
Acquired von Willebrand syndrome (AVWS) is an acquired coagulation disorder reported in Waldenström’s Macroglobulinemia (WM). Multiple pathogenic mechanisms are described in AVWS, including selective, pathologic adsorption of von Willebrand factor (VWF) on tumor cells, increased proteolysis of VWF and presence of neutralising or non-neutralising anti-VWF antibodies. In order to assess the frequency of AVWS in WM patients (pts), we measured ristocetin cofactor (VWF:RCo) activity and VWF antigen (VWF:Ag) in 58 pts with WM and 25 additional pts with IgM MGUS or other lymphoproliferative disorder (non-WM). Mean serum monoclonal immunoglobulin M component (IgM) were 1.8 and 0.7 g/dL, respectively (p<0.0001). Seven WM pts presented with acquired von Willebrand syndrome (AVWS) defined by VWF:RCo<50% (40% for blood group O) and 28 pts with VWF:RCo>150%, without feature for inflammatory disorder. Excluding the latter’s, there was a significant relationship between serum IgM and VWF:Ag and VWF:RCo (R²= 0.37 and 0.38 respectively, p<10⁻⁴ for both linear regression analyses). Five of the 7 pts with AVWS presented with haemorrhagic syndrome (mainly epistaxis). Inhibitory activity (ELISA) was absent in all tested pts. Long term reduction of IgM by WM treatment (3 pts) and short term reduction of IgM with plasmapheresis were associated with increase in VWF:Ag and VWF:RCo. Bone marrow trephine biopsy, cataract surgery and insertion of plasmapheresis device required haemostatic treatment (desmopressin or replacement therapy) in 2 cases, whereas hip surgery could be performed without specific treatment in 1 long-term responding pt. Pts with VWF:RCo>150% had significantly shorter overall survival and survival after first-line therapy than other WM patients (p=0.01), although there was no difference in WM characteristics in both groups of pts. We conclude that VWF activity should be systematically assessed in WM pts especially before diagnostic procedure as low VWF:RCo levels can be found in some patients (AVWS). In those patients we observed a significant relationship between IgM and VWF activity but no inhibitory activity. Forty-eight percent of WM pts presented with an increased VWF:RCo activity associated with an adverse prognostic value. Acquired VWF abnormalities in WM warrant further studies.