ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2023 October 26; 11(30): 7261-7507

Published by Baishideng Publishing Group Inc

WJCC

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 11 Number 30 October 26, 2023

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 30 October 26, 2023

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 30 October 26, 2023

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Ravindra Shukla, MBBS, MD, Additional Professor, Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, Jodhpur 342001, Rajasthan, India. ravindrashukla2@rediffmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJCC* as 1.1; IF without journal self cites: 1.1; 5-year IF: 1.3; Journal Citation Indicator: 0.26; Ranking: 133 among 167 journals in medicine, general and internal; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

PUBLICATION DATE

October 26, 2023

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2023 October 26; 11(30): 7485-7491

DOI: 10.12998/wjcc.v11.i30.7485

ISSN 2307-8960 (online)

CASE REPORT

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

Yi Yu, Qian-Qian Wang, Li Jian, Deng-Can Yang

Specialty type: Rheumatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Glumac S, Croatia; Pavlidis TE, Greece

Received: August 4, 2023
Peer-review started: August 4, 2023
First decision: August 24, 2023
Revised: August 26, 2023
Accepted: September 25, 2023
Article in press: September 25, 2023
Published online: October 26, 2023

Yi Yu, Department of Critical Care Medicine, Guangdong Provincial Hospital of Traditional Chinese Medicine, Guangzhou 510006, Guangdong Province, China

Qian-Qian Wang, Department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510000, Guangdong Province, China

Li Jian, Department of Critical Care Medicine, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou 510006, Guangdong Province, China

Deng-Can Yang, Anesthesiology Department, The Central Hospital of Shaoyang, Shaoyang 422000, Hunan Province, China

Corresponding author: Yi Yu, Doctor, Department of Critical Care Medicine, Guangdong Provincial Hospital of Traditional Chinese Medicine, No. 55 Daxuecheng Neihuanxi Road, Guangzhou 510006, Guangdong Province, China. 1191922959@qq.com

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

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.

Citation: Yu Y, Wang QQ, Jian L, Yang DC. Infrequent organ involvement in immunoglobulin G4-related prostate disease: A case report. *World J Clin Cases* 2023; 11(30): 7485-7491
URL: https://www.wjgnet.com/2307-8960/full/v11/i30/7485.htm
DOI: https://dx.doi.org/10.12998/wjcc.v11.i30.7485

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

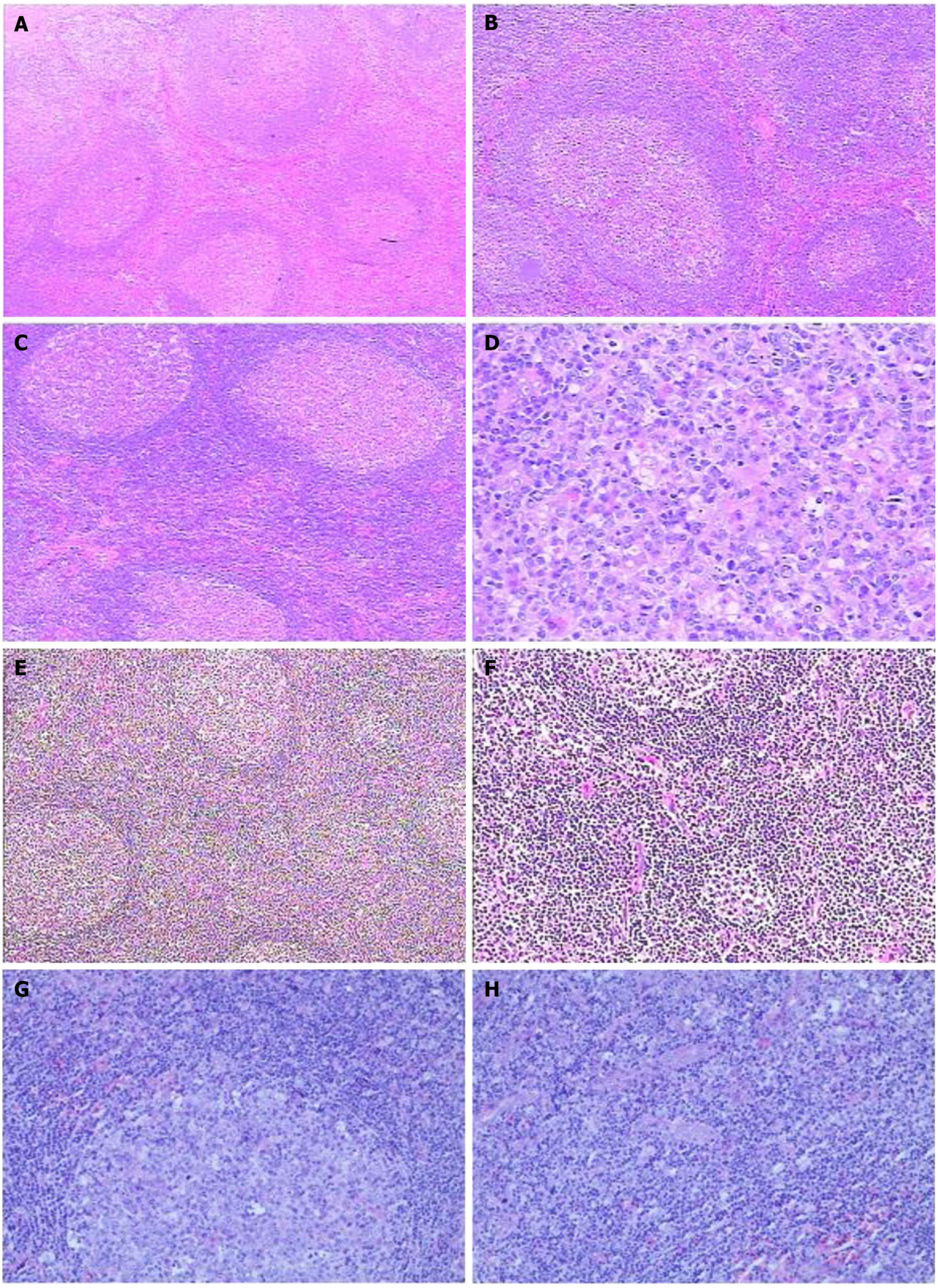
The patient had a cough and expectoration in February 2015. A peanut-sized mass was found in the right mandibular. The mass was not painful and showed a progressive increase in size accompanied by pharynx itch and sensation of a foreign body in the pharynx. In June 2015, the patient gradually developed 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.



DOI: 10.12998/wjcc.v11.i30.7485

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/IgG4 > 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 lymphadenopath **ies** (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).

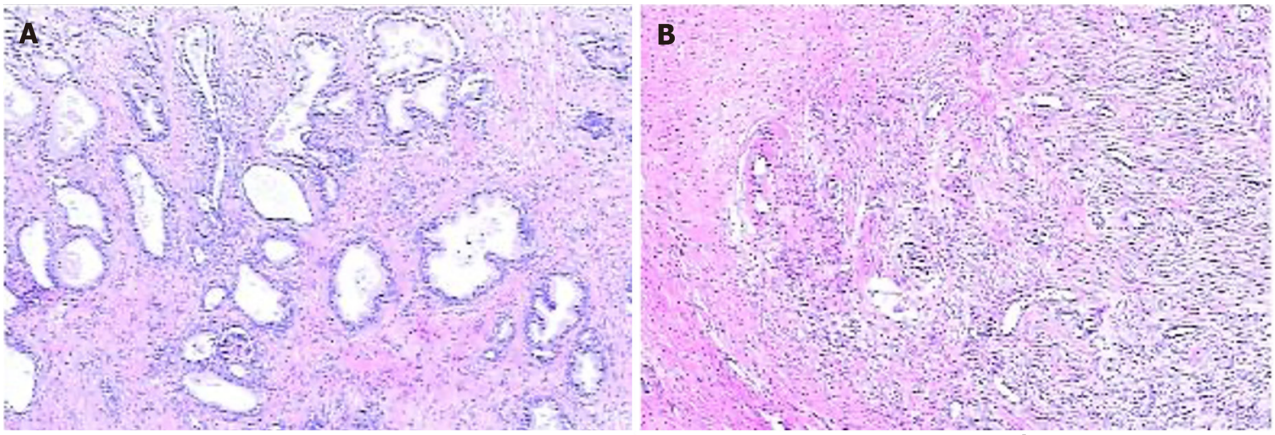
OUTCOME AND FOLLOW-UP

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

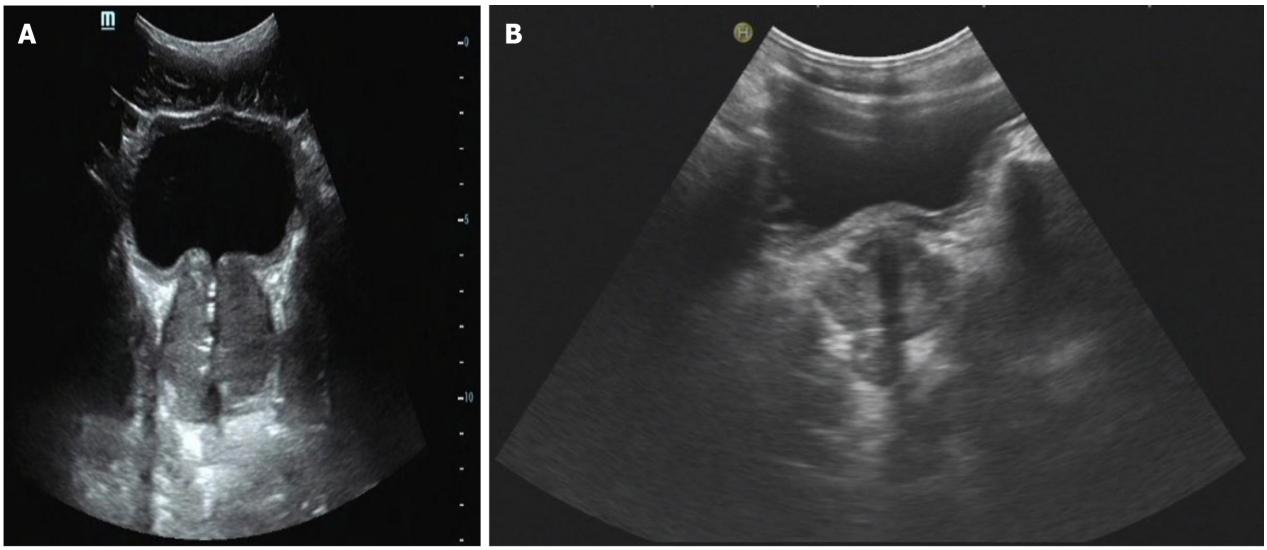
The concept of IgG4-RD was first introduced by Kamisawa *et al*[7] and the condition was named in 2010. At present, IgG4-RD is considered to be an autoimmune syndrome involving multiple organs and tissues, and chronic and progressive. Due to the extensive proliferative infiltration and sclerosis of IgG4-positive 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



DOI: 10.12998/wjcc.v11.i30.7485 **Copyright** ©The Author(s) 2023.

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, × 400.



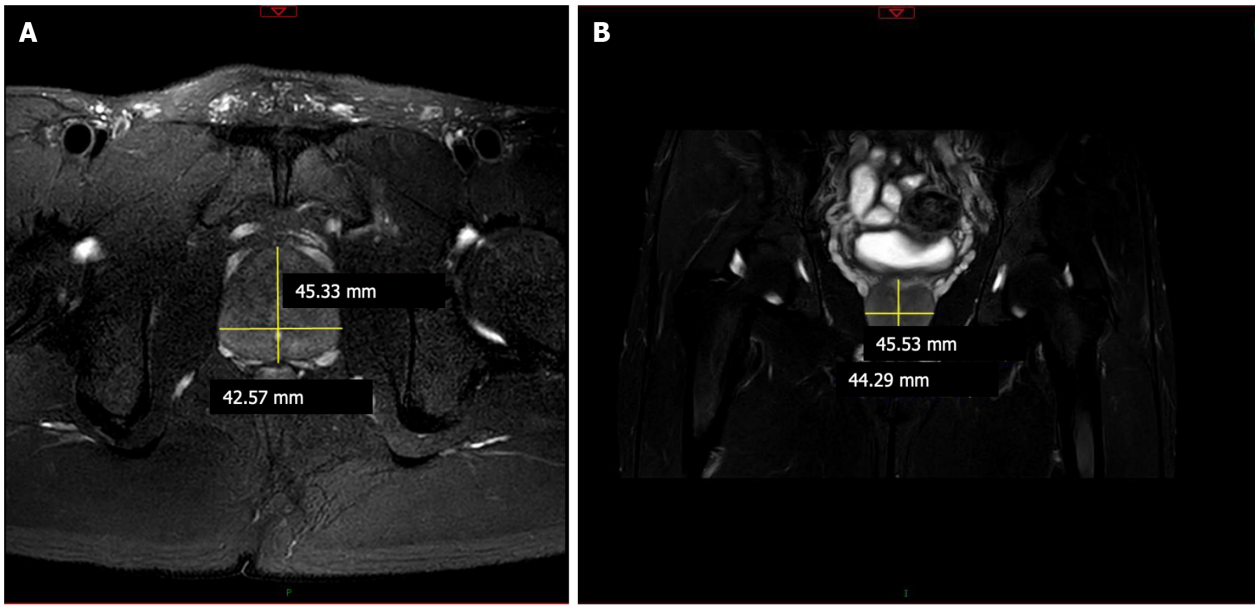
DOI: 10.12998/wjcc.v11.i30.7485 **Copyright** ©The Author(s) 2023.

Figure 3 Ultrasound of the prostate. A: The prostate section was 5.5 cm × 4.1 cm × 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 × 3.2 cm × 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.



DOI: 10.12998/wjcc.v11.i30.7485

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.

Supported by the Guangdong Provincial Bureau of Traditional Chinese Medicine, No. 20222065; Science and Technology Planning Project of Guangdong Province of China, No. A2021100; and National Natural Science Foundation of China, No. 82104989.

Informed consent statement: Informed written consent was obtained from the patients for the publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country/Territory of origin: China

ORCID number: Yi Yu 0000-0002-3122-2402.

S-Editor: Chen YL
L-Editor: A
P-Editor: Zhang XD

REFERENCES

1 **Deshpande V**, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, Klöppel G, Heathcote JG, Khosroshahi A, Ferry JA, Aalberse RC, Bloch DB, Brugge WR, Bateman AC, Carruthers MN, Chari ST, Cheuk W, Cornell LD, Fernandez-Del Castillo C, Forcione DG, Hamilos DL, Kamisawa T, Kasashima S, Kawa S, Kawano M, Lauwers GY, Masaki Y, Nakanuma Y, Notohara K, Okazaki K, Ryu JK, Saeki T, Sahani DV, Smyrk TC, Stone JR, Takahira M, Webster GJ, Yamamoto M, Zamboni G, Umehara H, Stone JH. Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 2012; **25**: 1181-1192 [PMID: 22596100 DOI: 10.1038/modpathol.2012.72]

2 **Stone JH**, Zen Y, Deshpande V. IgG4-related disease. *N Engl J Med* 2012; **366**: 539-551 [PMID: 22316447 DOI: 10.1056/NEJMra1104650]

3 **Yadlapati S**, Verheyen E, Efthimiou P. IgG4-related disease: a complex under-diagnosed clinical entity. *Rheumatol Int* 2018; **38**: 169-177 [PMID: 28681251 DOI: 10.1007/s00296-017-3765-7]

4 **Martínez-de-Alegría A**, Baleato-González S, García-Figueiras R, Bermúdez-Naveira A, Abdulkader-Nallib I, Díaz-Peromingo JA, Villalba-Martín C. IgG4-related Disease from Head to Toe. *Radiographics* 2015; **35**: 2007-2025 [PMID: 26473450 DOI: 10.1148/rg.357150066]

5 **Umehara H**, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, Matsui S, Sumida T, Mimori T, Tanaka Y, Tsubota K, Yoshino T, Kawa S, Suzuki R, Takegami T, Tomosugi N, Kurose N, Ishigaki Y, Azumi A, Kojima M, Nakamura S, Inoue D; Research Program for Intractable Disease by Ministry of Health, Labor and Welfare (MHLW) Japan G4 team. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. *Mod Rheumatol* 2012; **22**: 1-14 [PMID: 21881964 DOI: 10.1007/s10165-011-0508-6]

6 **Takahashi H**, Yamamoto M, Suzuki C, Naishiro Y, Shinomura Y, Imai K. The birthday of a new syndrome: IgG4-related diseases constitute a clinical entity. *Autoimmun Rev* 2010; **9**: 591-594 [PMID: 20457280 DOI: 10.1016/j.autrev.2010.05.003]

7 **Kamisawa T**, Funata N, Hayashi Y, Eishi Y, Koike M, Tsuruta K, Okamoto A, Egawa N, Nakajima H. A new clinicopathological entity of IgG4-related autoimmune disease. *J Gastroenterol* 2003; **38**: 982-984 [PMID: 14614606 DOI: 10.1007/s00535-003-1175-y]

8 **Rollins-Raval MA**, Felgar RE, Krasinskas AM, Roth CG. Increased numbers of IgG4-positive plasma cells may rarely be seen in lymph nodes of patients without IgG4-related sclerosing disease. *Int J Surg Pathol* 2012; **20**: 47-53 [PMID: 21911432 DOI: 10.1177/1066896911420562]

9 **Matsuo T**, Ichimura K, Yoshino T. Local recurrence as immunoglobulin G4 (IgG4)-related disease 10 years after radiotherapy to ocular adnexal extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. *J Clin Exp Hematop* 2011; **51**: 125-133 [PMID: 22104312 DOI: 10.3960/jslrt.51.125]

10 **Oyama T**, Takizawa J, Nakamura N, Aoki S, Aizawa Y, Abe H. Multifocal mucosa-associated lymphoid tissue lymphoma associated with IgG4-related disease: a case report. *Jpn J Ophthalmol* 2011; **55**: 304-306 [PMID: 21584726 DOI: 10.1007/s10384-011-0003-9]

11 **Sato Y**, Kojima M, Takata K, Morito T, Mizobuchi K, Tanaka T, Inoue D, Shiomi H, Iwao H, Yoshino T. Multicentric Castleman's disease with abundant IgG4-positive cells: a clinical and pathological analysis of six cases. *J Clin Pathol* 2010; **63**: 1084-1089 [PMID: 20974624 DOI: 10.1136/jcp.2010.082958]

12 **Li D**, Kan Y, Fu F, Wang S, Shi L, Liu J, Kong L. IgG4-related prostatitis progressed from localized IgG4-related lymphadenopathy. *Int J Clin Exp Pathol* 2015; **8**: 11747-11752 [PMID: 26617921]

13 **Chang J**, Zhang W. Infrequent organ involvement of IgG4-related diseases: a literature review. *Clin Rheumatol* 2018; **37**: 1153-1159 [PMID: 29502226 DOI: 10.1007/s10067-018-4048-8]

14 **Wallace ZS**, Zhang Y, Perugino CA, Naden R, Choi HK, Stone JH; ACR/EULAR IgG4-RD Classification Criteria Committee. Clinical phenotypes of IgG4-related disease: an analysis of two international cross-sectional cohorts. *Ann Rheum Dis* 2019; **78**: 406-412 [PMID: 30612117 DOI: 10.1136/annrheumdis-2018-214603]

15 **Bledsoe JR**, Della-Torre E, Rovati L, Deshpande V. IgG4-related disease: review of the histopathologic features, differential diagnosis, and therapeutic approach. *APMIS* 2018; **126**: 459-476 [PMID: 29924455 DOI: 10.1111/apm.12845]

16 **Umehara H**, Okazaki K, Kawano M, Mimori T, Chiba T. How to diagnose IgG4-related disease. *Ann Rheum Dis* 2017; **76**: e46 [PMID: 28283514 DOI: 10.1136/annrheumdis-2017-211330]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com