When Tissue Becomes the Issue:
A Lesson on Atypical Complications of Waldenström Macroglobulinemia

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Introduction

Waldenström macroglobulinemia (WM) frequently presents with pancytopenia placing patients at risk of infection and bleeding. However, other less common complications can occur with similar presentations. This case highlights an apparent case of osteomyelitis and bleeding diathesis, that with a systematic diagnostic approach was identified as: (1) plasmacytoma-like infiltrative extramedullary WM and (2) acquired von Willebrand syndrome (aVWS) in a patient with progressive WM.

Case Description

A 73-year-old man with Waldenström macroglobulinemia, pancytopenia, and peripheral neuropathy presented with progressive dorsalgia, epistaxis, and 30-pound weight loss with initial imaging concerning for lumbar osteomyelitis. He reported no fever, headaches, vision changes, or weakness, and had no neurologic deficits on exam except for decreased peripheral pinprick sensation.

Studies demonstrated hyperviscosity and an acquired von Willebrand syndrome (shown on right). Repeat MRI (shown on right) remained concerning for osteomyelitis. Infection continued to be the most likely etiology, but a biopsy was pursued to guide antimicrobial selection, and to provide diagnostic confirmation. Given the patient's hyperviscocity syndrome and aVWS, his surgical biopsy was delayed one week while he required plasmapheresis with cryoglobulin and VWF/FVIII concentrates (Humate-P®). Vertebral biopsy revealed clusters of plasma cells indicative of infiltrative extramedullary WM. He was initiated on therapy for WM with bortezomib and dexamethasone. Rituximab was held due to elevated IgM.

Case Data

Pertinent Studies:

Chemistry & Other

Basic metabolic panel	normal
Total protein	13.2 g/dL
Albumin	2.1 g/dL
IgM	>5850 mg/dL
vWF antigen	low
vWF activity (ristocetin cofactor)	low
Factor VIII	low
Viscosity	8.72 centipoises (high)

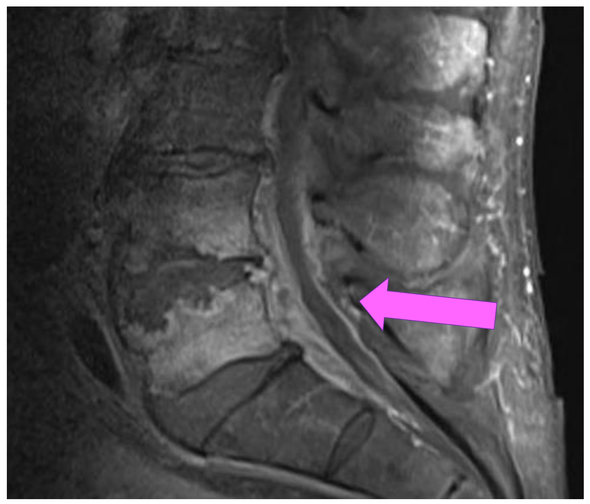
Hematology

Leukocytes	2820/mL
Neutrophils	1480/mL
Hemoglobin	7.9 g/dL
Platelets	119,000/mL
INR	1.17
aPTT (normalized with mixing study)	56.7 sec.
Fibrinogen	95 mg/dL
ESR	>120 mm/hr

Cultures:

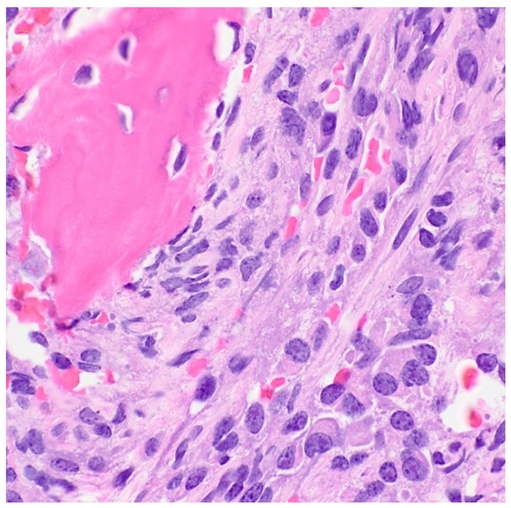
- Blood & vertebral cultures: no growth

Imaging (Lumbar MRI):



MRI T1 post-gadolinium of lumbar spine showing abnormal T1 hypo-intensity and post-contrast enhancement in L4-L5 vertebral bodies and L5 pedicles with abnormal thickening and enhancement of epidural soft tissues at L5-S1, ventral more than dorsal. L4-5 high grade stenosis. Compression fracture of L5 vertebral body. Abnormal post-contrast enhancement involving medial portion of bilateral psoas muscle without abscess.

Representative Pathology:



Example microscopy of a plasmacytoma in a patient with multiple myeloma with plasma cell infiltration and osteolytic destruction[2]

Pathology:

- L4-5 vertebral biopsy: hypo-cellular marrow with lambda light chain producing plasma cells.

Proposed Mechanisms for Acquired von-Willebrand Syndrome in Waldenström Macroglobulinemia[1]

- Phagocytosis of von Willebrand factor by plasma cells
- Plasma cells make antibodies against vWF
- Shear force from increased viscosity

Discussion

- Unlike multiple myeloma, there is no clear association between Waldenström macroglobulinemia and plasmacytoma. However infiltrative extramedullary WM may present on imaging as an infiltrative mass with pathology resembling plasmacytoma.[3]
- It is estimated extramedullary disease is only present in 4.4% of WM cases with the common locations involving the lungs, CSF, soft tissue, and bone.[3]
- There is a clear association between acquired von Willebrand syndrome (aVWS) and monoclonal gammopathies. A retrospective study shows an association between increasing IgM levels and risk of aVWS.[1]

Teaching Points

1. Importance of evaluating coagulation disorders in patients with mild thrombocytopenia & new bleeding
2. Benefits of adhering to a systematic diagnostic approach and maintaining a broad differential diagnosis
3. Reinforces the importance of tissue biopsy to not only guide antibiotic selection, but assure the correct diagnosis.

References

1. Castillo, J., et al. (2017). Acquired Von Willebrand Disease in Patients with Waldenström Macroglobulinemia. *Blood, 130*(Supp 1), 1088.
2. Crane, G.M. Plasmacytoma. PathologyOutlines.com website. http://www.pathologyoutlines.com/topic/lymphomaplasmacytoma.html. Accessed October 25th, 2018
3. Banwait, R., et al. (2015). Extramedullary Waldenström macroglobulinemia. *American Journal of Hematology, 90*(2), 100-104.