

PARAPROTEIN-DRIVEN ACQUIRED VON WILLEBRAND SYNDROME IN A PATIENT WITH MGUS AND UROTHELIAL CARCINOMA

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Background. Acquired von Willebrand syndrome (AVWS) is an autoimmune bleeding disorder characterized by the development of autoantibodies against coagulation factors. It has been described in association with autoimmune diseases, the postpartum period, drugs, and malignancies, including solid tumors and hematologic disorders. The aim of this report is to describe a case of von Willebrand syndrome (AVWS) occurring in a patient with monoclonal gammopathy and urothelial carcinoma, and to explore the possible pathogenetic link between coagulation factor inhibitors and underlying proliferative disease.

Case Report. We report a single case of a 71-year-old male patient with known monoclonal gammopathy and urothelial carcinoma. The diagnosis of a coagulation disorder suggestive of acquired hemophilia was made during pre-operative hospitalization for surgical removal of the urothelial neoplasm. Standard coagulation tests were performed, including activated partial thromboplastin time (aPTT), factor VIII activity, and specific assays for coagulation factor inhibitors, together with laboratory assessment of underlying hematologic and oncologic conditions. The patient exhibited prolonged aPTT (ratio 1.42), reduced factor VIII activity (38%), and markedly decreased VWF functional activity (VWF:RCO 16%), consistent with an acquired defect of the VWF-FVIII

axis. Although no classical FVIII or VWF-neutralizing antibodies were detected, the coexistence of MGUS suggests a paraprotein-related mechanism of VWF dysfunction. Two non-mutually exclusive hypotheses are proposed: (i) functional inhibition of VWF by monoclonal immunoglobulin through steric hindrance or epitope masking, and/or (ii) accelerated clearance or adsorption of VWF-FVIII complexes mediated by immunoglobulin-VWF interactions. The concomitant urothelial carcinoma may have acted as a trigger for immune dysregulation amplifying paraprotein pathogenicity. Following tumor resection, progressive normalization of coagulation parameters and reduction of the monoclonal component were observed.

Conclusions. This case supports a mechanistically plausible association between MGUS-associated paraproteinemia and AVWS, potentially mediated by functional interference or enhanced clearance of VWF rather than classical neutralizing inhibitors. The temporal resolution of both monoclonal gammopathy burden and hemostatic abnormalities after tumor removal suggests a dynamic, tumor-driven modulation of paraprotein pathogenicity. These findings reinforce the concept that AVWS in plasma cell disorders may extend beyond antibody-mediated inhibition to include structural and kinetic disruption of VWF function.