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Retrospective analysis of secondary AL amyloidosis in patients diagnosed with Waldenstrom Macroglobulinemia: a single-center experience

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Waldenstrom Macroglobulinemia (WM) is a rare variant of indolent B cell lymphoma, characterized by the presence of an IgM-paraprotein, clonal lymphoplasmacytic cells in the bone marrow, and in over 90% of cases, the presence of the MYD88 mutation. Its clinical manifestations vary from IgM-related symptoms to clonal B cell proliferation and overall survival (OS) varies from 10-12 years.

Light chain amyloidosis (AL amyloidosis) is a hematological disorder characterized by the deposit of amyloid fibrils, fragments of light chains leading to organ dysfunction. Virtually all types of tissue can be damaged by deposits of amyloid fibrils. WM-associated AL amyloidosis (WM-AL amyloidosis) occurs in approximately 10% of patients

Our aim was to identify patients with these characteristics and analyze disease evolution and clinical outcomes to further increase our understanding of WM-AL amyloidosis.

We collected data from patients diagnosed with WM between 2008 and 2023. 21 patients met criteria for diagnosis of WM and were concomitantly evaluated for AL amyloidosis due to a serological/clinical suspect.

WM-AL amyloidosis was identified in four patients. Two were diagnosed with WM-AL amyloidosis and two were diagnosed with AL amyloidosis after initial diagnosis of WM.

Patient 1 had cardiac and renal involvement due to AL amyloidosis with WM at diagnosis and began first-line treatment with CDR (Cyclophosphamide, Dexamethasone, Rituximab), progressed after 4 months, and started second-line treatment with MCP (Melphalan, Cyclophosphamide, Prednisone) obtaining a partial response (PR) and a Progression Free Survival (PFS) of 24 months; third-line treatment with Bortezomib and Dexamethasone (Vel-Dex) was necessary due to cardiac relapse, obtaining a complete response (CR). OS was 7 years.

Patient 2 was diagnosed with WM-AL amyloidosis with cardiac involvement. CDR was selected as first line treatment; the patient obtained a CR with a PFS of 8 years. Second-line treatment with Cyclophosphamyde, Velcade, Dexamethasone (CyBorD) was performed but the patient progressed and started third-line treatment with Melphalan, obtaining a PR. OS was 12 years.

Patient 3 was diagnosed with symptomatic WM and received first-line treatment (CDR). Due to increase of renal symptoms, disease re-evaluation was performed, and renal amyloidosis was identified. Therefore, the patient began second-line treatment with Vel-Dex obtaining a partial response. The patient is currently in follow up

Patient 4 was diagnosed with WM and received first-line treatment (Fludarabine, Cyclophsphamide, Rituximab) obtaining a CR with a PFS of 8 years. Second-line treatment was Bendamustine, interrupted after three cycles due to AEs. Subsequent treatment with Ibrutinib lasted for 6 months, interrupted due to relapse as a rare bilateral breast deposit of amyloid fibrils. Subsequently, the patient received multiple salvage treatment without obtaining a response and died shortly after. OS was 11 years.

WM-AL amyloidosis is a rare disease involving two disorders with few lines of treatment available. A correct first-line treatment is fundamental as it has been shown to increase OS. More research is needed to identify biological and genetic markers to further increase survival of these patients. Despite the retrospective nature and the small number of patients evaluated, results are in line with the data reported in literature.