Acquired von Willebrand Syndrome: A Rare Presentation of Waldenstrom Macroglobulinemia
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INTRODUCTION

- Patients with Waldenstrom macroglobulinemia (WM) can develop symptoms related to infiltration of the bone marrow or other tissues (e.g., anemia, lymphadenopathy, hepatosplenomegaly) and/or symptoms related to the IgM monoclonal protein in the blood (e.g., hyperviscosity, peripheral neuropathy). Bleeding is common in WM and is secondary to hyperviscosity. While chronic oozing of blood from the nose or gums is common, bleeding may occur from the gastrointestinal tract during and/or after surgery. The frequent laboratory abnormality related to coagulation is the prolongation of thrombin time, a reflection of the inhibition of fibrin polymerization by the IgM paraprotein.
- Acquired von Willebrand syndrome AVWS is not often suspected in a bleeding patient but can be seen in patients with autoimmune, myeloproliferative, lymphoproliferative disorders, and cardiac conditions. WM is one of the lymphoproliferative disorders that can develop aVWS. In some rare cases, aVWS can be the presenting finding.

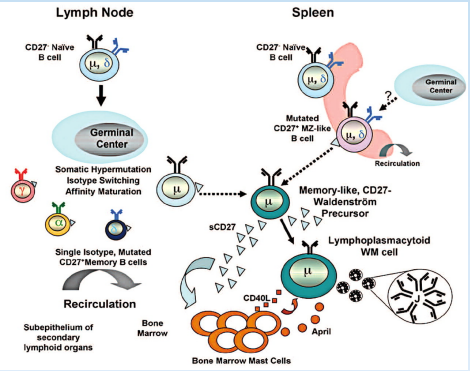

Figure 1. The WM cell could arise from a "memory-like", somatically mutated precursor that has lost classic memory markers such as CD27 due to shedding from the surface

Published in Haematologica 2010

Pathophysiology of Waldenström's macroglobulinemia M. Ocio | I. Treon

CASE DESCRIPTION

Waldenstrom macroglobulinemia (WM) is a lymphoproliferative disorder characterized by the production of serum monoclonal immunoglobulin M (IgM) and bone marrow infiltration by lymphoplasmacytic cells. Acquired von Willebrand syndrome (aVWS) is an uncommon complication and an even less common presenting feature.

We present the case of a 51-year-old man who had excessive postoperative bleeding following a Hartmann procedure reversal. The patient had a significantly elevated protein gap concerning for underlying paraproteinemia. Subsequent evaluation detected markedly elevated serum IgM and bone marrow biopsy with lymphoplasmacytic infiltrate. Von Willebrand's studies were consistent with aVWS. He underwent plasmapheresis with a target IgM level of 4,000 mg/dL before starting chemoimmunotherapy.

This case illustrates the importance of prompt and accurate evaluation of a lymphoproliferative disorder when an elevated protein gap is present. Furthermore, aVWS should be part of the differential diagnosis of bleeding in a suspected lymphoproliferative disorder.

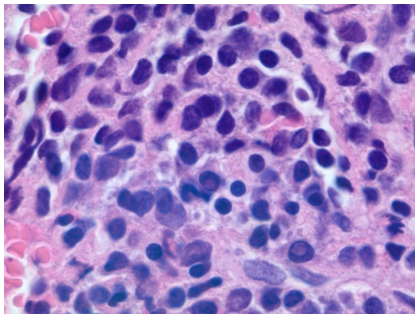

Figure 2. Bone marrow aspiration and biopsy H&E 100x Immersion lens, displaying Dutcher bodies

We would like to thank Dr. Sharon Swierczynski, hematopathologist at Reading Hospital, for providing pathology images for this presentation.

DISCUSSION

- Acquired von Willebrand syndrome (aVWS) is a rare bleeding disorder characterized by structural or functional alterations in von Willebrand factor (VWF) that is not inherited and causes bleeding.
- The prevalence of aVWS is not well known with less than 700 reported cases among all hematologic malignancies.
- One study demonstrated that 13% of patients with WM also met the criteria for aVWS. Multiple pathogenic mechanisms are postulated in aVWS, including selective VWF adsorption on tumoral cells, increased VWF proteolysis, immunoglobulin (Ig) G anti-VWF autoantibodies, or a complex interaction between VWF and WM monoclonal IgM.
- Treatment of aVWS is aimed at addressing the underlying disorder, which can lead to resolution of the bleeding diathesis. Patients with IgG autoantibodies and paraproteins have previously demonstrated good response to IVIG, however, this is not the case for IgM paraproteinemia.
- Plasmapheresis has been shown to deplete autoantibodies and paraproteins of any immunoglobulin class and has been reported in patients with aVWS resulting from IgM-MGUS. A recent case report demonstrated IgM reduction, increase in serum VWF levels, and improvement in hemostasis with Ibrutinib in AVWS secondary to WM.

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