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Infrequent organ involvement in immunoglobulin G4-related prostate disease: A case report

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Abstract

BACKGROUND

Immunoglobulin G4-related prostate disease (IgG4-RPD) characterized by a high count of IgG4-positive plasma cells has distinctive serological and radiological findings. Here we report a case of a patient who was successfully treated for IgG4-RPD, which manifested as frequent micturition, dysuric, and systemic lymphadenopathy.

CASE SUMMARY

The patient was a 33-year-old man who was referred to our hospital because of urinary tract symptoms that had persisted for 4 years. A physical examination revealed systemic lymphadenopathy and blood tests showed hyperglobulinemia with an IgG level of 18.90 g/L and an IgG4 level of 18.40 g/L. Computed tomography (CT) revealed bilateral lacrimal gland, right parotid gland and prostatic enlargement. Based on these findings, IgG4-RD was suspected, and further pathological examination and follow-up results showed expected results. Finally, the patient was diagnosed with IgG4-RPD based on clinical symptoms, pathological examination, therapeutic effects, and follow-up results. He received 50 mg oral prednisolone (the dose was gradually reduced and a low dose was used for long-term maintenance) in combination with cyclophosphamide 1.0 g *via* an intravenous drip for 6 mo. One year after the treatment was initiated, he was free of urinary or other complaints and his serum IgG4 level normalized.

CONCLUSION

In IgG4-RPD with severe urinary tract symptoms, radiological findings should be carefully examined. IgG4-RPD prognosis is good because the disease responds well to glucocorticoids. Furthermore, it is urgent for clinicians and pathologists to improve their understanding of IgG4-RPD.

Key Words: Immunoglobulin G4-related prostate disease; Infrequent organ involvement; Systemic disease; Pathological examination; Glucocorticoids; Case report

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Core Tip: Immunoglobulin G4-related prostate disease (IgG4-RPD) characterized by a high count of IgG4-positive plasma cells has distinctive serological and radiological findings. Here we report a case of a patient who was successfully treated for IgG4-RPD, which manifested as frequent micturition, dysuric, and systemic lymphadenopathy.

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INTRODUCTION

IgG4-related disease (IgG4-RD) is a chronic and systemic disease that can involve multiple organs. It has been recently recognized as an emerging clinicopathological entity characterized by several features[1,2]. Its clinical symptoms vary depending on the affected organs, but they are relatively mild, and organ swelling may be the only diagnostic clue in many patients. IgG4-RD is diagnosed by a combination of clinical, serological, and radiological findings along with pathological features[3]. IgG4-related prostate disease (IgG4-RPD) is a comprehensive term for prostate lesions associated with IgG4-RD[4]. In view of the general lack of understanding of the disease and the small number of cases reported at home and abroad, in order to improve the understanding, diagnosis, and treatment of the disease, the clinical characteristics and experience of the diagnosis and treatment of IgG4-RPD are discussed[5,6]. Here, we describe a case of highly advanced IgG4-RPD presenting as mass-like regions with urinary tract symptoms.

CASE PRESENTATION

Chief complaints

frequent urination, dysuric, and urinary hesitancy for 4 years.

History of present illness

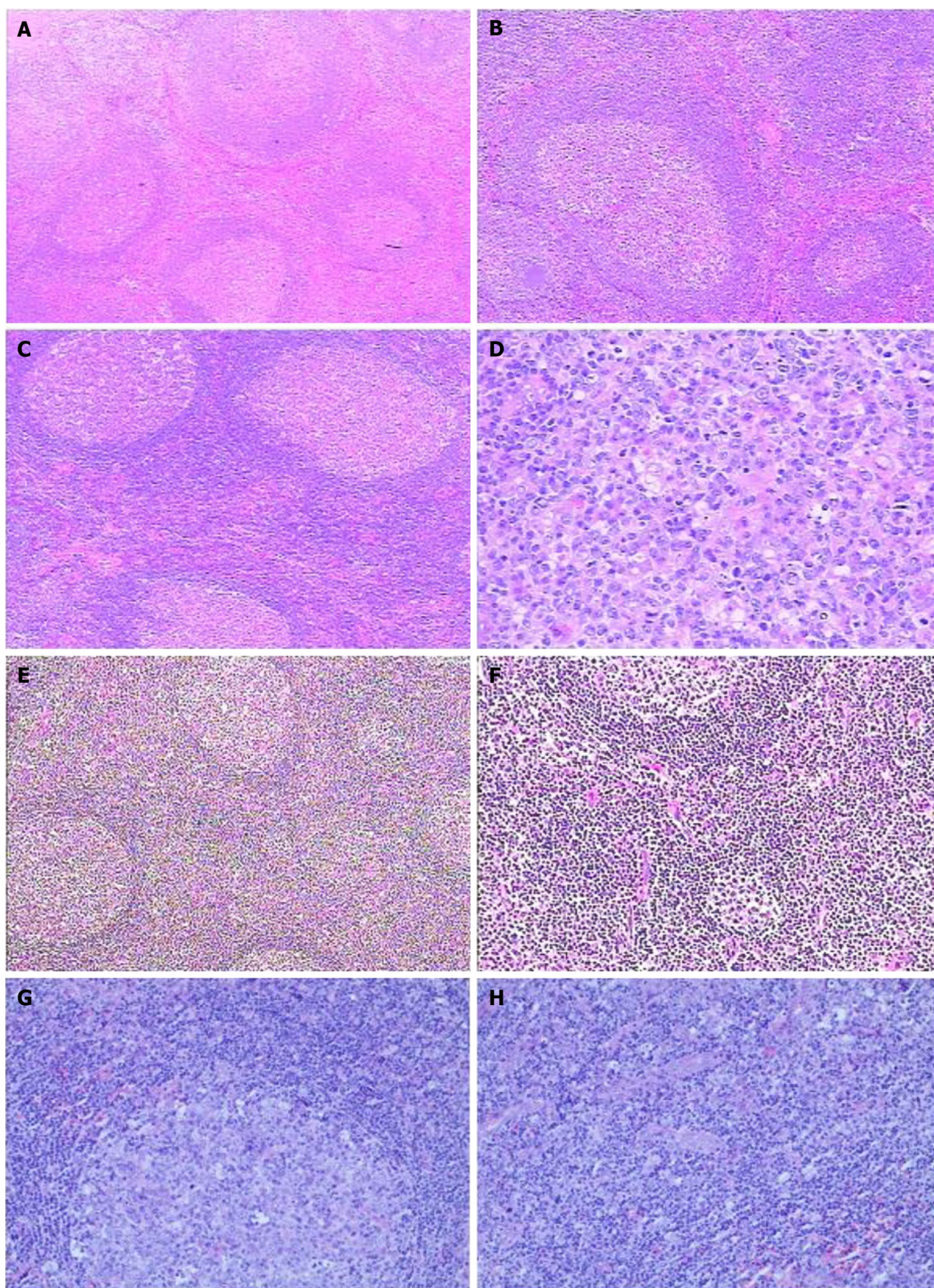
The patient had a cough and expectoration in February 2015. A peanut-sized mass was found in the right mandibular. The mass was not painful and showed a progressive increase in size accompanied by pharynx itch and sensation of a foreign body in the pharynx. In June 2015, the patient gradually developed urinary tract symptoms including frequent urination, nocturia, and urinary retention. Positron emission tomography/computed tomography (CT) showed multiple enlarged lymph nodes in the pelvic cavity. Prostatic posterior metabolism was active and the lesions were considered benign. Biopsy of right submaxillary lymph nodes suggested Castleman's disease (CD) (Figure 1). Thus, two courses of the R-cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP) regimen (mabthera 600 mg d1, cyclophosphamide 1.4 g d2, doxorubicin 30 mg d2, vincristine 2 mg d2, and prednisone 100 mg d2-6) was administered. The patient was administered prednisone 100 mg for 3 d after discharge. The mandibular lymph nodes significantly reduced after treatment. However, the patient required treatment with lenalidomide 25 mg qd for 3 years, but was irregular in taking his medication. The patient was treated with the IL-6R antibody at the department of lymphomatology of our hospital 13th August 2018.

History of past illness

He doesn't have a chronic illness.

Personal and family history

No special medical history.



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Figure 1 Hematoxylin and eosin staining and immunohistochemistry of lymph node biopsy. A: The structure of lymph nodes is normal; the number of lymphoid follicles increased, and the volume of most follicles increased. The germinal center indicated proliferation and enlargement, and the germinal center cells were mixed; B: Macrophage phagocytosis was observed, and a few follicular cuff regions were pushed and thinned. A few follicular germinal centers shrank, and the

sleeve area thickened. Lymph node follicular reactive hyperplasia; C: Most follicular germinal centers enlarged, and some showed apoptotic cells and nuclear fragments; D: A few follicular germinal centers shrank, and follicular epithelioid small vessel hyperplasia was observed. A few eosinophils proliferated; E: Some lymphoid follicles had atrophic with vitreous vessels in the center of the germinal center, onion skin-like structure in the covering area; F: and obvious proliferation of blood vessels with hyalinization in the paracentric region; G and H: Immunohistochemistry immunoglobulin G (IgG) and IgG4 (mostly located in the follicular germinal center, with a few located in the follicular area; IgG4/IgG > 40%) (G). Kappa and lambda plasmacytes (kappa plasmacytes > lambda plasmacytes). magnification, × 100 (H).

Physical examination

The patient's eyelids of both eyes were found to be slightly swollen and the eyeballs appeared slightly prominent. Furthermore, bilateral cervical lymph nodes were enlarged, about 3 cm × 3 cm, in size and elliptical; the texture was soft, the surface was smooth, and there was no adhesion with the surrounding tissue and no tenderness. There was no deformity in the skull; slight edema was noted on the head and face. Bilateral inguinal lymph nodes might have been enlarged.

Laboratory examinations

Prostate gland biopsy: Immunohistochemical examination showed a large number of IgG4-positive plasma cells and the IgG4/IgG ratio was more than 50% (Figure 2).

Imaging examinations

B ultrasonic and magnetic resonance imaging examination revealed prostatic enlargement and multiple lymphadenopathies (Figures 3 and 4).

FINAL DIAGNOSIS

He had multiple lymphadenopathies. The patient's serum IgG4 level was > 1.89 g/L, and prostate gland biopsy indicated an IgG4/IgG ratio of > 40%, which was in accord with the diagnostic criteria of IgG4-RPD.

TREATMENT

The patient was additionally treated with an intravenous drip of cyclophosphamide 1.0 g for 6 mo and oral prednisolone (the dose was gradually reduced and a low dose was used for long-term maintenance).

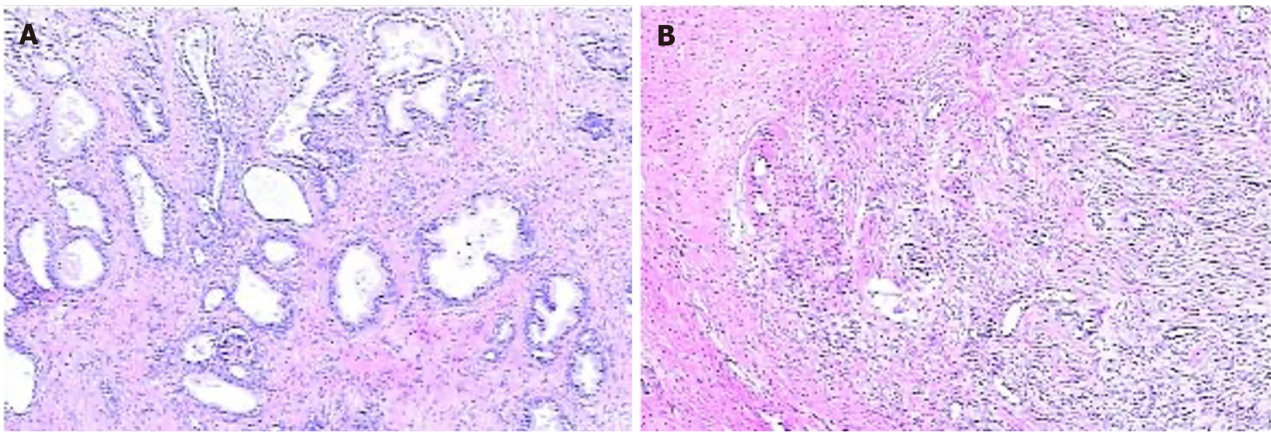
OUTCOME AND FOLLOW-UP

One year later (25th December 2019), we documented substantial reductions in the levels of serum IgG (1.22 g/L) and IgG4 (1.18 g/L). In the following 12 mo, the patient's medical condition remained stable, and he was free of urinary or other complaints. A repeat prostate B-ultrasound showed significant reduction of the prostate gland, indicating an obvious effect.

DISCUSSION

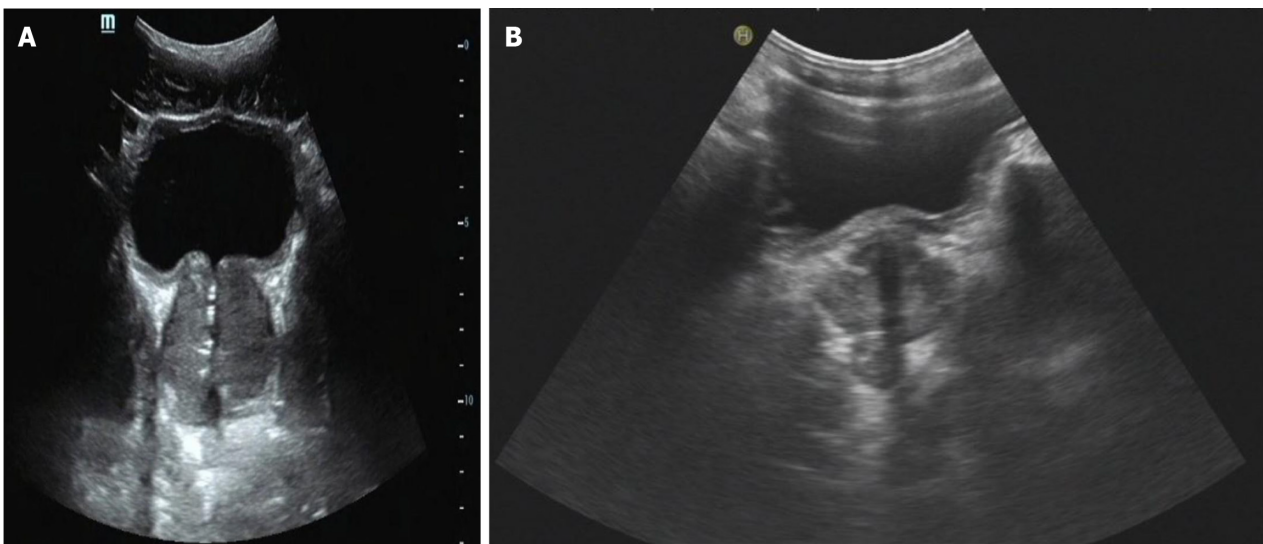
The concept of IgG4-RD was first introduced by Kamisawa *et al*[7] and the condition was named in 2010. At present, IgG4-RD is considered to be an autoimmune syndrome involving multiple organs and tissues, and chronic and progressive. Due to the extensive proliferative infiltration and sclerosis of IgG4-positive plasmacytes in organs or tissues, one or more organs often show tumor-like swelling and enlargement. This characteristic makes it difficult to distinguish the disease from other lymphoproliferative diseases such as CD or lymphoma, especially in the early stages. IgG4-RD is an autoimmune-mediated inflammatory fibrotic disease, which has been gradually recognized. The disease can involve many organs or systems, resulting in tissue damage, organ enlargement, and even organ failure.

In recent years, IgG4-associated lymphadenopathy has been in focus. The histologic characteristics of lymphadenopathy are varied and can be summarized as follows: CD, lymphoid follicular reactive hyperplasia, follicular plasmacytes, immunoblastoma, progressive transformation of the germinal center, and inflammatory pseudotumor. However, not all IgG4-RD patients who have the histologic characteristics of lymphadenopathy mentioned above. Only few patients had increased IgG4-positive plasma cells. For example, in a study conducted 26 patients, the histological characteristics of lymph nodes were similar to those associated with CD. Follicular proliferative and interstitial plasmacytes increased in one patient, but only one patient showed an increase in the number and proportion of IgG4-positive plasma cells in the lymph nodes[7,8]. The risk of malignant tumor is increased in IgG4-RD, especially malignant lymphoma. The clinical manifestations of lymphoma can be similar to the primary disease, which can easily result in



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Figure 2 Prostate gland biopsy. A: No findings were suggestive of prostatic carcinoma. Immunohistochemical examination showed a large number of immunoglobulin G4 (IgG4)-positive plasma cells and the IgG4/IgG ratio was higher than 50%; B: In addition, an increased number of IgG4-positive cells were visible within the acini. magnification, $\times 400$.



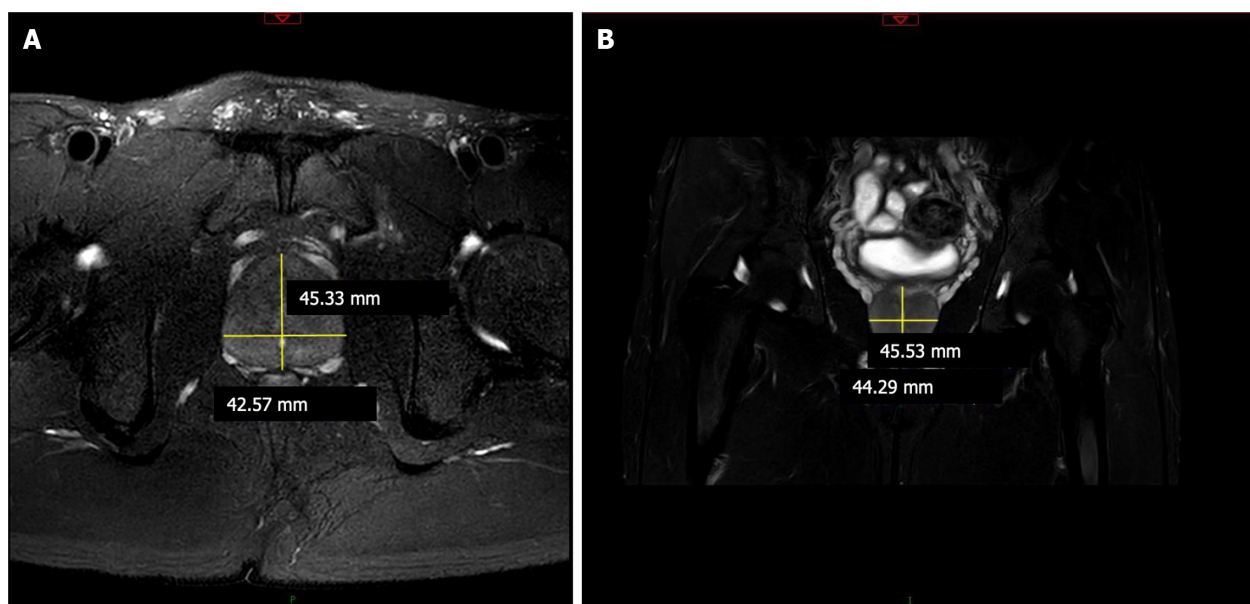
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Figure 3 Ultrasound of the prostate. A: The prostate section was 5.5 cm \times 4.1 cm \times 4.6 cm in size, full in shape, and showed uneven distribution of internal light spots. A few strong echo spots were observed; B: The prostate section was 3.5 cm \times 3.2 cm \times 3.0 cm in size 14 mo later.

misdiagnosis or delayed diagnosis and treatment, and should be paid attention to by clinicians. However, the tumor can progress in the later stage, and clinicians are highly suspicious of the tumor. Lymphoma is often diagnosed at the same time as IgG4-RD or after the diagnosis of IgG4-RD. Two studies reported that patients diagnosed with IgG4-RD had MALT lymphoma at the same time or at different times[9,10]. In another study, three patients with IgG4-RD were misdiagnosed with multicentric CD[11].

Multiple lymphadenopathies are a common clinical manifestation of CD and IgG4-RD. Diffuse lymphoplasmacytic infiltration, fibrosis, and a high percentage of IgG4 (+) plasmacytes are the histopathological features of IgG4-related diseases. The pathological characteristics of IgG4-RD and CD intersect to some extent. The differential diagnosis of IgG4-RD and CD is thus very difficult, and comprehensive evaluation is necessary as diagnosis cannot be solely based on serological, pathological, or immunohistochemical results. IgG4-RPD is a comprehensive term for prostate lesions associated with IgG4-RD, prostate involvement with IgG4-RD is very rare, patients were often presented with urine retention symptoms[12,13].

Because IgG4-RD and polycentric CD have their own effective and different treatment schemes, antidiastole is very important[14]. Polycentric CD is mostly invasive, and the treatment usually involves combination chemotherapy. Combination chemotherapy regimens such as CHOP and cyclophosphamide, vincristine, and prednisone can be used. The use of glucocorticoids alone can alleviate the clinical symptoms of CD to some extent but the duration of maintenance is short. Patients with IgG4-RD responded well to glucocorticoids[15]. Therefore, a definite diagnosis is helpful to guide treatment and avoid unnecessary chemotherapy or surgery due to the misdiagnosis of the tumor.



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Figure 4 Magnetic resonance imaging of the prostate gland. A: Prostate: Prostate enlargement, about 46 mm × 41 mm. The boundary between the central gland and the peripheral zone of the prostate was unclear. T2WI signal decreased diffusely; B: Enhanced scanning of the prostate showed uneven enhancement. The fat gap around the prostate was clear.

To avoid misdiagnosis or delayed diagnosis of patients with injury or organ dysfunction, it is urgent for clinicians and pathologists to improve the understanding of IgG4-RD. Thus far, for the diagnosis of IgG4-RD, clinicians need to determine clinical, serological, imaging, and pathological features, but the diagnosis cannot be solely based on a single examination or pathological results alone[16]. IgG4-RD responds well to glucocorticoid therapy, resulting in a good prognosis. Therefore, it is very important to correctly diagnose and distinguish this disease.

CONCLUSION

The lesson from this case is that as this is a new disease, not many cases of IgG4-RPD have yet been reported and that doctors' understanding of the disease is inadequate. Therefore, it is of great significance to improve pathologists' understanding of the disease and to treat the disease correctly.

FOOTNOTES

Author contributions: Yu Y and Wang QQ prepared the manuscript; Jian L collected material of this case; Yang DC critically reviewed the manuscript for important intellectual content and approved the final manuscript.

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