W22: Bleeding disorders associated with IgM paraproteinemia and response to treatment: Illustrative Case series from Waldenstrom Macroglobulinaemia United Kingdom (WMUK) Forum

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Waldenstrom macroglobinaemia (WM) can rarely be associated with Acquired Von Willebrand syndrome (VWS) and other bleeding disorders. These patients often present with bleeding diathesis such as epistaxis or Gastrointestinal bleeds or peri-procedural bleeds. Treatment of IgM paraproteinemia often helps to resolve the Acquired VWS. We surveyed case series from various United Kingdom hospitals to understand the presenting features, serological levels of IgM paraprotein, Von Willebrands antigen, RICOF levels, FVIII levels, FXI levels, treatment offered and to assess response to treatment.

We would like to illustrate clinical features of 4 patients with IgM paraprotein who were found to have acquired bleeding disorders.

75 year old man was found to have IgM paraprotein of 34 g/L on evaluation for anaemia (Hb 103 g/L) and chest infections. He also had profuse epistaxis and hence evaluated for bleeding disorders and found to have acquired VWS (FVIII 33%, RICOF 19%, and VWF Ag 23%). Bone marrow biopsy confirmed a diagnosis of WM. Imaging did not show any lymphadenopathy or splenomegaly. He was treated with Rituximab/ bendamustine and his acquired VWD syndrome went into complete remission while he achieved Partial response to WM; but achieved normalisation of full blood counts.

59 year old man with IgM paraprotein of 19 g/L was diagnosed with acquired VWS (FVIII 31%, RICOF <10%, VWF Ag 14.8%) following detection of abnormal clotting screen. Normal imaging and Full blood count. Patient has not presented with bleeding and has only been monitored so far.

73 year old woman with IgM paraprotein of 33 g/L found to have anaemia (Hb 100 g/L) and 30% bone marrow lymphoid infiltrate; presented with a large gluteal haematoma post bone marrow aspirate. On evaluation, found to have an acquired Factor XI deficiency (0.40 IU/L). Treated with dexamethasone/ cyclophosphamide/ rituximab x 1 followed by bortezomib/ dexamethasone x 6 led to excellent responses with improvement of FXI levels and complete resolution of WM.

94 year old man with relapsed WM post multiple lines of treatment with paraprotein of 32 g/L and anaemia (Hb 88 g/L); presented with profuse bleeding after biopsy of maxillary lesion and found to have acquired Factor XI deficiency (0.40 IU/L) . Given frailty and refractory

disease, he was not treated further for WM. He died of chest infection secondary to progressive disease.

Most patients are diagnosed following bleeding diathesis. Bleeding phenotype is often associated with high levels of paraprotein and treatment of WM leads to resolution of acquired VWS and acquired FXI deficiency. Detailed bleeding history and clotting screen prior to any invasive procedures should be considered for patients with WM. This case series underscores this rare but potentially life threating complication that should be should be diagnosed and managed early.