Case Report

Isolated testicular immunoglobulin G4-related disease: A mimicker of malignancy

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ABSTRACT

ImmunoglobulinG4 related disease (IgG4RD) is a systemic fibroinflammatory disease recognized recently. This usually presents with multiorgan involvement. We are reporting a case of a35-year-old male patient with isolated IgG4RD of the testis. This patient presented with right testis pain which responded to conservative treatment. However, later, he reported with hard swelling in the right testis which on imaging was suggestive of malignancy and hence underwent radical orchiectomy. Histopathology with immunohistochemical staining confirmed IgG4RD of the testis. To the best of our knowledge, this is the first report of purely isolated case of IgG4RD of testis in English literature.

Key words: Immunoglobulin G4 related disease, plasma cells, testes

INTRODUCTION

Immunoglobulin G4 related disease (IgG4RD) is a systemic fibroinflammatory disease recognized in the last decade. This disease usually presents as a systemic disease or rarely as an organ-specific disease. In the genitourinary system kidneys, ureters, urinarybladder, urethra, and prostate gland are commonly affected, but the involvement of testis by this disease is uncommon.

CASE REPORT

A 35-year- old male presented with pain in the right hemiscrotum of 5 days duration which was relieved following treatment elsewhere. Four weeks later, he reported with a 1 cm × 1 cm non tender hard nodule in the right testis. High-resolution ultrasound showed a hypoechoic lesion. Testicular tumor markers were normal. High inguinal orchiectomy was performed considering a diagnosis of testicular malignancy [Figure 1]. The histopathology showed testicular tissue with a lesion composed of dense inflammatory infiltrates predominantly plasma cells, lymphocytes, few eosinophils, and pigment-laden macrophages with dense areas of fibrosis. The inflammatory cells were seen infiltrating the interstitium surrounding the seminiferous tubules [Figure 2a]. No definite granuloma, necrosis, or atypical cells were seen. Immunohistochemistry showed extensive IgG staining of the plasma cells. More than 40% IgG4 staining strongly suggested IgG4RD of the testis [Figure 2b]. The IgG4 cell count was 120–130/hpf. However, serumIgG4 was normal. Investigations such as contrast enhanced computed tomography (CECT) of the thorax, abdomen, and pelvis did not show any systemic involvement.

DISCUSSION

IgG4RD is predominantly a systemic disorder usually with multiorgan involvement. It may also present with isolated organ involvement. In the genitourinary tract, the paratesticular involvement of IgG4RD has been reported. Primary testicular IgG4RD has been reported only once but with IgG4 related autoimmune pancreatitis.[1] Isolated

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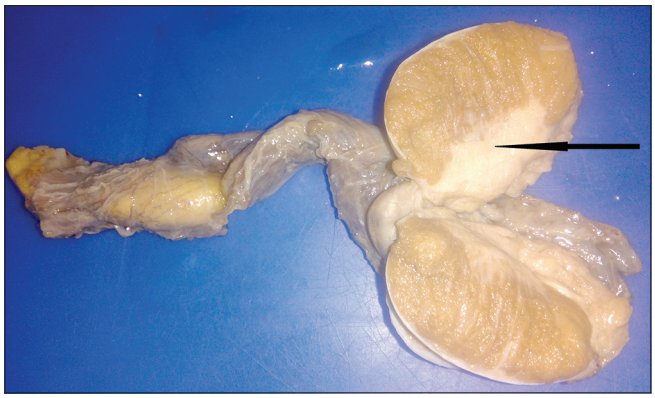

Figure 1: Cut section of testis showing the lesion (arrow mark)

primary testicular IgG4RD has not been reported till date to the best of our knowledge.

According to the consensus statement of international symposium on IgG4RD, the criteria for the diagnosis of IgG4RD include the presence of increased number of IgG4 plasma cells along with the presence of two out of three major histopathological criteria of dense lymphoplasmacytic infiltrate, fibrosis, and obliterative phlebitis.[2] Other associated features are increased number of eosinophils and phlebitis with out obliteration of lumen.[2,3] In our case, the percentage of fibrosis area was >75% but the characteristic storiform fibrosis was not seen. In organs such as lymphnode, lungs, minor salivary glands and lacrimal glands, storiform fibrosis may be absent.[2] There was dense lymphoplasmacytic infiltrate, obliterativephlebitis, and extensive fibrosis along with increased number of eosinophils. On histochemistry, increased numbers of IgG4 plasma cells were seen with an IgG4:IgG ratio of more than 40%, thus confirming the diagnosis of primary testicular IgG4RD.[2] There is no standard cut-off of the IgG4 cell count required for the diagnosis; however, it ranges from 10 to 200 cells/hpf according to the organ involved and the nature of the specimen.[2] The IgG4/IgG plasma cell ratio must be >40% for the histological diagnosis of IgG4RD. An elevated level of serum IgG4 is not mandatory for the diagnosis of IgG4RD.[2]

There are three classes of diagnoses with regard to IgG4RD. Our patient falls into the category of "histologically highly suggestive of IgG4RD." The other two categories include probable histological features of IgG4RD and insufficient histopathological evidence of IgG4RD. The differential diagnosis includes testicular malignancy, lymphoma, and inflammatory myofibroblastic tumor of the testis.[2]

de Buy Wenniger *et al*. Reported a case of testicular involvement in a patient diagnosed with multiorgan IgG4RD.[1] This patient initially presented with IgG4 related autoimmune pancreatitis and later developed orchitis. This patient underwent bilateral orchiectomy with the presumed

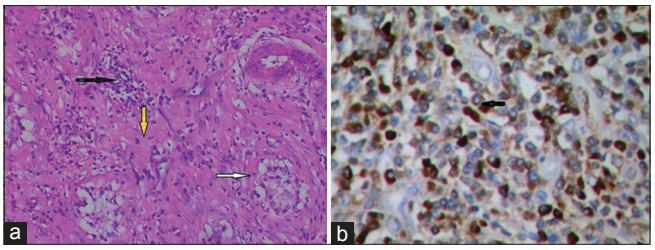

Figure 2: (a) H and E staining showing lymphoplasmacytic infiltrate (black arrow), obliterative phlebitis (white arrow) and fibrosis (yellow arrow). (b) ImmunoglobulinG4 staining showing ImmunoglobulinG4 stained plasma cells (arrow)

diagnosis of testicular malignancy on one side and later, a testicular abscess on the other side. In our case, the patient had testicular involvement only.

The pathogenic mechanism in IgG4RD is thought to be due to autoimmunity and infectious agents. This leads to over expression of cytokines such as interleukin-4, -5, -10, and transforming growth factor-β. These inturn contribute to eosinophilia, elevated serum IgG4, and progression of fibrosis.[4]

In the genitourinary tract, renal involvement is manifested as tubulointerstitial nephritis or membranous glomerulonephritis whereas involvement of ureter, urinary bladder, urethra, and testis presents as a pseudotumor.[3,4] Some cases of urethral caruncle are considered as IgG4RD as these have elevated levels of IgG4+ plasma cells. CECT of the thorax, abdomen, and pelvis are helpful in the systemic evaluation of the disease. CECT findings include mass lesions, diffuse or focal infiltration, and encasement by inflammatory and fibrotic tissue in the involved organs. In our case, there were no detectable changes in any of the organs on CECT.[5]

This condition is usually treated with steroids and majority respond to this. Those not responding or recurrence of the disease has been treated with novel agents such as rituximab. Possible sequelae of untreated cases include organ dysfunction and organ failure.[4] At 1-year follow-up, the patient remained asymptomatic.

A high index of suspicion is needed in the diagnosis of IgG4RD. In the presence of multiorgan involvement and elevated serum IgG4 levels, a biopsy can lead to accurate diagnosis and obviate ablative surgery as these patients respond to steroids.[4]

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Conflicts of interest
There are no conflicts of interest.

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