSOV. On of the cardiac surgery operation theater was kept on standby until the completion of the interventional procedure.

Preoperative anesthetic evaluation was done. Oral premedication in the form of tablet diazepam 5 mg HS and tablet alprazolam 0.5 mg an hour before the procedure were given. Premedication in the form of intramuscular injections were avoided for fear of an intra-muscular hematoma. Three thousand units of FVIII (Eloctate®, antihemophilic factor, Fc Fusion protein,

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Biogen, USA) were given intravenous (IV) 1 day before the procedure and another 3000 units were given 30 min before the procedure on the day of intervention as advised by the hematologist.

Four units of packed red blood cell, 4 units of platelet concentrate and 4 units of cryoprecipitate were arranged. Three vials of 3000 unit each were also arranged and the plan was to repeat 3000 units in the evening in case surgery was needed.

The patient was taken up for the procedure early morning as the first case. Monitoring included pulse oximetry, ECG, and noninvasive blood pressure. Intravenous cannulation was performed using 16 G cannula after local infiltration with insulin syringe. Injection midazolam 1 mg and injection fentanyl 100 μg were given intravenously. Anesthesia was induced with injection etomidate 20 mg and atracurium 40 mg IV was used as muscle relaxant. Trachea was intubated with 8.0 mm ID cuffed endotracheal tube and fixed at 22 cm. Anesthesia was maintained with oxygen, air, and isoflurane. End-tidal CO_2 monitoring was attached. Transesophageal echocardiography (TEE) probe was inserted gently avoiding any trauma [Figure 1]. Injection paracetamol 1 g IV was administered 30 min before the completion of procedure for adequate analgesia.

Catheters for loading the device were inserted through the femoral artery and the device was successfully deployed under fluoroscopic guidance [Video 1]. The procedure lasted for about 2 h and was uneventful. An occluder device (Amplatzer, 2.5 mm) was successfully placed to occlude the ruptured aneurysm [Figure 2 and Video 2]. The patient was extubated in the cath lab table and was shifted to the ward in a stable condition. No intraprocedure blood or blood product transfusions were required. Postprocedure FVIII levels were maintained for at least 7 days.

Discussion

Hemophilia A is a recessive X-linked disorder (XLR) with deficiency of FVIII. It represents 80% of all Hemophilia cases (FVIII and FIX deficiency).[1] Mutation in the long arm of chromosome X at F8 gene causes hemophilia A. This disease affects male offspring and female acts as carriers. The prevalence is as high as 1%–2% of the general population,[2] and one-third of the hemophilia patients have no family history.[3]

Factors VIII plays a crucial role in the clotting mechanism (the intrinsic pathway). It is essential for thrombin generation and fibrin formation. The plasma concentration of factors VIII is expressed as percentages of normal pooled plasma. 1 IU is the concentration of coagulation factor in 1 ml of normal pooled plasma. The normal range is 0.5–1.5 IU/ml or 50%–150%.[3]

Severe cases of hemophilia A (<2% FVIII activity) have spontaneous bleeding, predominantly in joints and muscles. Hemophilia A can be graded mild, moderate, and severe based on FVIII levels or activity percentage [Table 1] FVIII assay is diagnostic.[1] The hemophilia patients may present with spontaneous bleeding or trauma-related bleeding. Spontaneous bleeding is more common in severe hemophilia. Joints are in general the most affected, but any other part of the body, including central nervous system, may be subject to spontaneous hemorrhage.[4]

Desmopressin, a synthetic analog of the antidiuretic hormone vasopressin, increases plasma levels of FVIII and is primarily used to treat mild-to-moderate hemophilia A. A single IV infusion of 0.3 μg/kg increases the level of FVIII 3–6 times with peak response in 90 min. Desmopressin is ineffective in patients with severe hemophilia A and is of no value in hemophilia B. Tranexamic acid is an antifibrinolytic agent that promotes clot stability and is useful as adjunctive therapy in hemophilia.[1]

Management of patients with hemophilia with cardiac disease requires multidisciplinary involvement from cardiology, anesthesia, cardiac surgery, and hematology department [Table 2]. Although surgical treatment in the patient without bleeding diathesis presents low operative risk and has a high long-term survival rate, defect closure by intravenous placement of an occluder was chosen in our case to avoid the risk of increased bleeding subsequent to use of cardiopulmonary bypass and an open cardiac surgery.

Before any invasive procedure, the hematologist should rule out the presence of FVIII inhibiting antibodies, counsel about the stoppage of antiplatelet drugs 1 week before

Table 1: Severity of hemophilia A with respect to factor VIII levels and activity

Grading of severity	Factor VIII levels	Activity	Clinical presentation
Mild	0.05-0.40 IU/ml	5%-<40% of normal	Severe bleeding after major trauma/surgery. Spontaneous bleeding is rare
Moderate	0.01-0.05 IU/ml	1%-5% of normal	Prolonged bleeding after trauma/surgery. Occasional spontaneous bleeding
Severe	<0.01 IU/ml	<1% of normal	Spontaneous bleeding in joints and muscles most commonly can occur in other parts, for example, central nervous system.[4]

Table 2: Perioperative considerations in a patient with hemophilia A undergoing intervention procedures

Preprocedure assessment checklist
Detailed history
Type and severity of hemophilia
Previous blood or factor VIII transfusions
History of transfusion-related infections: HIV, Hepatitis B and C
Spontaneous bleed, joint deformities, contractures
Thorough airway examination: (rule out difficult airway, oral injuries)
Laboratory investigations: hemoglobin, platelet count (normal), PT (normal), aPTT (prolonged), Factor VIII assay (low)
Multidisciplinary involvement: hematologist, anesthesiologist, cardiologist, cardiac surgeon
Elective surgery scheduled early during the week and preferably in the morning
Adequate amount of blood and blood products as well as factor VIII should be readily available
Administer factor VIII 30 min before procedure[15]
Intra operative (procedure) considerations
Positioning: position on the operating table taking care of pressure points and any joint deformity
Avoid intramuscular injections
Care with vascular access and invasive monitoring. Consider early use of ultrasound
Risk–benefits for neuraxial block and regional blocks need to be assessed individually and in general avoided
Avoidance of tachycardia and hypertension because they lead to increased operative field bleeding
Avoid drugs such as succinylcholine to prevent muscle fasciculation which may worsen muscle and joint hemorrhage
Avoid oromucosal trauma: ETT should be well lubricated.
Care should be taken during the insertion of laryngoscope, temperature, and TEE probes. Bleeding may rapidly complicate airway management
Surgeon should pay special attention to small vessel hemostasis
Multimodal pain management (avoid NSAIDs); paracetamol is safe
Postoperative considerations
Factor VIII should be continuously monitored to maintain its postoperative levels from a minimum of 3 to 7 days depending on the type of procedure (noninvasive or invasive)

PT: Prothrombin time, APTT: Activated partial thromboplastin time, ETT: Endotracheal tube, TEE: Transesophageal echocardiography, NSAIDs: Nonsteroidal anti-inflammatory drugs

surgery, and assure the presence of adequate amounts of FVIII concentrate in the perioperative period.[5]

Hemophiliacs undergoing elective surgery should be evaluated for the status of joints, spontaneous hematomas, airway, and the presence of oral injuries. Induction of anesthesia should be smooth, and drugs such as succinylcholine are avoided to prevent muscle fasciculations, which may worsen already existing hemorrhage in muscle and joints.[6] Peripheral venous puncture sites generally do not tend to bleed excessively.[7] Intramuscular injections, difficult phlebotomy, and multiple arterial punctures should be avoided. We administered oral premedication instead of intramuscular injections in our case. Central venous access, if required, should be secured under ultrasound guidance.[8]

In hemophilia, major surgery should take place in a center with adequate laboratory support for monitoring of clotting factor levels, and preoperative assessment should include inhibitor screening. Elective surgery should be scheduled early in the week and early in the day for optimal laboratory and blood bank support.[1] Availability of sufficient quantities of clotting factor concentrates should be ensured before undertaking major surgery.

Patients with hemophilia need 80%–100% correction of their FVIII before any major surgical procedure and this must be confirmed before surgery.[3] Postoperatively, levels should be maintained for up to 6 weeks after orthopedic procedures and 1–2 weeks for other procedures.[4,9] A bag of fresh frozen plasma containing 70–250 ml of fresh frozen plasma contains 70–90 U/dl of FVIII, factor IX, von Willebrand factor, and other coagulation factors. It can replace 15%–20% FVIII with a volume of 800–1000 ml.[9] Cryoprecipitate extracted from fresh frozen plasma bags after slow thawing and centrifugation is rich in FVIII and fibrinogen. A volume of 20–30 ml of cryoprecipitate contains 60–100 FVIII units and 200–300 mg fibrinogen. It may be used in cases when FVIII concentrate is not available.[6]

Commercial preparations of factors VIII as lyophilized powder are available. It is free from the risk of transfusion-transmitted infections as seen with blood products, but the limiting factor is its high cost.[3] Calculation of the required dose of FVIII is based on the empirical finding that 1 IU of FVIII/kg body weight raises the plasma FVIII level by 2 IU/dL ($t_{1/2}$ 8–12 h). The dose to achieve a desired *in vivo* peak increase in FVIII level may be calculated from the following formula:[10]

Dose (IU) = Body weight (kg) × Desired FVIII rise (IU/dl or % of normal) × 0.5

The development of FVIII inhibitors complicates the management of hemophilia patients because it makes them refractory to FVIII therapy. These patients may be divided into low and high response groups as par the production of inhibitors. Therapeutic options for the patients with inhibitors include replacement with porcine FVIII, prothrombin complex concentrate, therapy with activated FVII, and even plasmapheresis as a palliative measure in emergency situations.[6,11]

Desmopressin is useful for patients with mild hemophilia who have obtained good response after a previous test with the drug. Desmopressin stimulates endogenous FVIII release by endothelial cells to the systemic circulation and may increase the levels of FVIII (2–3 folds). It is an alternative for less severe hemorrhages in mild

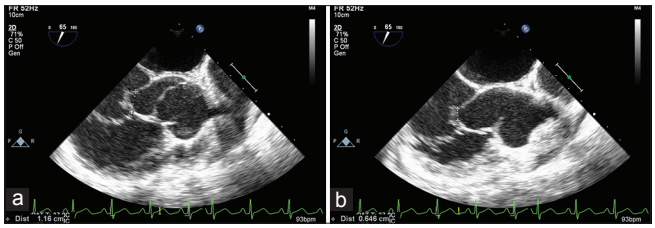

Figure 1: (a and b) The defect in the noncoronary sinus was clearly demonstrated in the ME AoV SAX view

hemophilia patients. The usual routes of administration are intravenous, subcutaneous, or nasal (spray for hemophiliacs). Intravenous dose is 0.3 μg/kg diluted in 30–50 mL saline and infused in 15–20 min. Nasal dose is 150 μg/kg for those weighing <50 kg and 300 μg/kg for those with >50 kg body weight.[6,12]

Antifibrinolytics are important adjuvant agents for hemorrhage prevention. Epsilon-aminocaproic acid and tranexamic acid may be administered.[1] Both drugs are contraindicated in the presence of hematuria and in patients with FVIII inhibitors being treated with prothrombin complex concentrate, due to the risk for thromboembolism.[6] Prothrombin concentrate complex is made up of prothrombin, factors IX and X, and variable amounts of FVIII. It is used in hemophilia A in patients with FVIII inhibitors in the dose range of 75–100 U/kg. It may be associated with thromboembolic problems.[6,9]

Care is also needed with insertion of probes, for example, temperature probe, TEE probe, and nasogastric tube because tongue and airway mucosal bleeding may rapidly lead to airway obstruction and obscure a clear vision for endotracheal intubation. Pharyngeal suctioning should be extremely delicate using lubricated soft catheters.[1] Postoperatively, FVIII levels should be maintained for up to 6 weeks after orthopedic procedures and 1–2 weeks for other procedures.[4,9] Postoperatively, analgesics such as aspirin and other NSAIDs should not be administered to hemophiliacs, as they can predispose these patients to gastrointestinal bleeding.[13] Patient-controlled analgesia is a safe and effective alternative to intramuscular injections.[14,15]

Conclusion

Management of hemophilia has undergone a sea change from transfusion of fresh whole blood in 1950s to administration of highly purified factor concentrates with greater efficacy today. In this report, we highlighted the role of a systematic examination, timely consultation, and execution of the management of a case of hemophilia with RSOV. A thorough and meticulous preoperative planning goes a long way in the management of a case of bleeding diathesis like hemophilia A as in our case. FVIII administration before any medical or surgical intervention as prophylaxis is a safe and very effective therapeutic strategy in patients of hemophilia A.

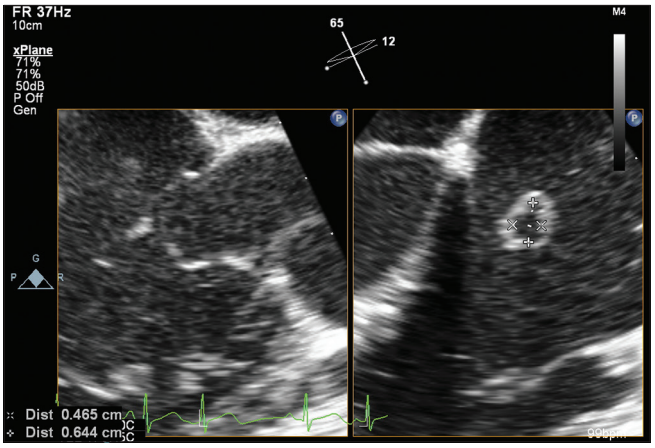

Figure 2: Using the orthogonal plane (X plane) view, the exact position was determined for the neck of the aneurysm and its dimensions were measured using calipers for choosing appropriate sized occluder

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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