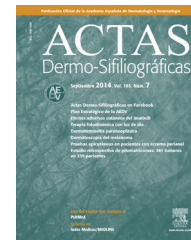




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RESIDENT'S FORUM

Dermatological Aspects of immunoglobulin G4 (IgG4)-Related Disease[☆]



RF-Perspectiva dermatológica de la enfermedad relacionada con la inmunoglobulina G4 (IgG4)

O. Yélamos

Servicio de Dermatología, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

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PALABRAS CLAVE

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Immunoglobulin G4-related disease (IgG4-RD) is a systemic disease characterized by lymphoplasmacytic inflammation, fibrosis, and elevated levels of IgG4 in tissues and eventually in the blood. IgG4-RD is a recently described disease and encompasses classic entities such as Riedel's thyroiditis, Mikulicz syndrome, and Küttner's tumor.¹ It is a rare disease that affects middle-aged men, especially Asians.^{2,3}

The etiology of IgG4-RD is poorly understood. Several potential triggers have been proposed, including genetic susceptibility, malignant tumors, and even some microorganisms such as *Helicobacter pylori*.³ Pathophysiologically, an increase in the Th2 and Treg responses has been described. This induces the release of cytokines such as IL-10 and TGF- β , which are responsible for the inflammation and the fibrosis characteristic of this disease.^{2,3}

IgG4-RD predominantly affects the pancreas, presenting with autoimmune pancreatitis, but can affect virtually every organ, including the salivary glands, the lacrimal glands, the orbits, the lungs, the kidneys, the liver, the thyroid, the hypophysis, the retroperitoneum, and the prostate.¹ Skin involvement is less common, and usually occurs after the onset of systemic symptoms. However, cutaneous involvement prior to the appearance of systemic symptoms has been described, as well as cases with exclusive involvement of the skin.⁴

Cutaneous IgG4-RD presents with erythematous papules, plaques, and particularly nodules, predominantly located on the head and neck.^{4,5} The differential diagnosis includes cutaneous lymphomas and pseudolymphomas, sarcoidosis, lupus, cutaneous metastases, and even deep skin infections such as syphilis and micobacteriosis.⁴ Histologically, the lesions are characterized by an infiltrate rich in lymphocytes and plasma cells, storiform fibrosis, obliterative phlebitis, and less frequently an infiltrate with few eosinophils.^{1,4,5}

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E-mail address: oyelamos@santpau.cat

Various diagnostic criteria for IgG4-RD have been proposed. These include the presence of compatible signs (mass or swelling in one or more organs) and a biopsy compatible with elevated levels of IgG4+ plasma cells (IgG4/IgG ratio > 40%; > 10 IgG4+ cells per high-power field), associated with elevated serum levels of IgG4 (> 135 mg/dL).² However, these criteria remain under discussion, as normal serum IgG4 levels can be found in patients with exclusive skin or single organ involvement.⁴ It is also important to note that an increase in serum IgG4 levels is not a pathognomonic finding in IgG4-RD as such increases have been described in other dermatoses such as pemphigus vulgaris, atopic dermatitis, some parasitic infections,⁵ and recently in marginal zone lymphomas.⁶

IgG4-RD has been treated using systemic corticosteroids, azathioprine, thalidomide, and even biologics such as rituximab and infliximab.^{1,3,4} The prognosis depends on the degree of dysfunction caused by the inflammation and fibrosis in the organs affected by the disease.

In summary, it is important that dermatologists consider IgG4-RD in patients presenting with a nodule or mass with an infiltrate rich in plasma cells. However, as IgG4-RD is a recently described and little-known disease, the diagnostic

limitations should be borne in mind. Further characterization of this disease is necessary to establish definitive diagnostic criteria.

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