

Bortezomib/ibrutinib/rituximab

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Various toxicities: case report

A 63-year-old woman developed Waldenstrom macroglobulinaemia (WM) and acquired von Willebrand syndrome (AVWS) flare during treatment with rituximab. Additionally, she developed peripheral neuropathy during treatment with bortezomib for WM and AVWS, and experienced rebound of WM and AVWS following the discontinuation of ibrutinib [*not all routes, dosages and outcomes stated; durations of treatments to reactions onsets not stated*].

The woman, who had history of Sjogren's syndrome, presented with mild bleeding symptoms including epistaxis and ecchymosis. Based on the results of a comprehensive evaluation, she was diagnosed with WM and associated AVWS along with L265 P MYD88 mutation. Following 6 months, first-line treatment was initiated with dexamethasone, rituximab and SC bortezomib. After initial doses of rituximab, a flare phenomenon of WM and AVWS occurred secondary to rituximab.

The woman was treated with several plasmapheresis sessions. Rituximab was stopped but she continued to receive bortezomib and dexamethasone for two more cycles achieving a serological partial response. However, bortezomib had to be discontinued due to the side-effect of grade 4 sensitive peripheral neuropathy. During the subsequent 21 months, her bleeding symptoms worsened; hence, second-line therapy with oral ibrutinib 420mg daily was initiated a year later. Within 2 months of treatment, a partial response was attained and haemostasis parameters were normalised. However, ibrutinib was discontinued for 20 days due to catarrhal symptoms and suspected SARS-CoV-2 infection, which was not confirmed. However, this interruption caused WM and AVWS flare (rebound effect). Thus, ibrutinib was again initiated that led to a rapid clinical and analytical response. After 26 months of ibrutinib use, a partial response was maintained with a good quality of life.

Poza M, et al. Ibrutinib effect in acquired von Willebrand syndrome secondary to Waldenstrom macroglobulinemia. *Therapeutic Advances in Hematology* 12: 28 Aug 2021.

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