

## **SYSTEMIC IGG4-RELATED LYMPHADENOPATHY: A CLINICAL AND PATHOLOGIC COMPARISON TO MULTICENTRIC CASTLEMAN'S DISEASE**

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IgG4-related disease sometimes involves regional and/or systemic lymph nodes, and often clinically and/or histologically mimics multicentric Castleman's disease (MCD) or malignant lymphoma. In this study, we examined clinical and pathologic findings of nine patients with systemic IgG4-related lymphadenopathy. None of these cases were associated with HHV-8 or HIV infection, and there was no T-cell receptor or immunoglobulin gene rearrangement. Histologically, systemic IgG4-related lymphadenopathy was classified into two types by the infiltration pattern of IgG4-positive cells: interfollicular plasmacytosis type and intra-germinal center plasmacytosis type. The interfollicular plasmacytosis type showed either Castleman's disease-like features or atypical lymphoplasmacytic and immunoblastic proliferation-like features. By contrast, the intra-germinal center plasmacytosis type showed marked follicular hyperplasia, and infiltration of IgG4-positive cells mainly into the germinal centers, and some cases exhibited features of progressively transformed germinal centers. Interestingly, eight of our nine (89%) cases showed eosinophil infiltration in the affected lymph nodes, and examined patients showed high elevation of serum IgE. Laboratory examinations revealed elevation of serum IgG4 and soluble IL-2 receptors. However, the levels of IL-6, CRP, and LDH were within normal limits or only slightly elevated in almost all patients. One patient showed a high IL-6 level whereas CRP was within the normal limit. Autoantibodies were examined in five patients and detected in four. Compared with the previously reported cases of MCD, our patients with systemic IgG4-related lymphadenopathy were significantly older and had significantly lower CRP and IL-6 levels. In conclusion, in our systemic IgG4-related lymphadenopathy showed pathologic features only partially overlapping those of MCD, and serum data (especially CRP and IL-6) are useful for differentiating the two. Our findings of eosinophil infiltration in the affected tissue and elevation of serum IgE may suggest an allergic mechanism in the pathogenesis of systemic IgG4-related lymphadenopathy.