Introduction to IgG4-related disease

Ming-Fei Liu MD, NCKUH, Tainan, Taiwan

IgG4-related disease is a newly recognized immune-mediated systemic disease which was characterized by fibroinflammatory condition with a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells in pathology. The disease was first described in patients with autoimmune pancreatitis in Japan about one decade ago. Since then, the spectrum of IgG4-related disease has been explosively expanded and been described in virtually every organ system including the biliary tree, salivary glands, periorbital tissues, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, and skin. It may present with an isolated single organ or affect simultaneously many organs. The histopathological features are strikingly similar across organs, regardless of the site of disease. IgG4-related disease mimics many malignant, infectious and inflammatory disorders and the nomenclature for IgG4-related disease continues to evolve.

The etiopathogenesis of IgG4-related disease remains to be elucidated. From the immunolopathological viewpoint, autoimmunity and infectious agents are potential immunologic triggers. Cytokines including IL- 4, 5, 10, and 13 and TGF-β are overexpressed, leading to the speculation that Th2 cells and Treg cells play a crucial role in the disease pathogenesis. These cytokines contribute to the eosinophilia, elevated serum IgG4 and IgE concentrations, and progression of fibrosis that are characteristic of IgG4-related disease. However, many recent investigations have shown clonal expansion of IL-1 β and TGF-β1-secreting CD4+ cytotoxic T lymphocytes in peripheral blood and inflammatory tissue lesions of patients with IgG4-related disease. However much remains unknown about the role of IgG4 in IgG4-related disease.

The gold standard for the diagnosis of IgG4-related disease is tissue biopsy. High serum IgG4 concentrations are neither sufficiently sensitive nor specific for the diagnosis. Imaging is a part of diagnostic approach, but the findings are non-specific and are only helpful to define the extent of organ involvement. So far several diagnostic criteria for specific organs have been developed for clinical use. Remission induction with glucocorticoids is the first-line therapy in active disease. Other treatment strategies are being investigated including anti-CD 20 biologics. The management and treatment guidance of IgG4-related disease by international consensus for practical use was published recently.