MANAGEMENT OF TRANSFORMED WALDENSTROM MACROGLOBULINEMIA

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ABSTRACT

Histological transformation (HT) occurs rarely in Waldenström macroglobulinemia (WM), with a higher incidence in *MYD88* wild-type patients. HT should be suspected in patients with WM that present physical deterioration, rapidly progressive lymphadenopathy, extranodal disease, sudden rise in LDH levels, and/or decreased serum IgM levels. Tissue biopsy is mandatory to diagnose HT-WM and may be directed by clinical or radiologic features (ie, by site of rapidly enlarging lymph nodes, or by site of increased avidity on ^{18F}FDG-PET/CT). Most transformation events are caused by diffuse large B-cell lymphoma of the activated B-cell subtype. Recommendations for the optimal management of HT-WM are limited by the lack of prospective studies. Treatment with intermediate-dose chemoimmunotherapy, such as R-CHOP, is the preferred option. Central nervous system prophylaxis with high-dose MTX should be considered if feasible and consolidation with autologous stem cell transplantation (SCT) should be discussed in fit patients responding to chemoimmunotherapy. Durable remission has been reported in autologous SCT with 3-year progression-free survival (PFS) of 44% and 3-year overall survival (OS) of 57%. In relapsed/refractory patients with HT-WM, chimeric antigen receptor T cells (CAR-T) therapy is associated with high efficacy (ORR 96%, CR 87%, 1-year PFS 73%, 1-year OS 80%) and no unexpected toxicity.