Various Aspects of IgG4-related Disease

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Key words: IgG4-related disease, IgG4-related kidney disease, lymphoma, Henoch-Schönlein purpura

(Intern Med 51: 1157-1158, 2012)
(DOI: 10.2169/internalmedicine.51.7451)

A clinicopathological entity associated with an elevated serum IgG4 level and abundant infiltration of IgG4-positive plasma cells is widely known as IgG4-related disease (IgG4 RD). IgG4RD has been identified with Mikulicz’s disease in relation to the aspect of autoimmune systemic disease (1), although such characteristics were first recognized in autoimmune pancreatitis (AIP) (2). Thereafter, many cases have been reported and it has been revealed that IgG4RD shows various changes in multiple organs. Recently, comprehensive diagnostic criteria have been published for the establishment of IgG4RD by the collaboration of two IgG4RD study groups organized by the Ministry of Health, Labor and Welfare of Japan (3). In particular, renal lesions are frequently detected and associated with the involvement of other organs. The main change in the kidney is tubulointerstitial nephritis, but other characteristics including glomerulopathy are also reported (4). From this point of view, diagnostic criteria for IgG4-related kidney disease (IgG4RKD) have also been published by the working group of the Japanese Society of Nephrology (5).

In the case reported by Oshima et al. (6), the diagnosis of definite IgG4RKD was established by both criteria (3, 5). This case has two interesting features, which are valuable for investigating the pathogenesis of IgG4RD. One is that the onset follows malignant lymphoma and lymphadenopathy, and the other is that Henoch-Schönlein purpura (HSP) is a complication. As for the former feature, IgG4RD categorized as plasmacytosis should be differentiated from lymphoma or other malignancies. However, it is possible that lymphoma may be a precursor of IgG4RD. Yamamoto et al. (7) showed that the standardized incidence ratio for malignancies including lymphoma in IgG4RD is substantially higher than that in general population. Accordingly, we should consider the relationship between IgG4RD and malignancies. Recently, it has been clarified that helper T2 and regulatory T cells (Treg) play a pivotal role in the pathogenesis of IgG4RD (8-10). On the other hand, it is known that Treg infiltrates are observed in a variety of cancers and are related to the prognosis of neoplastic diseases including lymphoma (11). Therefore it will be interesting to study the linkage of IgG4RD and neoplastic diseases through Treg mechanism. As for the latter feature, the complications of IgG4RKD and HSP have been reported in a few cases (12, 13). Clinical features, i.e., eosinophilia and a high level of serum IgE, show that IgG4RD is induced not only by autoimmunity but also by allergy. The preceding occurrence of HSP also suggests that allergy could be involved in the etiology of IgG4RD.

IgG4RD is a still mysterious disease entity, and it has various characteristics of autoimmune disease. The current case by Oshima et al. (6) presents intriguing problems of IgG4RD to researchers who confront this disease.

The author states that he has no Conflict of Interest (COI).

References
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