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Immunoglobulin G4 (IgG4) Sclerosing Disease

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Immunoglobulin G4 (IgG4) sclerosing disease is a recently described entity that is increasingly being recognized and diagnosed. The spectrum of associated organ systems is broad, but unifying histopathologic, clinical, and serologic findings is helpful when making the diagnosis.

Plasma cells are classified by the type of immunoglobulin they produce. Within the family of immunoglobulin G (IgG) plasma cells, a subset designated IgG4-positive plasma cells can be found. IgG4-positive plasma cells, the smallest fraction of the IgG subclass, typically account for only a minor fraction of circulating plasma cells.

In 2003, a new clinicopathologic entity involving IgG4-positive plasma cells and related sclerosis was described in the Far East. Since then, dozens of publications have appeared and demonstrated that the disease can affect anyone, most commonly middle age adults. First recognized in the pancreas in patients with autoimmune pancreatitis, IgG4-related disease has since been reported in nearly every organ system.

Often times, patients present with an inflammatory pseudotumor (a rapidly growing lesion that consists of plasma cells and other inflammatory cells) at the site of involvement. These pseudotumors can mimic malignant lesions both clinically and radiologically, leading to biopsy or surgical resection.

On histopathologic examination, the involved tissue is invariably overwhelmed with a rich lymphoplasmacytic infiltrate. In the appropriate clinical setting, infection and hematopoietic malignancies should be ruled out. Immunohistochemistry can help demonstrate a significant increase in the proportion of IgG4-positive plasma cells. Other histologic features include storiforming fibrosis and obliterative phlebitis. Importantly, a simple increase in the number of IgG4-positive plasma cells is insufficient, in most cases, to render a diagnosis of IgG4 sclerosing disease. Clinical laboratory tests, including elevated serum levels of IgG4, are also present in the majority of cases and can be useful when the diagnosis is suspected. International working groups have recently submitted proposed diagnostic criteria for IgG4 sclerosing disease based, in part, on the tissue at the involved site.

The exact pathogenesis of IgG4 sclerosing disease is unknown. Various theories have been postulated, among them, that the disease process may involve the dysregulation of various systems controlling immune and host response, or even allergy.

Though locally disruptive, pseudotumors and related inflammatory lesions often respond well to steroid therapy. However, there have been numerous documented cases of patients developing chronic disease and complications (eg, cirrhosis, retroperitoneal fibrosis, portal hypertension, etc) secondary to IgG4-related sclerosis. Patients with IgG4 sclerosing disease at one site may also develop IgG4-related pathologies at another site.

Reports linking lymphoma and other malignancies in patients with IgG4 sclerosing disease have also been made. Further data and long-term follow-up are necessary to better evaluate these relationships as well as the prognosis IgG4-related sclerosis carries.

With increasing awareness by pathologists, clinicians, and radiologists, the frequency of diagnosing IgG4-related sclerosis will likely increase in the near future. Using established guidelines, this team of physicians together can make appropriate diagnostic and treatment decisions for its patients.

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