

Acquired von Willebrand Syndrome *secondary to* Immunoglobulin Light Chain Amyloidosis *presenting as an* Intramuscular and Intraabdominal Bleed

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Introduction

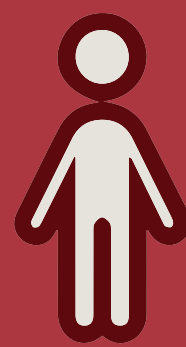
Immunoglobulin light chain (AL) amyloidosis

- A plasma cell dyscrasia: overproduction of monoclonal Ig light chain fragments by bone marrow plasma cells → improper folding → deposition into tissues¹
- Prevalence varies geographically: 1,275 to 3,200 new cases annually in the U.S.²
- Complications: Affects heart, kidneys, and nerves → cardiomyopathy, nephrotic syndrome, and neuropathy¹
- Less common: abnormal bleeding

Acquired von Willebrand Syndrome (AVWS)

- A rare bleeding disorder caused by loss of von Willebrand factor (vWF), a plasma protein that mediates platelet adhesion and aggregation
- vWF can be destroyed or absorbed by amyloid fibrils³

Case Presentation



Patient: Middle-aged man with a benign medical history until COVID-19 diagnosis.

Post-COVID-19 recovery: Spontaneous bilateral lower extremity pain, swelling, and bruising.

- Multiple visits with primary care, vascular surgery, and orthopedics.
- Venous doppler ultrasound: Chronic venous insufficiency and small hematoma in the left proximal thigh.
- Worsening leg pain despite conservative measures (naproxen, prednisone, compression socks).



Consultation with Hematology/Oncology due to abnormal CBC findings:

- Chronic leukocytosis with mild neutrophilia and monocytosis.
- Progressive thrombocytosis.
- New onset normocytic anemia.
- Repeat ultrasound: Left thigh hematoma tripled in length and quadrupled in width.



ED visit for abdominal pain, ultrasound revealing cholecystitis.

- Laparoscopic cholecystectomy with post-op hemorrhagic shock and 2.5cm x 2.5cm right abdominal wall hematoma.
- Returned to operating room for diagnostic laparoscopy, abdominal washout, and repair of bleeding trocar sites with multiple blood clots in the omentum.
- Stabilization following platelets and pRBCs administration, discharge on post-operative day three.



Two weeks later, emergency department visit due to progressive left lower extremity swelling.

- CT contrast: Left thigh hematoma expanded throughout vastus intermedius, lateral side of the rectus femoris, and distal vastus medialis.



Diagnostic Assessment

Differential Diagnoses

- Platelet dysfunction
- Coagulation factor disorder
- Myeloproliferative neoplasm (MPN)

Workup for platelet dysfunction and coagulation factor disorders

- vWPanel, Factor X assay, CBC:
- Acquired von Willebrand disease (vWD): low ristocetin, absent high molecular weight multimers
 - Echocardiogram negative for aortic stenosis
 - Factor X deficiency
 - Thrombocytosis (1 million/mm3)

Evaluation for MPN

- Negative JAK2 V617F, JAK2 exon 12-13, CALR, and MPL genes → no polycythemia vera, essential thrombocythemia, JAK2 exon 12-13-positive MPN, CALR-positive MPN, or primary myelofibrosis
- Serum Protein Electrophoresis (SPEP) and multiple myeloma labs:
 - Bence Jones proteinuria
 - Multiple myeloma FISH panel normal
 - Low kappa:lambda light chain ratio
- Bone marrow biopsy:
 - Positive Congo red stain: diagnostic of AL amyloidosis.

Treatment

- Initially treated with hydroxyurea to lower platelets, while receiving recombinant von Willebrand factor and replacement Factor X
 - No resolution of symptoms and values
- Subsequently treated following standard systemic light chain amyloidosis guidelines after diagnosis
 - Daratumumab-CyBorD (cyclophosphamide, bortezomib, and dexamethasone)

Outcome

- Positive response to CyBorD treatment
- Normalization of vWF levels
- Repeat bone marrow biopsies showed plasma cells less than five percent
- Complete resolution of symptoms
- No intention to proceed with hematopoietic stem cell transplantation (HCT) at this time though he did have a stem cell collection

Discussion

- Treatment response suggests bleeding was not solely from thrombocytosis, von Willebrand Disease, or Factor X deficiency, but also related to AL amyloidosis.
- In previous studies, identification of AVWS led to appropriate management of initial bleeding, including transfusions and medication adjustments.⁴
- Clues of AL amyloidosis throughout the patient's presentation, including atraumatic leg hematoma and elevated alkaline phosphatase (ALP) levels.
 - Not high on differential as classic presentation is end-organ damage
 - ALP can be a marker for biliary obstruction but also MPNs
 - COVID-19 related to increased serum amyloid A but less studied on primary amyloid concentrations
- Importance of thorough workup of underlying plasma cell disorders in patients with unexplained bleeding and abnormal coagulopathies.
- A limitation is the lack of information on the patient's long-term outcomes.
- Future studies can explore optimal management approaches for AL amyloidosis in the context of AVWS and thrombocytosis.
- Recognize and manage AL amyloidosis early to prevent complications and improve outcomes in patients with refractory bleeding complications.

Sources

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