

Introduction

A 67 year old African American male presents to the emergency department with bleeding from his Dexcom needle site for the past 3 days and shoulder pain.

Background

- Diagnosed with **Multiple Myeloma** 2018
 - Completed 5 months CyBorD chemotherapy
 - Autologous stem cell transplant 2019
 - Completed 8 months of Lenalidomide maintenance therapy
 - Bone Marrow Biopsy indicating remission 2022
- Myelodysplastic Syndrome** diagnosis in 2022
 - Chemotherapy initially with azacitidine
 - Transitioned to decitabine
- Past medical history** is significant for diabetes mellitus type 2, chronic kidney disease stage 3, rheumatoid arthritis, and carotid artery stenosis
- Medications** include Nifedipine, Metoprolol, Losartan, Insulin aspart, Gabapentin, Empagliflozin, Duloxetine, Atorvastatin, Acetaminophen, Folic Acid, and Omeprazole
- No significant past surgical history
- Social history was negative to tobacco use and drug use. Positive for social alcohol use

Presentation

- Reports persistent oozing from his Dexcom needle site for the last three days and has not been able to get it to stop. This is his second presentation to the emergency department in the last three days but his first presentation to ECU Health Medical Center Greenville
- Review of Systems:** Acute on chronic shoulder pain, new onset bruising. Denies recent trauma, neurologic complaints, chest pain, abdominal pain, or shortness of breath
- Vitals/Exam:** BP 105/66, HR 57, RR 16, afebrile. African American male with scattered ecchymosis across the right upper anterior chest, abdomen with persistent trickle of blood, swelling and pain on palpation/movement of the right shoulder, hematoma of the left wrist that is extended to the distal 1/3 of the forearm. He is neurovascularly intact and otherwise has no other pertinent physical exam findings.
- Pertinent Labs:** Hgb 7.0, Hematocrit 23.7, MCV 100.4, WBC 2.13, Platelet 37, INR 1, PT 11.4, PTT 88.5, Cr 2.64, GFR 38
 - Mixing Study:** Corrected PPT to 51
 - Factor Analysis:** Factor VIII%: <1%
 - Bethesda Inhibitor Assay:** 172

Hospital Course and Follow Up Care

- Emergency Department Care:** Direct firm pressure over bleeding, TXA, 1 unit RBC, 5 units of Platelets
- Hospital Day 1:** Admitted to the Heme/Onc where he received TXA, Kcentra, 5 units of Platelets, 1 unit FFP, and 1 unit RBC's. Hematology was consulted. His Hgb continued to drop from 7 down to 6.4. Started on 100 mg of Prednisone PO daily
- Hospital Day 2:** Hgb dropped to 6.1 for which he received TXA, a 3rd unit of RBC's and scheduled dosing of Kcentra 50u/kg BID
- Hospital Day 3 - Discharge:** Hemostasis obtained and Hgb recovery occurred after the addition of Rituximab 900 mg IV infusion on day 3. Discharged home after 7 day hospital stay on a long steroid taper with plans of rituximab infusion cycle outpatient. Planned to start Emicizumab outpatient.
- Outpatient Course:** Prednisone taper was completed, however the patient had a bounce back to the hospital for gastrointestinal bleeding. On repeat testing he was found to have recurrent Factor 8 deficiency. He was restarted on his original Prednisone taper regimen with cessation of bleed and no further intervention.

Pertinent Physical Exam Findings



Figure 1: Spontaneous deep tissue bruising (not shown posterior upper arm bruising with extension to the shoulder, forearm, and chest wall) Shared with informed consent from the patient for educational and research purposes over a recorded line.

DISCUSSION

- Occurring **1-1.5 in 1 million people per year**, characterized by autoantibodies directed against circulating coagulation factor VIII in individuals with no previous history of abnormal bleeding patterns. The new bleeding diathesis has a **mortality rate of 15-25%** [1-2].
- Associations:**
 - Older Males with autoimmune disease such **RA** and **SLE** [4]
 - Medications: Alectuzumab, Omalizumab, Interferon Alfa, Clopidogrel, Aspirin, Warfarin, Apixaban, Amoxicillin [5]
 - Young females in pregnancy/postpartum state [6]
- Napolitano et al.**, found 105 case reports during systemic review [7]
 - 60 cases solid tumor cancer (GI, GU, and Lung)
 - 45 cases hematological cancer (**MDS, MM, and Lymphoma**)
- Diagnosis is with laboratory testing revealing normal PT/INR, prolonged PTT, incomplete mixing study, and **factor analysis showing reduced Factor VIII activity level and elevated Bethesda Inhibitor Assay** [8-10]
- Disease severity is based on Clotting Factor Activity [11-13]:
 - Mild Disease: FVIII: >5-40%
 - Moderate Disease: FVIII 1-5%
 - Severe Disease: FVIII <1%
- Case Reports of management provided updates to International consensus AHA guidelines in 2020 with a goal of hemostasis and autoantibody eradication [15]
 - Hemostasis medications: direct compression, TXA, recombinant Factor VIIa, aPCC, recombinant FVIII, desmopressin for mild to moderate disease [16], plasmapheresis
 - Autoantibody Eradication: First line with prednisone following the addition of second line agent's cyclophosphamide or rituximab
 - Emicizumab has shown benefit in some case series and is approved for congenital AHA by FDA however other case reports show increased thrombotic complications and increased mortality with off label use [17-19]
 - Several case reports and case series have shown efficacy with mycophenolate mofetil, tacrolimus, vincristine, and Bortezomib as second line agents [19]

Teaching Points

- AHA is easily missed due to rarity of the disease and carries a high mortality rate
- Diagnosis is made by easily obtained routine lab work
- Ideal management is still poorly defined and due to a lack of resources of appropriate therapy rapid transfer to a tertiary care center is imperative

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