Case Report

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IgG4-Related Disease in a 90-Year-Old Man with an 18-Year Disease Course: A Case Report

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ABSTRACT

IgG4-related disease (IgG4-RD) is a multi-organ inflammatory immune-mediated illness caused by IgG4-secreting plasma cells infiltrating the tissue. This condition usually affects elderly men. A 90-year-old Chinese male was diagnosed with IgG4-RD based on the new 2019 ACR/EULAR classification criteria, as he had multiple organ involvement. After receiving treatment with glucocorticoids, leflunomide, and gamma-globulin, the patient's clinical symptoms significantly improved, confirming the accuracy of the diagnosis. The patient had an 18-year medical history during which the disease progressively worsened due to delayed diagnosis and treatment. Although the relevant symptoms were alleviated with appropriate medication, the overall treatment process encountered challenges. Due to the patient's relative lack of adrenocortical function, he experienced symptoms such as nausea, exhaustion, and loss of appetite during the hormone reduction process. Therefore, timely intervention is especially crucial to address the side effects of hormone therapy.

Keywords: Case report, Glucocorticoid, Hypophysitis, IgG4-RD, Retroperitoneal fibrosis

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INTRODUCTION

IgG4-RD is an immune-mediated, multi-organ (1) disease that resembles a number of infectious, inflammatory (2), and neoplastic conditions. It typically affects older males. No prior papers have provided a thorough account of the clinical course. Here, we discuss a case of a patient with IgG4-RD who was already 90 years old but had involvement of multiple organs: pancreas, lungs, pituitary, and retroperitoneum. The pancreatic space-occupying lesions were initially found in 2004 and the patient's medical history spanned eighteen years. It was not until 2021 that IgG4-RD was identified and treated.

For treatment, we employed methylprednisolone, leflunomide, and gamma-globulin. However, due to the relative lack of adrenocortical function, the patient experienced nausea, exhaustion, loss of appetite, and other symptoms during the hormone reduction process. After the prescription was changed, the symptoms eventually went away. After reviewing the medical history, we came to the conclusion that, considering the negative effects of hormone therapy, it was especially crucial to consider how to determine the IgG4-RD's progression and when to begin treatment.

CASE PRESENTATION

Patient's Information

A 90-year-old male was found to have left iliac artery stenosis with tumor-like dilatation in the annual physical examination in August 2020. Abdominal CT revealed soft tissue shadow around the left common iliac artery (Fig. 1), accompanied by involvement of the left ureter, and slightly dilated hydronephrosis of the ureter, renal pelvis and calyx above the plane. The patient had no corresponding clinical manifestations.

He had a medical history of kidney stones, diabetes, hypertension, and fatty liver. Furthermore, the space occupying lesions of the pancreas was found by ultrasound in 2004. Malignant tumors were highly suspected, and a cycle of chemotherapy was carried out that year. However, considering the patient's advanced age, the chemotherapy was terminated and there was no corresponding surgical treatment. No significant increase in pancreatic mass was found during the follow-up. The patient had routine physical examination every year, and no imaging indications of an intrusion into other systems were discovered.

Until 2011, interstitial inflammation of the lower lobe of both lungs was found for the first time, but no specific treatment was administered because the patient insisted on being followed up and observed. The elderly man started exhibiting clinical symptoms in June 2017 that were consistent with bulbar paralysis, including coughing, difficulty in swallowing, hoarseness, etc. Pituitary magnetic resonance imaging (MRI) indicated pituitary hypertrophy and thickening of pituitary stalk. During the period, the patient had two PET/CT examinations and no typical malignant tumor-like hypermetabolic lesions were found. After cerebral hemorrhage and stroke had been ruled out, more frequently, pituitary inflammation was considered. We are unaware of the specific treatment the patient received after being transferred to another hospital. There were no significant findings in the patient's family history. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Clinical Findings

The blood pressure of the patient was 154/70 mmHg on admission, and no obvious abnormality was found in the physical examination of heart, lung and abdomen. The pulse of the dorsalis pedis artery was considered weak on palpation.

The results of laboratory testing revealed the following: complement C3 0.60 g/L (reference range 0.7-1.4 g/L), complement C4 0.06 g/L (reference range 0.1-0.4 g/L), erythrocyte sedimentation rate 37 mm/h (reference range 0-20 mm/h), and C-reactive protein 5 mg/L (reference range 0-10 mg/L).

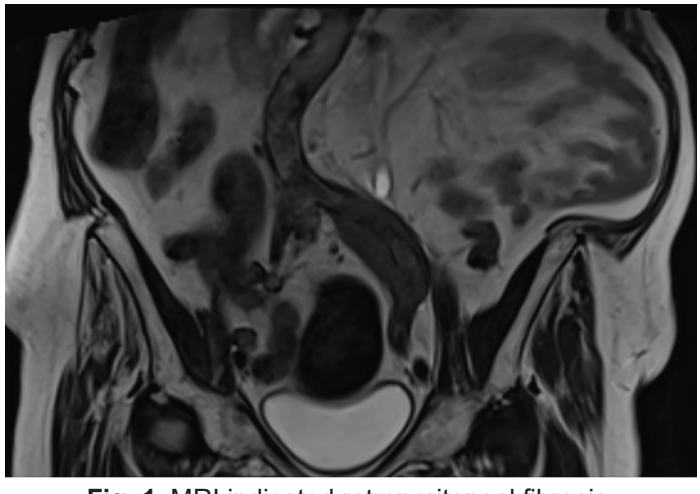

Fig. 1. MRI indicated retroperitoneal fibrosis.

The results of a serological examination revealed that the levels of prolactin were 325.48 ulU/mL (reference range 44.52-375.24 uIU/mL), luteinizing hormone was 0.93 mIU/mL (reference range 1.5-9.3 mIU/mL), and follicle stimulating hormone was 5.24 mlU/mL (reference range 1.4-18.1 mlU/mL). The levels of IgG were slightly elevated, coming in at 19.9 g/L (reference range 8.6-17.4 mg/dL).

Anticardiolipin antibodies, anti-glycoprotein 1 antibodies, pANCA, cANCA, ASO, RF, and interferon-γ associated with mycobacterium TB were negative. Additionally, other autospecific antibodies—such as those against SSA and SMB, and others—were negative.

Abdominal ultrasound showed that there was still pancreatic mass (1.47*0.96cm). No obvious abnormality was found in pituitary magnetic resonance imaging. Interstitial alterations were visible on pulmonary CT in the lower lobes of both lungs' basal segments.

Then the patient was diagnosed as IgG4-RD due to the involvement of pituitary, pancreas, lungs and retroperitoneum according to the new 2019 ACR/EULAR classification criteria (3). With a cumulative score of 29 points, he met all inclusion requirements, but none of the exclusion criteria. These included uninformative biopsy (0 points), normal serum IgG4 levels (0 points), peribronchovascular and septal thickening (4 points), diffuse pancreas enlargement and capsule-like rim with decreased enhancement (11 points), hypocomplementemia (6 points), and imaging showing anterolateral soft tissue around the iliac arteries (8 points). Considering the side effects of the hormone, the patient's family did not agree to glucocorticoid treatment. They decided to continue monitoring and observing the patient. However, in March 2021, the patient developed fatigue, anorexia, dizziness, nausea, significant blood pressure fluctuations and other related symptoms. And medical data indicated that during the final week of March 2021, the patient's maximum urine production was 6400ml per day, with an average of 4475ml per day. The urine osmotic pressure also significantly decreased to 324mOsm (reference range 600-1000mOsm). He did not complain about visual field loss. Laboratory tests showed serum corticotropin and cortisol-II decreased. Pituitary magnetic resonance imaging (MRI) indicated pituitary hypertrophy and thickening of pituitary stalk (Fig. 2). We suspected the disease was progressing. Despite the lack of pathological data, the patient was given diagnostic treatment. The clinical manifestation of the patient was prominently relieved, which proved that the treatment was effective. After 6 months of treatment, we followed up with the patient and observed a significant reduction in the size of the pituitary gland (Fig. 3), and in addition, retroperitoneal fibrosis was alleviated. CRP, ESR and other indexes also returned to normal. However, the pituitary secretion function has not yet fully recovered. After one year of treatment, laboratory tests showed that testosterone was still at a low level (0.2 nmol/L; reference range 6.07-27.1 nmol/L)) and prolactin remained at a high level (432.35 ulU/mL; reference range 44.52-375.24 uIU/mL).

Gamma globulin, leflunomide, and glucocorticoids were utilized in therapy.

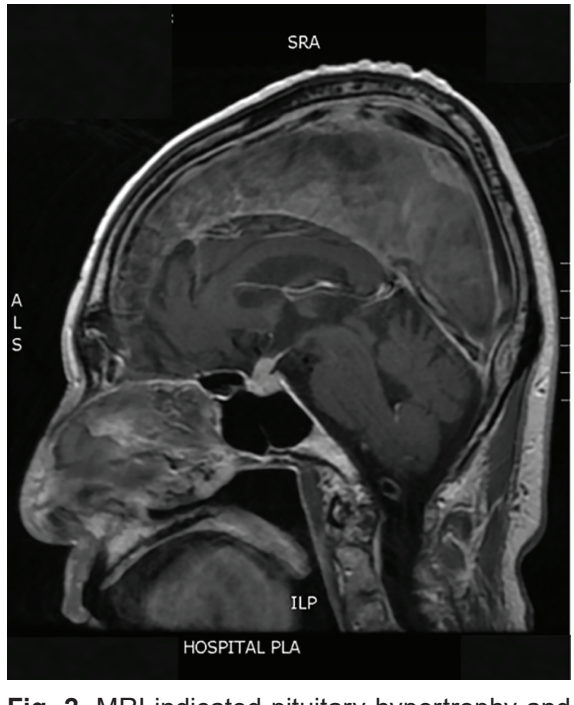

Fig. 2. MRI indicated pituitary hypertrophy and thickening of pituitary stalk.

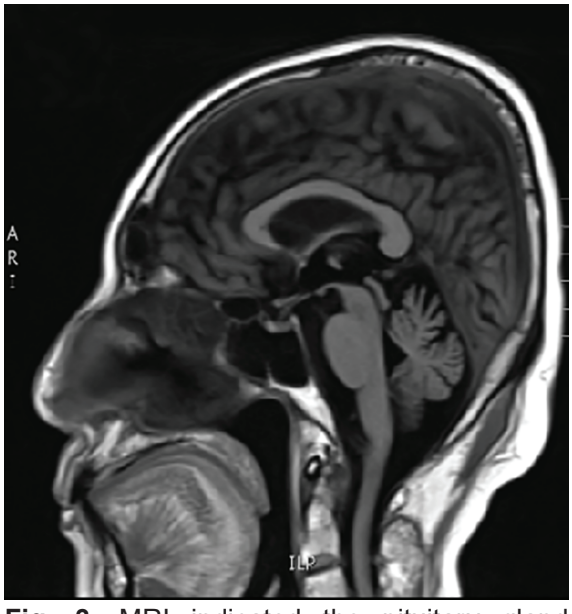

Fig. 3. MRI indicated the pituitary gland significantly shrank after 6 months of treatment.

The patient did, however, have to endure nausea, tiredness, loss of appetite, and other symptoms during the hormone reduction process due to the relative absence of adrenocortical activity. These symptoms were alleviated after the hormone dosage was increased appropriately. Fig. 4 depicts the progression of the diagnosis, the course of treatment, and the prognosis in this case.

DISCUSSION AND CONCLUSION

It seems that the development of the IgG4-RD is relatively slow by reviewing our patient's medical history, during which the condition of the patient did not have any associated negative effects even without glucocorticoid management. The appropriate timing of intervention is crucial because once the disease has advanced and vital organs are affected, it may result in irreparable damage such as renal atrophy.

However, negative effects associated with glucocorticoids can impact all major organ systems (4). It is particularly important to determine whether the disease is active and requires hormone therapy. Imaging is an important means to monitor the progress of the disease. Sonography is recommended as a modality for the screening of IgG4-RD, because it is easy to use, effective, involving no radiation exposure (5). Regrettably, IgG 4 related disease can involve any organ. There are some cases that have been reported to describe the invasion of gastrointestinal tract (6), heart (7), and testicle (8), etc. Hypophysitis, retroperitoneal fibrosis and most involvement of organs can be shown on computerized tomography (CT). Nevertheless, the imaging findings are usually not specific except for autoimmune pancreatitis. PET can be useful in monitoring disease activity and in defining the degree of organ involvement. Evaluation before treatment showed in most cases a good correlation of 2-[18F]-fluoro-2-deoxy-D-glucose–positron emission tomography/computed tomography (FDG-PET/CT) results with disease activity (9). However, the cost is indeed high.

There are few specific serological markers, presently, to indicate the activity of IgG4-RD. It is still unclear if blood IgG4 levels are a reliable indicator of disease activity. Even as

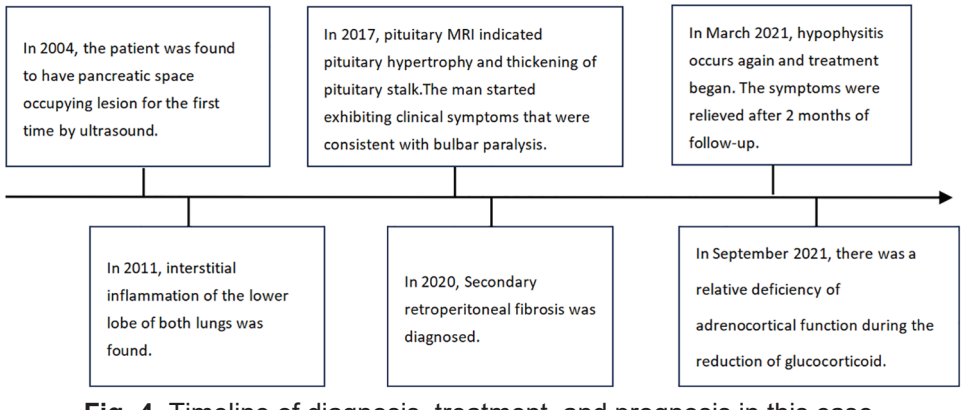

Fig. 4. Timeline of diagnosis, treatment, and prognosis in this case.

the disease progresses, approximately 50% of individuals with IgG4-related disorders identified by biopsies exhibit normal serum IgG4 concentrations (10). Our patient had low serum IgG4 concentrations throughout the course of the disease. While some patients showed normal IgG4 levels at the beginning of treatment, others had a sharp decline or normalization of increased IgG4 levels (11).

IgG4 levels are not able to effectively monitor the progression of the disease, nor do they sufficiently predict the emergence of comorbidities or even relapse (12).

Oligoclonal expansions of plasmablasts may be a useful indicator for disease activity (13). A favorable correlation was seen between the peripheral CD19+CD24-CD38hi plasmablast/plasma cell population and serum IgG4 levels, organ involvement, and the IgG4-RD Responder Index in individuals with IgG4-RD who were not receiving treatment (14). Through an abnormal production of plasmablasts, the thymus and activation-regulated chemokine (TARC) may have a role in the development of IgG4-RD (15).

The clinical progression of certain instances implies that serum complement serves as a biomarker for the disease activity. Clinical improvement was noted in correlation with serum complement normalization, and a decline in serum complements predated the disease's progression (16). A valuable biomarker for fibrotic disorders, CC-chemokine ligand 18 (CCL18) (17) is also helpful in assessing the disease activity of IgG4-RD (18).

We reported here a case diagnosed as IgG4-RD with a more than ten-year disease course. The patient's disease course indicates the existence of the resting period of the IgG4-RD. We reviewed some clinical supplementary examinations that monitor the progression of the disease and several serological markers indicating the activity of the disease to expect patients with IgG4-RD to be intervened at an appropriate time to reduce glucocorticoid complications.

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AUTHORS' CONTRIBUTION

QTR and YJC conceived the project and wrote the manuscript. YMB performed image post-processing and editing. YJ, PL, and GXZ, QXY participated in the discussion and language editing. YJC reviewed the manuscript. All authors contributed to the article and approved the submitted version.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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