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Case Report

Aortic Valve Replacement Surgery Caused by IgG4-Related Aortic Regurgitation

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Abstract

While IgG4-related disease affects different organs, it is uncommon to associate it with the aortic valve. The clinical manifestations and prognosis of an uncommon IgG4-related aortic valve disease were examined by reporting it. After common activity, a 50-year-old man experienced shortness of breath and chest tightness. $IgG4^+$ was expressed at a level of 4.23 g/L. The aortic valve had severe reflux, and the ascending aorta and aortic sinus were dilated, as evidenced by transesophageal echocardiography. Pathological results suggested that the ratio of $IgG4^+$ cells to IgG^+ cells was over 40%. Thus, the patient was diagnosed with aortic valve disease caused by $IgG4^+$. Surgical treatment was executed. In clinical practice, IgG4-associated aortic regurgitation is uncommon and has the same clinical manifestations as general aortic valve disease. Nevertheless, there was a significant increase in serum $IgG4^+$ levels. There was an association between the two. The pathology of valves can be proven.

Keywords

chronic autoimmune diseases; IgG4-related diseases; aortic valve disease; $IgG4^+$

Introduction

Multiple organs and systems are affected by IgG4-related disease, which is a chronic and progressive autoimmune disease [1]. Its characteristic pathological tissue is fibrotic and rich in IgG4-positive plasma cells, as well as elevated serum $IgG4^+$ levels [2]. The incidence of IgG4-related diseases is low, and there are certain similarities with other diseases in clinical, pathological, and laboratory examinations, which can easily lead to misdiagnosis [3]. If there is no involvement of other systems, the diagnosis of $IgG4^+$ involvement in the heart can only be made through postoperative pathological diagnosis [4]. Currently, there are not many reports that involve the cardiovascular system [5]. The disease we report is related to $IgG4^+$ and involves the aorta with regurgitation of the aorta valve. The CARE checklist was used when writing this case report (**Supplementary Fig. 1**).

Case Presentation

Six months ago, a 50-year-old man experienced shortness of breath and tightness in his chest after common activity. During an echocardiogram at a local hospital, it was discovered that the left coronary valve of the aortic valve had undergone abnormal development with moderate regurgitation. Multiple solid nodules were visible on the left lower lung during the chest computerized tomography scan (CT), with a maximum diameter of 17 × 10 mm (see Fig. 1A). Hepatitis B, syphilis, and thalassemia were among her medical history. The patient has been a smoker for 20 years. The admission examinations were as follows: body temperature: 36.5 °C, heart rate: 75 beats/min, respiratory rate (R): 18 beats/min, blood pressure: 109/28 mmHg, and blood oxygen saturation: 100%. The heart rhythm is neat. A continuous rumbling noise of the III grade can be heard between the left III ribs of the sternum. The right side of the sternum has a continuous III-grade rumbling noise between the II–III ribs. According to the serological tests, $IgG4^+$ was 4.23 g/L, which is more than twice the normal value. High sensitivity c-reactive protein (HSCRP) exceeds the normal value by nearly 13 times, erythrocyte sedimentation rate (ESR) and IL-6 exceed the normal value, and n-terminal pro-brain natriuretic peptide (NT proBNP) reaches 2635 pg/L, which is 10 times the normal value. Transesophageal echocardiography showed that the aortic valve was a three-leaf valve, the left coronary valve of the aortic valve was small, the aortic valve was severely refluxing,

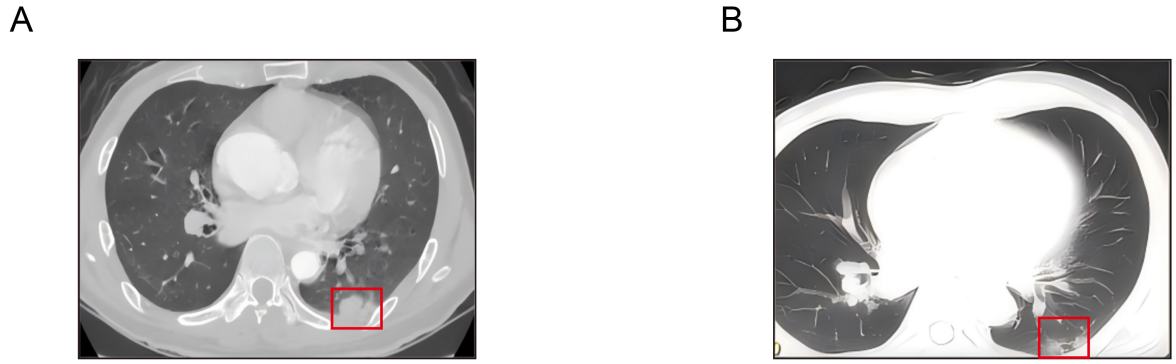

Fig. 1. Chest computerized tomography (CT) results. (A) Preoperative chest CT nodule (box); (B) Postoperative chest CT nodule (box).

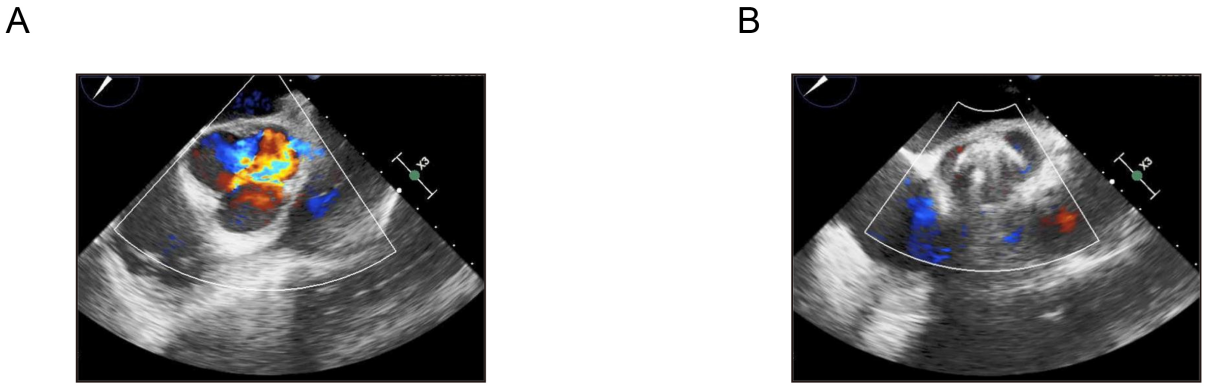

Fig. 2. Cardiac ultrasonography results. (A) preoperative transesophageal echocardiography. Aortic regurgitation beam; (B) postoperative transesophageal echocardiography. Metal aortic valve echo.

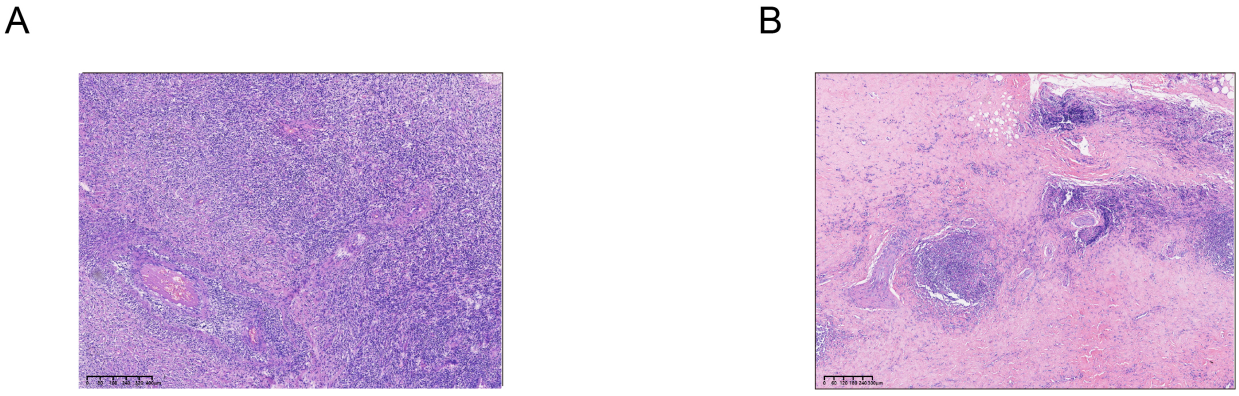

Fig. 3. Pathological results of nodule and aortic valve. (A) Hematoxylin-eosin (HE) staining of pulmonary nodules. (B) HE staining of the aortic valve. Original magnification: 200×.

and the ascending aorta and aortic sinus were dilated (see Fig. 2A). The results of head CT, coronary angiography, aortic computerized tomography angiography (CTA), abdominal ultrasound, bilateral lower limb artery ultrasound, and neck vascular ultrasound showed no significant abnormalities. The diagnosis and the surgical indications were clear. It was recommended to accept surgical treatment and receive routine glucocorticoid therapy after surgery.

The excised valve cusps and a portion of the aortic wall were removed and sent for histopathologic examination. Special stains for common microorganisms gave negative results using a microscope. Hematoxylin-eosin (HE)

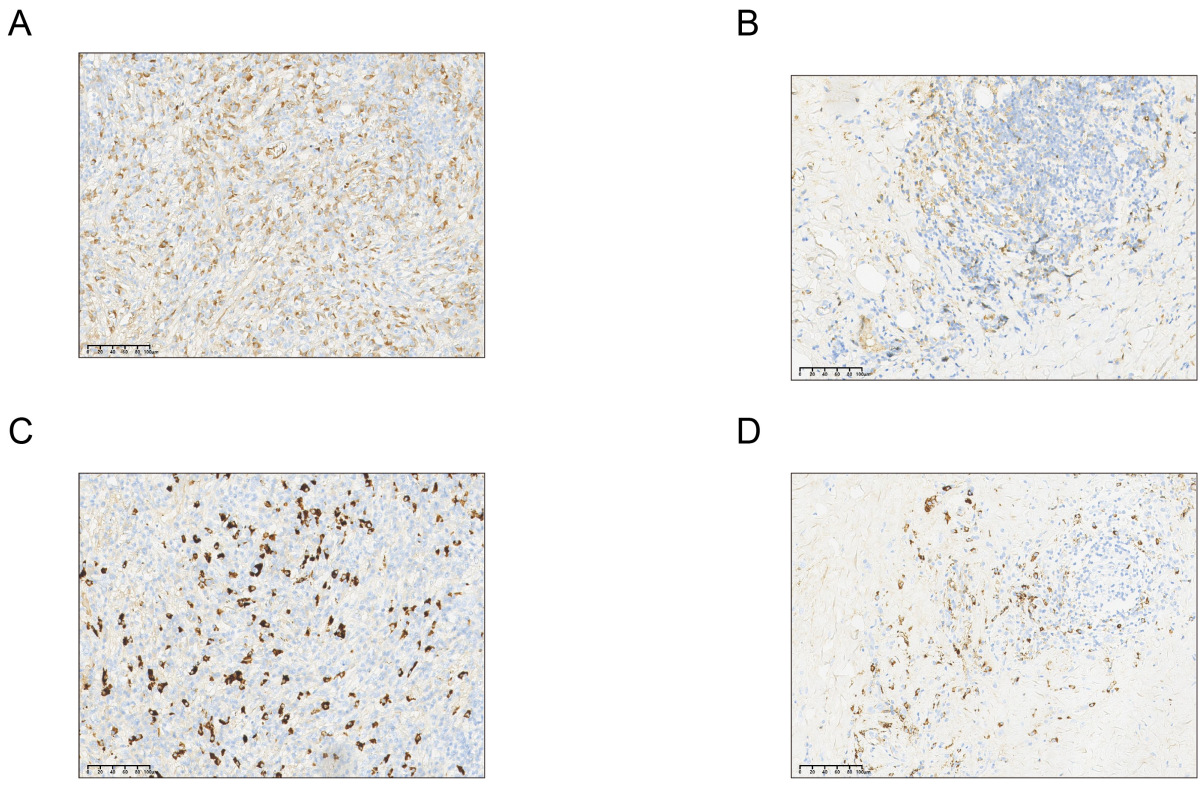

Fig. 4. Immunohistochemical results of nodule and aortic valve. (A) Immunohistochemical staining of IgG in pulmonary nodules. (B) Immunohistochemical staining of aortic valve with IgG. (C) Immunohistochemical staining of $IgG4^+$ in pulmonary nodules. (D) Immunohistochemical staining of aortic valve with $IgG4^+$. Original magnification: 200×.

staining of the lower pulmonary nodules on the left revealed massive proliferation of lymphocytes and plasma cells. There was a significant infiltration of neutrophils and eosinophils. Some blood vessels showed inflammatory changes (see Fig. 3A). The results of aortic valve HE staining suggested that a large number of plasma cells and lymphocytes infiltrated. Lymphocyte-based inflammatory cell infiltration was seen around the small blood vessels. There were lymphoid follicles formation, fibrous tissue hyperplasia with hyalinization and cellulose exudation (see Fig. 3B). According to the immunological staining of left lower pulmonary nodules and aortic valves, there were a great deal of IgG plasma cells (see Fig. 4A,B). As showing in the results of $IgG4^+$ immunohistochemical staining, the infiltration of $IgG4^+$ plasma cells were greater than 10/HPF and the ratio of $IgG4^+$ to IgG^+ cells was more than 40% (see Fig. 4C,D).

The echocardiography of the patient before discharge revealed that the aortic valve was an artificial valve with a fixed valve frame and there were no abnormalities in valve leaflet activity. With a valve velocity of 1.6 m/s and a peak pressure difference of 10 mmHg, the blood flow of the left ventricular outflow tract was smooth (see Fig. 2B). According to chest CT results, there have been changes in the lower left lung after surgery. There were scattered small nodules in both lungs, which did not change much (see Fig. 1B).

After half a year of follow-up, the patient's echocardiography showed no obvious perivalvular leakage after aortic valve prosthetic metal valve replacement. Chest CT results suggested postoperative changes in the left lower lung. There were scattered small nodules in both lungs, which did not change much.

Discussion

IgG4-related disease is a chronic autoimmune disease, and its pathogenesis is still unclear [6]. The main features are elevated serum $IgG4^+$ levels and typical histopathological changes: IgG4-positive plasma cell infiltration with striated fibrosis and occlusive vasculitis [7], which can involve systemic organs, such as the pancreas [8], coronary artery [9], lymph nodes [10] and central nervous system [11], etc. Involving different parts, clinical manifestations are different. At present, it is believed that a clear diagnosis of $IgG4^+$ related diseases requires the following conditions: (1) Typical focal/diffuse enlargement or mass formation of organ tissues; (2) Serum $IgG4^+$ level >1350 mg/L; (3) The pathological examination results indicate a large infiltration of lymphocytes and plasma cells with interstitial fibrosis. The infiltration of $IgG4^+$ plasma cells in organ tissues is greater than 10/HPF, and the ratio of $IgG4^+$ plasma cells to IgG^+ plasma cells is greater than 40%. Among them, there were

so few reports on the heart that the clinical diagnosis was difficult [12]. According to our search, we found one article summarizing 10 cases. The average level of $IgG4^+$ expression in serum of 6 cases exceeded normal levels. Extensive infiltration of positive plasma cells and lymphocytes was reported in 7 cases. Among them, 4 cases were treated with glucocorticoids, 7 cases were treated with surgery, and 2 cases were treated with cardiac pacemakers [13]. This case not only involved the aortic valve, causing aortic valve insufficiency, which has not been reported in previous literature, but also affected lung tissue. We are reporting for the first time.

Through the review of this case, it was suggested that in clinical practice, patients with IgG4-related diseases should be vigilant of the numerous organs and tissues involved, including cardiovascular diseases [4]. The clinical symptoms of IgG4-related aortic valve disease in this case were shortness of breath and chest tightness after activity, which was not significantly different from common aortic valve diseases. However, there were obvious abnormalities in serum detection. HSCRP was significantly higher than the normal value by nearly 13 times, and ESR was 7 times higher than the normal value, suggesting that the patient had autoimmune diseases. $IgG4^+$ was up to 4.34 g/mL, which was much higher than the diagnostic criteria. If combined with autoimmune-related diseases, the possibility of this disease should be considered. In clinics, doctors should be vigilant against such diseases. IgG4-associated large artery vasculitis has its uniqueness in terms of serology, imaging, and pathology. Understanding this disease will improve our clinical diagnosis and treatment level. During the treatment of the case, the postoperative care needs attendtion. Due to the patient's impatience, anxiety, and pessimism before surgery, postoperative care for pain and fever were particularly important. After surgery, in addition to routine use of anticoagulants, steroid glucocorticoid therapy was also given. Preoperative education to patients on the necessity and principles of the glucocorticoid therapy, as well as informing them of common adverse reactions from the glucocorticoid therapy.

At present, the etiology and pathogenesis of IgG4-related diseases remain unclear. Therefore, we should enhance our understanding of this disease, timely conduct serum $IgG4^+$ levels and pathological tissue examinations, achieve early diagnosis, avoid missed diagnosis and misdiagnosis. In addition, providing patients with sufficient preoperative emotional counseling, glucocorticoid medication usage instructions, and meticulous postoperative care has greatly benefited them.

Conclusions

IgG4-related diseases involving the aortic valve have same clinical symptoms as common aortic valve disease. It was easy to miss the diagnosis if serological changes were not observerd. The pathology findings of chest nodules and aortic valve were beneficial in making further diagnoses. IgG4-related diseases are chronic diseases that tipically involve multiple organs or systems, which is a significant charactercistic.

Abbreviations

HSCRP, high sensitivity c-reactive protein; ESR, erythrocyte sedimentation rate; NT-proBNP, n-terminal pro-brain natriuretic peptide.

Availability of Data and Materials

All data points generated or analyzed during this study are included in this published article.

Author Contributions

YW and HW was responsible for collecting and organizing datas, while YX's job was conducting pathological experiments. FX was responsible for conception of the article. WW was responsible for analysising the data and writing the article. YW and WW writed the article and FX edited the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The Institutional Ethics Committee of Fuwai Hospital granted ethical approval for this case report, as ethical approval is not necessary for individual case reports. The patient's consent was obtained before publishing the clinical and imaging data in the case report.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7879.

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