

A Case Series of Waldenström's Macroglobulinaemia and Multiple Myeloma

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Background

Considered distinct clinicopathological entities, Waldenström's Macroglobulinaemia (WM) and multiple myeloma (MM) can overlap or co-exist in the same patient. We describe the features of six patients at our centre.

Case series

Case 1. 65 M. Diagnosis of smouldering MM with faint IgMκ paraprotein, diagnostic bone marrow (BMAT) 15% isolated CD138⁺CD20⁺CyclinD1⁺κappa⁺ plasma cells. After 15 years, an IgGκ paraprotein emerged alongside skeletal lytic lesions and pathological fracture. Repeat BMAT extensively infiltrated by small CD20⁺CD56⁺CD138⁺CyclinD1⁺IgM⁺κappa⁺ plasmacytoid cells. FISH CCND1 translocation; MYD88^{L265P} detected. Progression through Bortezomib-Dexamethasone-Rituximab with cast nephropathy, kappa light chains 3507. Commenced Daratumumab-Velcade-Dexamethasone. Concurrent MM and WM, with IgMκ and IgGκ paraproteins, lymphoplasmacytic morphology, and MYD88^{L265P} and t(11;14).

Case 2. 74 M. Mild anaemia and two IgMκ paraprotein bands, alongside kappa light chains 507, ratio 5.2. BMAT 80% CD5⁺CD10⁺CD20⁺CyclinD1⁺ lymphocytes and 15% CD138⁺ plasma cells. MYD88^{L265P} detected. Commenced Rituximab-Bendamustine. MYD88^{L265P} WM with prominent plasmacytic differentiation and elevated kappa light chains.

Case 3. 50 M. Oromaxillary mass, cervical lymphadenopathy and skeletal lytic lesions. Biopsy demonstrated medium-large BCL6⁺CD5⁺CD10⁺CyclinD⁺CD20⁺ centroblastic lymphocytes. IgMκ paraprotein at 14g/L, with kappa light chains 427.7, ratio 47.52. BMAT 10% infiltration with CD20⁺IgM⁺PAX-5⁺CD19⁺CD23⁺ small cells and additional 50% sheets of medium-large sized cells with multiple nucleoli, CD20⁺CyclinD1⁺CD138⁺CD56⁺CD79a⁺cytoplasmicIgM⁺κappa⁺. MYD88^{L265P} detected, CD138-FISH 1q21 gain and TP53 deletion. Treated with 6 cycles R-CHP-Velcade to complete metabolic response (CMR), consolidative BEAM autologous transplant. Patient subsequently suffered CNS relapse. WM with MYD88^{L265P}, presenting with high-grade transformation to DLBCL. Additional concurrent plasmablastic myeloma with high-risk cytogenetics.

Case 4. 61 M. Known IgM lambda and IgA kappa MGUS. Hypopharyngeal mass and lytic femoral lesion emerged after three years. Biopsies confirmed a kappa⁺CD138⁺ plasmablastic cells. BMAT involved, but predominant infiltrate concurrent lambda-restricted small lymphoplasmacytoid cells. CD138-FISH 1q21 gain. HIV negative. Patient treated with R-CHP-Velcade to CMR. Disease progression after two years, with further lytic lesions and rising IgA paraprotein. Underwent induction with Dara-VTD, with subsequent melphalan ASCT. WM with concurrent IgA kappa plasmablastic disease, with 1q gain.

Case 5. 59 M. Mild pancytopenia alongside two IgMλ paraproteins, 9g/L. Diagnostic BMAT demonstrated a 30% lymphoplasmacytic infiltrate, with CD138⁺. Worsening anaemia 5 years later with a rise in IgM paraprotein to 20g/L. BMAT >90% CD20⁺IgM⁺ lymphoid infiltrate, occasional plasma cell only. MYD88^{L265P} detected. Treatment with rituximab and ibrutinib, with improvement in haemoglobin and decrease in paraprotein. Emergence of an additional IgA kappa paraprotein band a year later, rising to 47g/L. Kappa light chains 434, lambda 23, ratio 18. BMAT 10% residual LPL, with 60% concomitant kappa⁺ plasma cells. CD138-FISH 1q gain, 13q12 loss. CT unremarkable. Patient commenced Dara-VTD.

MYD88^{L265P} WM with heavy BM involvement, responding to rituximab-ibrutinib therapy but subsequent development of high-risk IgAk MM.

Case 6. 56 M. IgMk MGUS, subsequent IgGk paraprotein. BMAT after 17 years demonstrated 35% CD20+IgM+kappa+ lymphoplasmacytic infiltrate, with 7% CyclinD1-CD56-C138+IgM+kappa+ plasma cells. CD138-FISH TP53 mutation. MYD88^{L265P} not detected. MRI whole body normal. Under active observation. MYD88^{WT} LPL with TP53^{MUT} plasma cell infiltrate.

Case series

We report six cases with overlapping features of WM and MM, highlighting the need for clinician awareness and vigilance of changing disease phenotype.

15th July 2024

Dear Sir/Madam,

Re: International Workshop on Waldenstrom's Macroglobulinemia 12

I hereby confirm that Dr Oliver Tomkins is a PhD fellow at the UCLH Centre for Waldenstrom's Macroglobulinaemia and Related Conditions. He is also a haematology registrar in a training programme.

Yours sincerely,



Dr Shirley D'Sa
Consultant Haematologist and Honorary Associate Professor