

DISORDINI EMORRAGICI ACQUISITI: ASPETTI
DIAGNOSTICI E CLINICI

EFFICACY OF RITUXIMAB TREATMENT IN A CASE OF A RELAPSED AND REFRACTORY ACQUIRED VON WILLEBRAND DISEASE SECONDARY TO PRIMARY CUTANEOUS MARGINAL ZONE B-CELL LYMPHOMA

L. Gurgoglione¹, F. Saladino², E. Morsia², N. Viola³, S. Rupoli¹, A. Poloni²

¹Clinical Hematology, AOU delle Marche, Ancona, Italy; ²Università Politecnica delle Marche, Ancona, Italy; ³Clinical Immunology, AOU delle Marche, Ancona, Italy

Background. Acquired von Willebrand disease (AVWD) is a rare disorder of hemostasis characterized by reduced circulating von Willebrand factor (vWF) levels and impaired hemostasis, leading to spontaneous mucocutaneous bleeding manifestations, typically of mild to moderate degree. In AVWD, anti-vWF antibodies (predominantly IgG, and to a lesser extent IgM and IgA) may develop, impairing its hemostatic function by forming immune complexes (Ab-vWF) that accelerate its clearance from the circulation. The production of these antibodies is usually associated with hematologic malignancies and autoimmune diseases.

Case Report. We report the case of a 79-year-old woman who in October 2018 developed bleeding symptoms (spontaneous ecchymoses and mild gingival bleeding), with a negative family history. Coagulation studies showed an aPTT of 39 seconds and normal INR, with factor VIII (FVIII) at 16% and vWF at 14%. A desmopressin test was performed, with no response. The patient was initially diagnosed with congenital von Willebrand disease. At January 2020, a lesion appeared on the right forearm; biopsy led to a diagnosis of primary cutaneous marginal zone B-cell lymphoma stage I, with circulating clonal disease B1 (594/mm³ clonal lymphocytes with immunophenotype: CD19+, CD20+, CD5-, CD10-) [Figure 1]. The patient started a first-line treatment with anti-CD20 monoclonal antibody rituximab (administered at 375 mg/m² weekly for 4 weeks), achieving complete remission, with resolution of bleeding symptoms. In October 2024, a relapse of the cutaneous lymphoma occurred (with both a skin lesion and circulating clone), along with recurrence of mild bleeding symptoms. Coagulation studies showed INR 0.92, aPTT 42 sec, FVIII 97%, with vWF at 13%

and ristocetin cofactor activity (vWF:RCO) at 15%. Given her age at relapse (87 years), she initially received prednisone (0.5 mg/kg for 30 days), without improvement in coagulation parameters (vWF 12% and vWF:RCO 15%). She was therefore retreated with rituximab 375 mg/m² weekly for 4 weeks. At reassessment after 6 weeks, complete remission was again observed, with an INR of 0.96, aPTT of 27 sec, FVIII 117%, vWF 87%, vWF:RCO 44% and complete absence of the circulating clone. The patient is currently in follow up with complete response.

Conclusions. AVWD is a rare condition but should be considered in oncologic patients presenting with new-onset bleeding symptoms. A personalized treatment approach, taking into account the underlying malignancy, should be considered in these patients. In this case, treatment of the B-cell lymphoma with rituximab led to a response also in the coagulopathy, both at the onset and the relapse.

