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Inflammation and infection

IgG4-related disease presenting as a solitary paratesticular fibrous pseudotumor

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ABSTRACT

Paratesticular fibrous pseudotumors (PFP) have long been described in the literature. Since the recognition of IgG4-related disease (IgG4-RD) as a distinct clinical entity, cases of PFP with similar pathological characteristics have been described. A case of IgG4-RD presenting as an isolated PFP is presented.

Introduction

IgG4-RD is an immune-mediated fibroinflammatory disease characterized by lesions containing dense ("storiform") fibrosis with infiltration of IgG4 positive plasma cells that can develop in a variety of anatomical sites[1]. The 2019 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for IgG4-RD entry criteria requires characteristic clinical, pathologic or radiographic involvement of a typical organ (e.g. pancreas, salivary glands, bile ducts, orbits, kidney, lung, aorta, retroperitoneum, pachymeninges, or thyroid gland).[2] PFPs are uncommon benign lesions of the testicular tunica that can clinically mimic malignancy.[3] The majority of cases of PFP, prior to the recognition of IgG4-RD as a distinct entity in 2003,[4] were found to contain similar histology to IgG4-RD.[5] A case is presented in this article that represents a patient with a solitary PFP that meets the histologic and serologic but not the anatomic criteria for IgG4-RD.

Case

A 36-year-old male with no prior medical history presented with a small, painless right scrotal mass. Ultrasound of the mass revealed a solid 1.7 cm extratesticular mass centered within the epididymal tail (Fig. 1). He underwent surgical excision of the mass along with a vasectomy. No other abnormalities were identified during surgery. Histology of the mass showed storiform fibrosis (Fig. 2) with positive staining of IgG4+ (positive) plasma cells (Fig. 3) with IgG4/IgG ratio of over 50% and more than 50 IgG4+ cells per high power field (hpf). Serologic testing revealed elevated IgG4 levels of 166.8 mg/dL (reference range 6.0–130 mg/dL). Physical examination was otherwise normal. Computed tomography of the abdomen and pelvis performed 2 months after surgery was normal and showed no retroperitoneal fibrosis, abdominal organ mass or lymphadenopathy. Follow-up physical examination performed 4 months after surgery was normal without recurrence of a scrotal mass.

Discussion

Paratesticular fibrous pseudotumors (also known as chronic proliferative periorchitis, inflammatory pseudotumors, reactive periorchitis) are rare, benign, fibroinflammatory tumors that are found in the tunica vaginalis testes, spermatic cord or epididymis. Microscopic pathology of these tumors has been described as consisting of densely arranged fibrotic and myofibrotic proliferation with heterogenous inflammatory cells including plasma cells, lymphocytes, histiocytes, granulocytes and hyalinized areas.[5] Pathological analysis of these tumors prior to 2003 typically did not stain for IgG or IgG-4 and therefore cannot be confirmed as being definitive of IgG-4RD however the pathology of most of these tumors seem morphologically similar. Since IgG4-RD was first characterized, multiple anatomical sites of involvement have been

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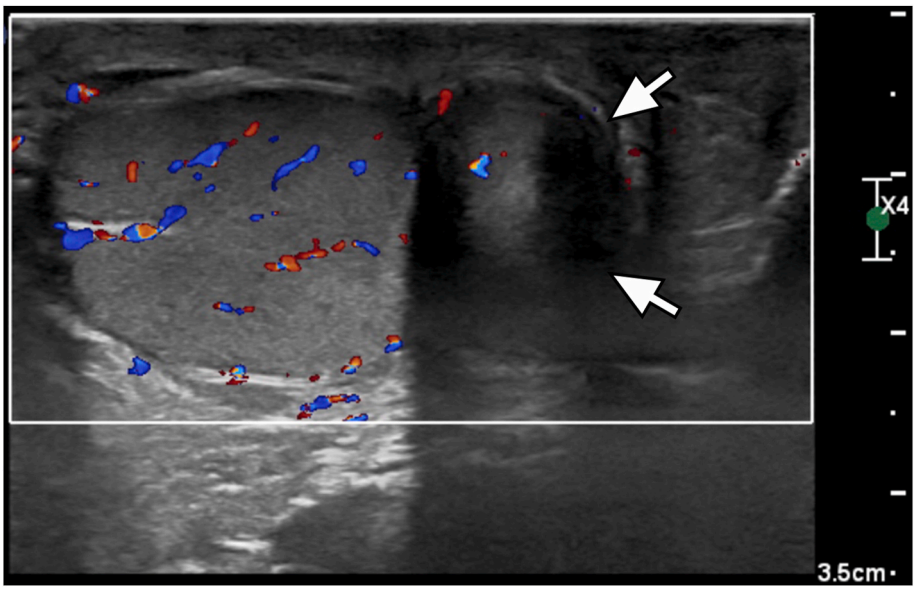

Fig. 1. Sagittal color Doppler ultrasound of the right testicle showed a solid, heterogeneous extratesticular mass (arrows) with acoustic shadowing around its periphery centered within the epididymal tail. Color Doppler flow was present within the mass. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

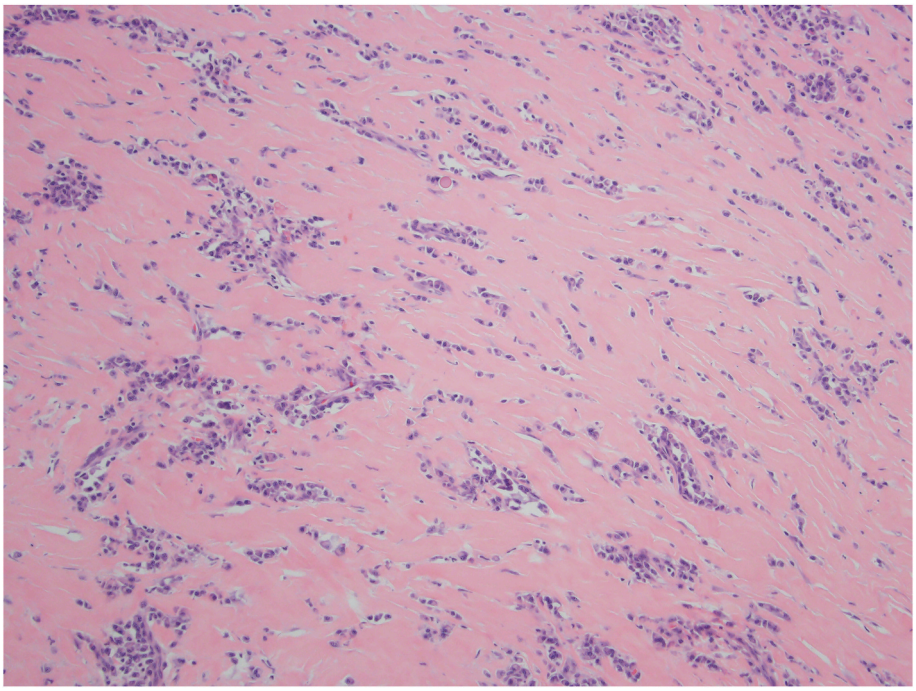

Fig. 2. The testicular excisional biopsy showed extensive storiform hyalinized fibrosis. A prominent admixed lymphoplasmacytic infiltrate with a markedly increased number of plasma cells was present. (Hematoxylin and eosin, 10×).

described including the lungs, kidneys, salivary glands, lacrimal glands, orbits, thyroid, pancreas, biliary tree, meninges, aorta and retroperitoneum.[2] Clinical syndromes include autoimmune pancreatitis, chronic aortitis, Reidel's thyroiditis, Mikulicz syndrome, retroperitoneal fibrosis and interstitial, bronchovascular and nodular lung disease.[1] The 2019 ACR/EULAR inclusion criteria for the diagnosis of the disease is supported by characteristic histology, the presence of IgG4 positive plasma cell infiltrates and the presence of elevated serum levels of IgG4[2]. The entry criteria (step 1) for classification requires "characteristic clinical or radiologic involvement of a typical organ (e.g. pancreas, salivary glands, bile ducts, orbits, kidney, lung, aorta, retroperitoneum, pachymeninges, or thyroid gland) OR pathologic evidence of an inflammatory process accompanied by a lymphoplasmacytic infiltrate of uncertain etiology in one of these same organs". After excluding for other diseases and various clinical, serologic, radiologic and pathologic items, histopathology (lymphocytic infiltrate and storiform fibrosis) and immunostaining (IgG4+/IgG+ ratio and number of IgG4+/hpf) criteria are weighted.

The presented case does meet the defined histopathology, immunostaining and serologic criteria of the 2019 ACR/EULAR criteria for IgG4-RD. The case however does not meet entry criteria as the affected area was not in a specifically defined organ or anatomical area. The authors

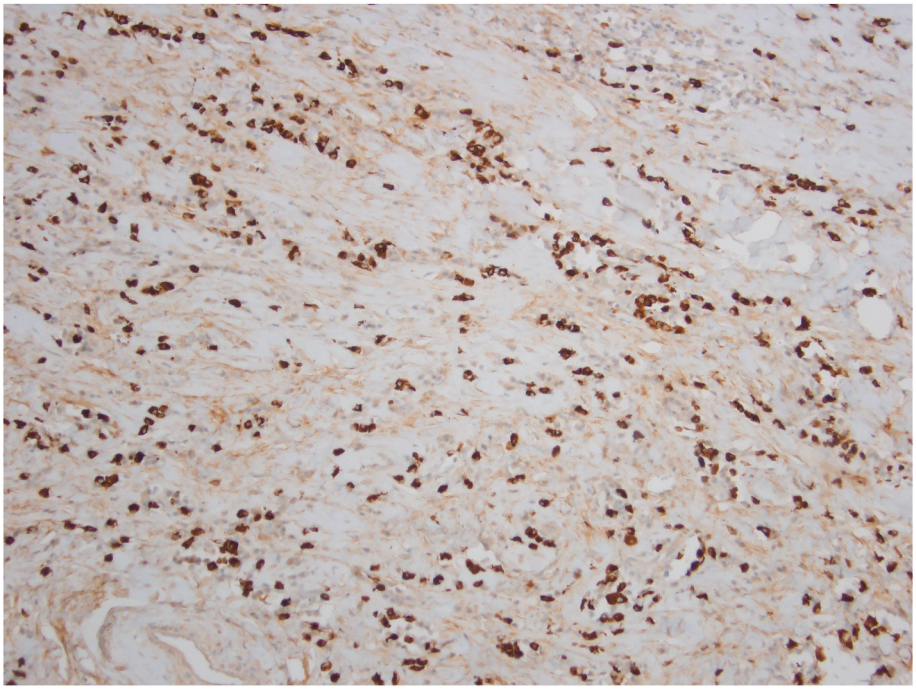

Fig. 3. Immunostains showed a markedly increased number of IgG4+ plasma cells as well as an increased IgG4+/IgG+ ratio. (IgG4 immunostain, 10×).

of the paper do mention in their discussion that the criteria are not intended for use in clinical practice as the basis of establishing a diagnosis. As explained, the criteria were set up to attain the highest possible specificity while retaining moderately high sensitivity. IgG4-RD is a systemic inflammatory disease that can affect many different anatomical systems. Patients presenting with the clinical picture of an apparent isolated paratesticular pseudotumor with pathology consistent with IgG4-RD should therefore undergo further evaluation for other potential areas of anatomical involvement.

Declaration of competing interest

None.

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