

Clinical Features and Prognostic Analysis of Lymphoplasmacytic Lymphoma/Waldenström Macroglobulinemia with Concurrent Autoimmune Hemolytic Anemia

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Abstract:

Introduction : Lymphoplasmacytic lymphoma/Waldenström macroglobulinemia (LPL/WM) complicated by autoimmune hemolytic anemia (AIHA) is a rare clinical entity, with the majority of available evidence derived from isolated case reports. Consequently, the clinical features, optimal management, and prognostic determinants in this unique patient subset remain largely unexplored. Given the therapeutic challenges posed by the concurrent neoplastic and autoimmune processes, a systematic characterization of this population is urgently needed to inform clinical decision-making.

Methods: This was a retrospective cohort study conducted at the Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences, encompassing a total of 504 patients with a confirmed diagnosis of LPL/WM between January 2012 and December 2025. AIHA was defined based on the presence of hemolytic anemia with a positive direct antiglobulin test (DAT), in the absence of other identifiable causes of hemolysis. This study was approved by the institutional review board of the hospital, and informed consent was waived due to the retrospective nature of the analysis.

Results: Among 504 patients, 40 patients (7.94%) were identified as having concurrent autoimmune hemolytic anemia (AIHA). The median age in patients with AIHA was 57.1 years which was younger than that without AIHA (57.1 vs 61.6, $P=0.017$). Among 40 patients with AIHA, 27 patients were male and 13

patients were female. The median hemoglobin was 81.6g/L, which was significantly lower than patients without AIHA (81.6 vs 94.7 g/L). Besides, these patients with AIHA exhibited higher indirect bilirubin (23 vs. 9.83, $P<0.001$), higher lactate dehydrogenase levels (274 vs. 172, $P<0.001$), lower MYD88 positivity rate (50% vs. 73.9%, $P=0.02$) and lower IgM level (22.6 vs 36.8 g/L, $P<0.001$). No statistically significant differences were observed between the two groups in terms of IgH gene rearrangement positivity rate or IGH mutation rate (89.2% vs. 78.3%, $P=0.122$; 91.3% vs. 84.87%, $P=0.378$, respectively) and the CXCR4 mutation rate (29.6% vs. 27.6%, $P=1$). Among AIHA patients, Coombs testing showed that 77.5% (31/40) had warm antibody type C3, and 50% (20/40) tested positive for cold agglutinins. The median PFS was 47.2 in AIHA which was shorter than that with the patient without AIHA (59.8). The median overall survival (OS) of the AIHA group was 109.5 months which was also shorter than 147.0 months of the non-AIHA group; For different treatment, The PFS and OS in different treatments group had no significantly difference. Lymphocyte subset analysis indicated a lower total B-cell percentage and lower NK cells in patients with AIHA ($P<0.05$).

Conclusion: AIHA in the context of LPL/WM exhibits distinctive clinical and prognostic features that set it apart from LPL/WM patients without this complication..

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