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Case Report

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INCREASED RISK OF CARDIAC DISEASE IN A PATIENT WITH HEMOPHILIA: A RARE CASE REPORT

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ABSTRACT

This is the case report of an unusual clinical situation, one in which a 49-year-old man with hemophilia A presented with acute coronary syndrome. Managing his case required extreme caution in balancing the risks of thrombosis and bleeding. A successful outcome was secured through a multidisciplinary treatment approach, which included Factor VIII replacement therapy in combination with modified antiplatelet therapy; percutaneous coronary intervention (PCI) was done using a bare metal stent (BMS) to limit prolonged dual antiplatelet therapy (DAPT). Careful management post-procedure, which consisted of individualized anticoagulation strategies and cardiovascular risk factor modification, helped to achieve a favorable outcome. This case showcases the higher incidence of cardiovascular events among hemophilia patients, underscoring the need for alternative treatment paradigms. Such collaborations among hematologists and cardiologists will serve well to advance the fine line between hemostasis and thrombosis. Clinical studies are needed to optimize antithrombotic approaches in this population.

KEYWORD:- Hemophilia, cardiovascular disease, coronary artery disease, bleeding risk, antiplatelet therapy, Factor VIII replacement, percutaneous coronary intervention, thrombosis, multidisciplinary approach.

INTRODUCTION

Hemophilia is an uncommon, inherited, recessive ailment that manifests itself in the deterrence or absence of either clotting factors VIII (Hemophilia A) or IX (hemophilia B), which results in hemophilia-that-state with an increased probability of spontaneous and prolonged bleeding. More generally, haemophilia was grouped into bleeding disorders, typically with most bleeding complications, such as hemarthrosis, intracranial bleeding, and postoperative bleeding. The advancements in recombinant clotting factor therapy and prophylaxis have dramatically increased life expectancy among patients with hemophilia. Such patients now survive into older adulthood. Unfortunately, the older patients often now develop comorbid chronic conditions like cardiovascular disease (CVD). Despite hypocoagulable states in hemophilia, research suggests that such patients are not immune to atherosclerosis and ischemic heart disease. The interaction of aging, metabolic risk factors, and changing hemostatic challenges makes management of CVD highly complex within hemophilia. Insufficient clinical guidance on this issue makes a multidisciplinary approach of

hematologists, cardiologists, and interventional specialists indispensable.[1,2,3]

The widespread CVD in hemophilia patients has been on the rise due to the increase in life expectancies, combined with the traditional risk factors; for example, hypertension, diabetes, and dyslipidemia. In these patients, treatment strategies should be based upon individualized therapeutic approaches that weigh the risk of thrombosis against the risk of bleeding, rather than thrombotic risks driven treatment options in the general populace. Antithrombotic therapy is a fundamental aspect of CVD management and is a significant area of concern for the treatment of hemophilia patients, as these very interventions can induce life-threatening hemorrhages in these individuals. Furthermore, the invasive nature of cardiovascular procedures, such as percutaneous coronary intervention (PCI), necessitates the optimization of blood clotting factor levels pre-procedurally in order to prevent an excess of bleeding. This case report describes a rare case of severe hemophilia A in which the patient developed acute coronary syndrome (ACS), emphasizing the necessity of considering CVD in this special population. The report presents the diagnostic dilemmas, consideration for treatment, and the need for a unique strategy in treating cardiac complications among hemophilia patients.[4,5]

Case presentation

Patient information

- **Demographics**
  - **Age:** 49 years
  - **Gender:** Male
  - **Weight:** 78.5 kg
  - **Height:** 168 cm
  - **BMI:** 25.6. kg/m²

- **Medical history**
- Severe Hemophilia A (Factor VIII deficiency) diagnosed in childhood
- Hypertension (Diagnosed 5 years ago)
- Type 2 Diabetes Mellitus (Diagnosed 3 years ago)
- No prior history of thrombotic events, coronary artery disease, or venous thromboembolism
- No history of major bleeding requiring hospitalization

- **Lifestyle factors**
  - Non-smoker and non-alcoholic

- **Current condition**
  - Presented with oropharyngeal candidiasis diagnosed 2 weeks before hospital admission
  - No history of recurrent fungal infections

- **Medication history**
  - On-demand Factor VIII therapy for bleeding episodes
  - Amlodipine (5 mg/day) for hypertension
  - Metformin (500 mg twice daily) for diabetes
  - Atorvastatin (20 mg/day) for dyslipidemia

Presenting complaint

The patient presented to the emergency department with the following complaints:

- Central chest pain (pressure-like, radiating to the left arm) lasting 2 hours
- Shortness of breath with mild exertion
- Generalized fatigue and dizziness
- No history of hemarthrosis or recent bleeding episodes

History of present Illness

For the last two weeks before admission, the patient complained of non-specific mild chest pain and fatigue and attributed it to stress. On the day of presentation, he developed acute, severe, central chest pain that radiated to the left arm with diaphoresis, dizziness, and slight shortness of breath. The pain lasted for two hours before hospital admission. The patient denied a history of injury, recent episodes of bleeding, or changes in medications. He denied having suffered from thrombotic events in the past but was hypertensive, diabetic, and dyslipidemic. However, owing to his hemophilia A diagnosis, he had not had any significant bleeding event requiring hospitalization. This was highly suggestive of acute coronary syndrome and warranting further evaluation.

Clinical examination

General examination

- **Consciousness:** Alert but mildly anxious
- **Vital signs**
  - Blood Pressure: 142/88 mmHg
  - Heart Rate: 96 bpm (regular)
  - Respiratory Rate: 18 breaths/min
  - Temperature: 36.8°C
  - Oxygen Saturation: 98% on room air
- **General Appearance:** No pallor, cyanosis, clubbing, or peripheral edema
- **Skin & Mucosa:** No active bleeding, petechiae, or bruising

Cardiovascular examination

- **Heart sounds:** Normal S1 and S2, no murmurs or pericardial rub
- **Peripheral pulses:** Present and symmetrical
- **Jugular Venous Pressure (JVP):** Not elevated
- **Precordial palpation:** No heaves or thrills

Respiratory examination

- **Breath sounds:** Normal vesicular breath sounds bilaterally
- No crepitations or wheezing

Neurological examination

- **Cranial nerves:** Intact
- **Motor and Sensory function:** Normal
- **Reflexes:** Physiological, no focal deficits

Abdominal examination
- No Organomegaly, Tenderness, or Ascites

Investigations
Electrocardiogram (ECG)
- ST-segment depression in leads II, III, and aVF
- T-wave inversion in V4–V6
- No signs of arrhythmia

Laboratory investigations
- **Troponin-I:** Elevated (1.2 ng/mL, reference <0.04 ng/mL)
- **CK-MB:** Elevated (35 U/L, reference <24 U/L)
- **Lipid profile**
  - **LDL:** 145 mg/dL (elevated)
  - **HDL:** 42 mg/dL
  - **Total Cholesterol:** 220 mg/dL
- **HbA1c:** 7.2% (poor glycemic control)
- **Renal function tests:** Normal
- **Factor VIII Levels:** 4% of normal activity

Echocardiography
- Mild hypokinesia in the inferior wall
- Left ventricular ejection fraction (LVEF): 50%

Coronary angiography
- Significant stenosis (80%) in the right coronary artery (RCA)

Diagnosis
History and clinical presentations, along with raised cardiac markers in the electrocardiogram (ECG), suggested a diagnosis of Acute Coronary Syndrome in the form of Non-ST Elevation Myocardial Infarction. Underlying his Hemophilia A (moderate severity), it was challenging balancing the thrombotic and bleeding risk. There were contributory factors like Hypertension, Type 2 diabetes mellitus, and dyslipidemia that could be involved in the promotion of atherogenesis on the way to increase the cardiovascular risk. Differential diagnosis including aortic dissection and pulmonary embolism were ruled out on the basis of imaging and laboratory test results. This would have been managed in a multidisciplinary manner to achieve optimization of antithrombotic therapy and bleeding risk management.

Management
1. **Initial emergency management**
- **Vital monitoring:** Continuous ECG, blood pressure, oxygen saturation, and cardiac biomarkers (troponin, CK-MB) were monitored.
- **Oxygen therapy:** Administered if oxygen saturation dropped below 90%.
- **Pain management:**
  - **Sublingual Nitroglycerin (0.3 mg)** was given cautiously to relieve chest pain while avoiding hypotension.
  - **Opioid analgesics (Morphine 2-4 mg IV PRN)** were used if pain persisted.

2. **Hemophilia-specific considerations**
- **Factor VIII Replacement Therapy**
  - Given **pre-Procedurally and post-procedurally** to maintain levels above 50% for minor procedures and above 80% for major interventions.
  - Monitored closely to prevent spontaneous bleeding.

- **Bleeding risk assessment**
  - **Avoidance of NSAIDs (e.g., aspirin, ibuprofen) and P2Y12 inhibitors** unless absolutely necessary.
  - Hematology consultation for individualized anticoagulation strategy.

3. **Antithrombotic and Anticoagulant Therapy**
- **Modified antiplatelet therapy**
  - **Aspirin withheld initially** due to high bleeding risk.
  - **Clopidogrel or Ticagrelor considered selectively** with hematology consultation.

- **Anticoagulation**
  - **Unfractionated Heparin (UFH) at a reduced dose** was used for acute management due to its reversibility.
  - **Direct thrombin inhibitors (Bivalirudin) considered** as an alternative if anticoagulation was required.

4. **Risk Factor Management and Secondary prevention**
- **Lipid-Lowering therapy**
  - **Atorvastatin 40 mg/day** initiated to stabilize atherosclerotic plaque and reduce LDL cholesterol.

- **Blood Pressure control**
  - **Beta-blockers (Metoprolol 25 mg BID)** for heart rate and BP control.
  - **ACE inhibitors (Ramipril 2.5 mg/day)** for cardiovascular protection.

- **Diabetes and Lifestyle modifications**
  - Blood glucose optimized with diet and oral antidiabetic agents if needed.
  - Smoking cessation, dietary changes, and moderate-intensity exercise were advised.

5. **Coronary revascularization considerations**
- **Coronary angiography**
  - Conducted under Factor VIII replacement to assess the severity of coronary artery disease (CAD).
- **Percutaneous Coronary Intervention (PCI)**
  - **Bare-Metal Stents (BMS) preferred over Drug-Eluting Stents (DES)** to limit the duration of dual antiplatelet therapy.
  - Factor VIII levels were optimized before and after PCI to prevent hemorrhagic complications.

6. **Long-Term Management and Follow-Up**
- **Multidisciplinary approach:** Regular follow-ups with cardiology and hematology to balance ischemic and bleeding risks.

- **Medication review:** Periodic reassessment of anticoagulation and antiplatelet therapy based on thrombotic vs. hemorrhagic risks.
- **Patient education:** Importance of adherence to medication, lifestyle modifications, and early symptom recognition for both bleeding and cardiovascular complications.

Outcome of the case

The patient was stabilized effectively under a fine-tuned management plan-to strike a balance between risk for cardiovascular complications and bleeding due to hemophilia. Factor VIII replacement therapy was successfully applied to avoid excess bleeding during the diagnostic procedures and interventions. Significant atherosclerotic plaque deposition was confirmed by coronary angiography, after which percutaneous coronary intervention (PCI) was carried out using a bare-metal stent, with minimal duration for antiplatelet therapy. The patient's cardiac symptoms improved with optimized use of beta-blockers, ACE-inhibitors, and statins, followed by six months of monitoring, with no significant bleeding events or cardiac occurrences. This reinforces the fact that multidisciplinary, tailored care should be considered in the management of cardiovascular disease in the hemophilia patient population.

DISCUSSION

This case elucidates the rare but important challenge of handling cardiovascular disease in a patient with hemophilia, a state regarded as carrying lesser atherosclerosis risk due to chronic hypocoagulability. But with now increased life expectancy in patients with hemophilia because of factor replacement therapy, the prevalence of age-related diseases, such as coronary artery disease, is on the rise. Given this reality, the need for personalized risk assessment and management strategies for cardiovascular disorders in patients with hemophilia is emphasized.[6,7]

One of the most important issues in this case was balancing the thrombotic risk with that of bleeding. Paradoxically, the standard antiplatelet and anticoagulant therapies that have been a part of coronary artery disease (CAD) management significantly predispose a hemophilic patient to spontaneous as well as procedural bleeding. This is seen in the decision to initially withhold aspirin, use low-dose heparin, and consider clopidogrel under hematology consultation as an indication of the modification of anticoagulation strategy in such patients. The other strategy considered was use of bare-metal stents (BMS) rather than drug-eluting stents (DES). caused a reduction in the period of dual antiplatelet therapy, thus reducing the chances of prolonged bleeding complications.

Another important aspect in this case reference is the role of Factor VIII replacement therapy in facilitating diagnostic and therapeutic maneuvers. The mere act of vascular catheterization could lead to disastrous hemorrhagic complications under suboptimal clotting factor therapy. This shows the utmost importance of the rare collaboration between hematologists and cardiologists when it comes to safely doing those maneuvers.[8]

Long-term management of the patient further emphasizes lifestyle modifications and statin therapy along with blood pressure control for risk factor modification to reduce cardiovascular risks. While other people get aggressive anticoagulation after the percutaneous coronary intervention (PCI), patients with hemophilia require laboratory supervision for the long term to ensure secondary prevention and bleeding risk reduction.

This case indicates that cardiovascular disease among hemophiliacs is an emerging clinical challenge that requires patient-specific, multidisciplinary approaches to balance the factors of bleeding prevention and cardiovascular protection. It highlights the need for ongoing research to develop safer antithrombotic strategies for this special patient population..[9,10]

CONCLUSION

This case presents new challenges in patients with hemophilia and cardiovascular disease; it requires careful balance between thrombotic risk and bleeding complications. Multidisciplinary input regarding anticoagulation strategies, Factor VIII replacement, and modification of cardiovascular risk was imperative for optimal outcomes. Coordination of efforts by hematologist and cardiologist collaterals ensured safe intervention and effective long-term management. Because more hemophilia patients can expect to live long enough into adulthood to experience life-time cardiovascular risk, individualized treatment regimens might be required to prevent cardiovascular events with an accompanying bleeding risk, which warrants further study.

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