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【 CASE REPORT 】

IgG4-related Pericarditis in which Oral Corticosteroid Therapy Was Effective

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Abstract:
IgG4-related diseases (IgG4-RDs) have recently been reported in many organs other than the salivary, pancreatic and hepatobiliary systems. A 64-year-old woman was referred to our department for her abdominal fullness and cardiomegaly on chest X-ray. After draining the pericardial fluid, her symptom promptly diminished, and pericardial friction rubbing became clearly audible. Elevated serum levels of IgG and IgG4 and ureteral wall thickening on computed tomography suggested IgG4-RD. After the initiation of oral corticosteroid therapy, the pericardial effusion was resolved, and she has been in a steady-state condition for the past two years.

Key words: corticosteroid, IgG4-related disease, pericardial fluid, pericarditis

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Introduction

Cases of IgG4-related diseases (IgG4-RDs) have recently been reported in the salivary, pancreatic and hepatobiliary systems. However, these entities have additionally been found to involve many organs and to occur concomitantly (1, 2). The number of patients is increasing due to the widespread recognition of this new entity. We experienced a case of IgG4-related pericarditis with massive effusion in which oral corticosteroid therapy was effective.

Case Report

A 64-year-old woman who had been treated for hypertension and bronchial asthma at a nearby clinic was referred to our department with a 1-month history of abdominal fullness and cardiomegaly with a 72% cardio-thoracic ratio on chest X-ray (Fig. 1a). Her blood pressure was 167/100 mmHg, and her pulse showed regular sinus tachycardia of 114 beats per minute. She had mild pretibial pitting edema but did not show goiter, cardiac murmur or friction rubbing.

Findings of initial blood tests performed mainly on admission are shown in Table. The values of thyroid hormone, liver enzymes, white blood cell count and C-reactive protein were within normal ranges. An electrocardiogram showed sinus rhythm and low R-wave voltage on precordial leads. Chest plain computed tomography (CT) demonstrated massive effusion around the heart (Fig. 2a) with no significant findings in either lung field, the mediastinum or aorta. An echocardiogram showed no specific findings suggestive of the cause of pericardial effusion. After draining 1 L of light-yellowish exudative effusion by transapical puncture (Fig. 1b), her symptom of abdominal fullness was promptly alleviated without significant changes in blood pressure and heart rate, and pericardial locomotive friction rubbing was clearly audible the next day.

Findings on additional blood laboratory tests, such as those assessing tumor markers and serum autoantibodies relating to collagen diseases, were within normal ranges, and pericardial fluid cytology and culture were negative for malignancies and infections. However, abdominal plain CT showed ureteral wall thickening in the right renal hilum (Fig. 2b, c), which led us to suspect that the pericardial effusion had been caused by IgG4-RD (3). Coronary artery CT and subsequent coronary angiography showed no steno-

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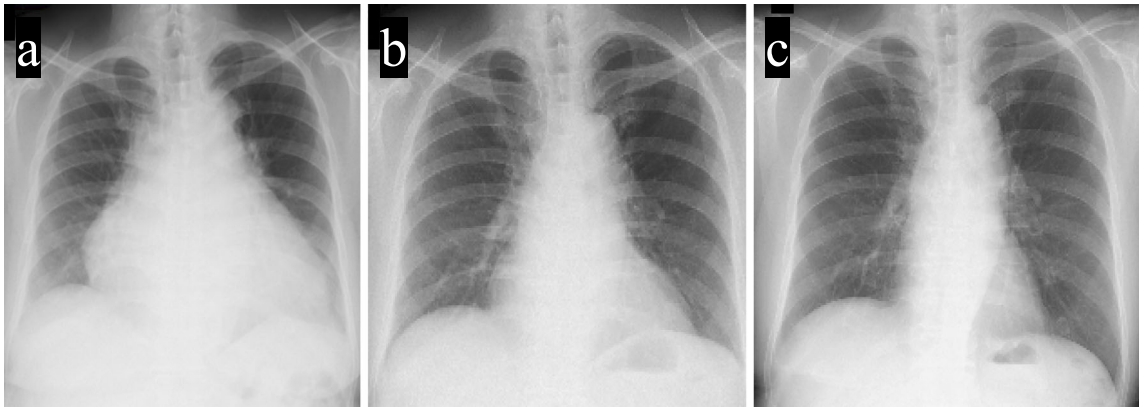

Figure 1. **Serial changes on chest X-ray. Cardiomegaly at the outpatient visit (a) was improved immediately after pericardial drainage (b) and after six months (c).**

Table. **Blood Chemistry Test on Admission.**

<Hematology>		<Immunology>	
White blood cell	3,520 /μL	IgG	2,058 mg/dL
Red blood cell	448 ×10⁴/μL	IgG4	962 mg/dL
Hemoglobin	13.9 g/dL	IgE	685 mg/dL
Hematocrit	41.9 %	ANA	40 ×
Platelet	19.8 ×10⁴/μL	Anti-DNA Ab	3.2 IU/mL
		RF	4 IU/mL
<Biochemistry>		C3	93.0 mg/dL
Total protein	7.6 g/dL	C4	25.1 ng/dL
Albumin	3.7 g/dL	CH50	43 U/mL
Total bilirubin	1.0 mg/dL		
AST	65 IU/L	<Coagulation>	
ALT	22 IU/L	D-dimer	0.9 μg/mL
γ-GTP	80 IU/L		
Blood urea nitrogen	16.6 mg/dL	<Tumor marker>	
Creatinine	0.91 mg/dL	CEA	2.7 ng/mL
C-reactive protein	<0.30 mg/dL	CA19-9	3.5 U/mL
Brain natriuretic peptide	10 pg/mL	CA125	123.4 U/mL
<Thyroid function>			
Thyroid stimulating hormone	3.62 μIU/mL		
free T4	1.09 ng/dL		

ALT: alanine aminotransferase, ANA: anti-nuclear antibody, AST: aspartate aminotransferase, CH50: 50% hemolytic unit of complement, γGTP: γ-glutamyl transpeptidase, RF: rheumatoid factor

tic, aneurismal or periarterial tumorous lesions. The levels of serum IgG, particularly IgG4, and IgE were found to be markedly elevated [2,058 mg/dL (normal range: 870-1,700 mg/dL); 962 mg/dL (4-108 mg/dL); and 685 mg/dL (<175 mg/dL), respectively]. Accordingly, IgG4-related pericarditis was strongly suspected. However, we observed no lesions other than ureteral wall thickening in the right renal hilum that were readily accessible for a biopsy, such as those in the salivary glands and lymph nodes, although the diagnostic criteria require pathological findings for a definitive diagnosis (2). We therefore diagnosed this patient with possible IgG4-RD and started oral steroids therapy.

High-dose oral prednisolone (PSL) of 45 mg (0.6 mg/kg body weight) daily was initiated and continued for the first 2 weeks (4) and gradually decreased over the period of 9 months to the maintenance dose of 5.0 mg daily at present. Accordingly, the serum levels of IgG4 gradually decreased (Fig. 3), and no further accumulation of pericardial effusion has been noted in the past two years (Fig. 1c).

Discussion

We experienced a case of IgG4-related pericarditis with massive effusion in which oral corticosteroid therapy was effective (5, 6).

In 2001, Hamano et al. reported the elevated levels of se-

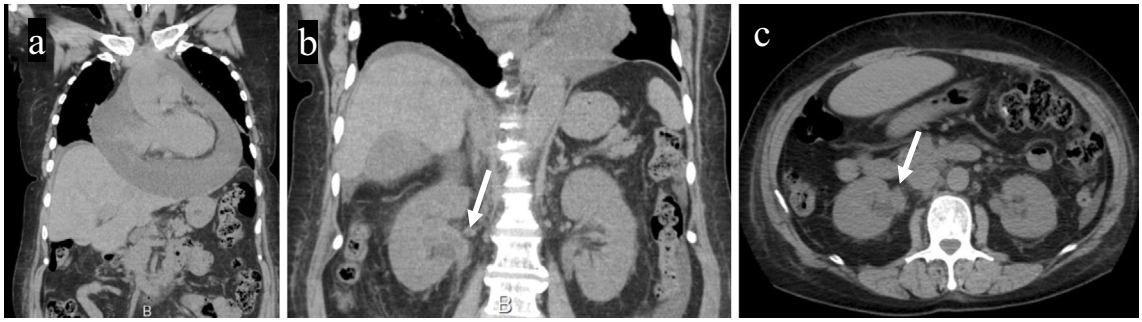

Figure 2. **Plain chest and abdominal computed tomography findings. Massive pericardial effusion had accumulated at the outpatient visit (a). The white arrow indicates ureteral wall thickening in the right renal hilum (b, c).**

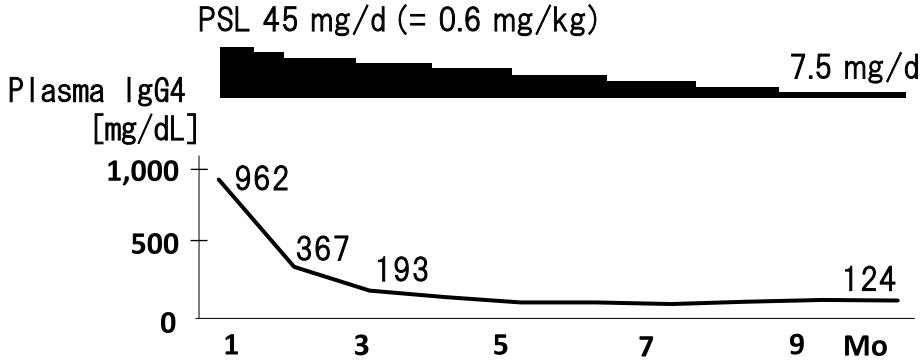

Figure 3. **Serial changes in the doses of corticosteroids and values of plasma IgG4. The values of IgG4 gradually decreased after starting corticosteroid therapy.**

rum IgG4 in patients with autoimmune pancreatitis (AIH) (1). Subsequently, the clinicopathological entity of this disease has been adapted to many other organs, including the conventional salivary gland diseases of Mikulicz disease and Sjögren syndrome as well as renal organ diseases (7, 8). Thus, the new clinicopathological entity of IgG4-RD has been established and is now widely accepted. IgG4-RD often involves multiple organs concomitantly (9). IgG4-related cardiovascular lesions include inflammatory abdominal aortic aneurysm (IAAA), coronary periarteritis and pericarditis (3, 10-14). Kasashima showed that 12 of 252 aortic aneurysms were IgG4-RD, about half of which were IAAA, accounting for 5-10% of abdominal aneurysms (15). However, since most of the reports of IgG4-related coronary periarteritis and pericarditis are limited to solitary cases (14, 16), the precise frequency of these lesions is unclear. In general, cases with the acute accumulation of pericardial fluid often demonstrate hemodynamic changes, including hypotension, whereas cases with chronic pericardial fluid collection usually do not (17). Similar to almost all previous case reports of IgG4-related pericarditis, the present case also followed a chronic course, which we think was why the present case did not show significant hemodynamic changes aside from tachycardia despite massive pericardial fluid collection (16).

The diagnostic criteria of IgG4-RD consist of the combination of the following findings (18): clinically characteristic imaging findings, such as diffuse or localized enlarged, tumorous, nodular or hypertrophic lesion in one or more organs; high levels of serum IgG4 (≥135 mg/dL); and the pathological tissue findings of the marked infiltration of lymphocytes or plasma cells, fibrosis and IgG4-positive cell infiltration. Depending on the combination of these findings, the diagnostic level is determined to be definite, probable or possible. The present case was at the possible diagnostic level, but several additional tests have been proposed for achieving a more definitive diagnosis. Surgical pericardiotomy to identify IgG4-positive cells in the pericardial specimen might have been useful; however, we did not perform pericardiotomy because the procedure requires general anesthesia, and there was a sufficient amount of pericardial fluid for a safe puncture in the present case (16). Although the usefulness of ^{18}F-fluorodeoxyglucose positron emission tomography/CT and ^{67}gallium single-photon emission CT have been indicated in terms of the sites and activities of inflammation and evaluating responses to steroid therapy, the findings of neither of these procedures are included in the current diagnostic criteria (13, 19, 20). The levels of IgG and IgG4 in pericardial fluid have not been described in the limited number of available reports; we therefore believe that the significance of this measurement remains unclear.

As mentioned above, many patients with IgG4-RD and with IgG4-related pericarditis follow a chronic course, and most respond to steroid therapy (13, 20, 21). However, the patient's prognosis depends on the time between the initiation of the disease and the first visit or initial diagnosis, so

some patients suffer a fatal outcome (13). Furthermore, no epidemiological studies of IgG4-related pericarditis among patients with IgG4-RD or with pericardial fluid collection have been performed. Therefore, the levels of serum IgG4 should be routinely measured in patients with more than a moderate amount of pericardial effusion in order to accumulate data and establish epidemiological evidence for the usefulness of IgG4 levels. However at present, we recommend the levels be measured at an early stage, at least in cases with impaired hemodynamics, organ failure, relapsing pericardial effusion and pericardial effusion of unknown cause, even after initial screening tests, or in patients scheduled to receive steroid administration.

For the treatment of IgG4-RD, oral steroid therapy is the first choice (4, 22), and immuno-suppressive agents are occasionally added in combination. After the initiation of high-dose steroid therapy, the dose is gradually reduced according to the symptom severity, imaging findings and serum levels of IgG, IgG4 and γ-globulin, with low-dose therapy maintained for half a year to three years (4, 22).

Steroid therapy is effective in half to two-thirds of IgG4-RD cases, and the time until the response to steroid therapy is usually two weeks to several months (9). Such therapy may be discontinued if remission is achieved. However, dose reduction or discontinuation causes the recurrence of IgG4-RD in about half of cases, and a complete cure cannot be expected. Furthermore, patients whose levels of serum C-reactive protein and IgG4 fail to decrease tend to show a poor response to steroid therapy and are at risk of recurrence. In the present case, the patient's symptoms of asthma attack and wheezing have also been suppressed since steroid therapy was started.

Previous cases of refractory pericarditis before the discovery of IgG4-RD, in which empirical steroid therapy was found to be effective, might have included pericarditis caused by IgG4-RD. In cases of chronic retention of pericardial effusion in which the cause cannot be determined after the initial evaluation, the possibility of IgG4-related pericarditis should be considered. Searching for body surface lesions, such as those in the salivary glands and lymph nodes, in a histopathological evaluation might increase the diagnostic certainty according to the established criteria.

The authors state that they have no Conflict of Interest (COI).

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