INTERNAL MEDICINE

□ CASE REPORT □

Pericardial Involvement in IgG4-related Disease

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Abstract

We herein report the case of a 65-year-old man with pericardial involvement associated with autoimmune pancreatitis. Chest CT imaging showed pericardial thickening. The patient responded to corticosteroid therapy, and the pericardial thickening resolved. Multiple organs are involved in immunoglobulin G4 (IgG4)-related disease (IgG4-RD); however, only a few cases of IgG4-related chronic constrictive pericarditis have been reported. To our knowledge, this is the first reported case of IgG4-RD with pericardial involvement at an early stage. This case indicates that recognizing pericardial complications in autoimmune pancreatitis is important and that CT imaging may be useful for obtaining the diagnosis and providing follow-up of pericardial lesions in cases of IgG4-RD.

Key words: IgG4-related disease, pericardial involvement, computed tomography

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Introduction

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is an increasingly recognized syndrome whose etiology remains unknown. In 2003, Kamisawa et al. reported multiple extrapancreatic lesions in patients with autoimmune pancreatitis (AIP) and proposed the existence of a novel entity termed "IgG4-related autoimmune disease," organ manifestations of which include involvement of the pancreas, bile ducts, retroperitoneum and salivary glands (1, 2). There are a few reports of IgG4-RD cases complicated by constrictive pericarditis diagnosed using pericardiectomy specimens or at autopsy (3-5). We herein report a case of IgG4-RD in which AIP was associated with pericardial involvement that improved after steroid therapy.

Case Report

A 65-year-old man with a history of dyslipidemia was admitted to our hospital to evaluate of his liver function. He had experienced nausea and epigastric discomfort three days earlier and noted brown urine two days before admission. Prior to admission, he had visited a nearby clinic, and routine laboratory examinations detected abnormal liver function parameters. He was therefore referred to our hospital for a close examination and treatment. On a physical examination, his blood pressure was 124/72 mmHg, his pulse rate was 66 beats per minute and his body temperature was 36.6°C. The conjunctiva was yellow, and cardiac auscultation was unremarkable; specifically, there were no audible murmurs, gallops or signs of pericardial friction rub. The patient's abdomen was slightly distended, and the edge of the liver was four finger-widths below the right costal margin in the midclavicular line. No edema was evident in the

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Table 1. Laboratory Data.

WBC	7,000	/μL	d-Bilirubin	6.8	mg/dL	Anti-SS-B	7.0	U/mL
RBC	426×10⁴	/μL	UA	4.2	mg/dL	ANA	×80	
Hb	13.5	g/dL	BUN	9	mg/dL	homo	×80	
Ht	39.3	%	Cr	0.63	mg/dL	speckled	×80	
Plt	35.1×10⁴	/μL	TC	160	mg/dL	IgG4	637	mg/dL
CRP	0.60	mg/dL	TG	197	mg/dL	IgA	152	mg/dL *
TTT	7.7	McLagan U	Na	143	mEq/L	IgM	59	mg/dL *
ZTT	12.7	Kunkel U	K	4.1	mEq/L	IgD	0.9	mg/dL *
AST	284	IU/L	t-Protein	7.0	mg/dL	IgG	1,351	mg/dL *
ALT	529	IU/L	Alb	60.8	% *	IgE	483	IU/mL *
ALP	1,194	IU/L	α1	2.6	% *	FT3	2.90	pg/mL
LDH	240	IU/L	α2	7.8	% *	FT4	1.03	ng/dL
γGTP	1,402	IU/L	β	10.3	% *	TSH	2.81	μU/mL
ChE	275	IU/L	γ	18.5	% *	CEA	2.0	ng/dL
CPK	57	IU/L	RF	3>	IU/mL	CA19-9	19	U/mL
Amylase	263	IU/L	CH50	38.7	U/mL	Urine	protein (-)	glucose (-)
t-Bilirubin	8.0	mg/dL	Anti-SS-A	7.0	U/mL		urobili (0.1)	OB (-)

(* measured under corticosteroid therapy)

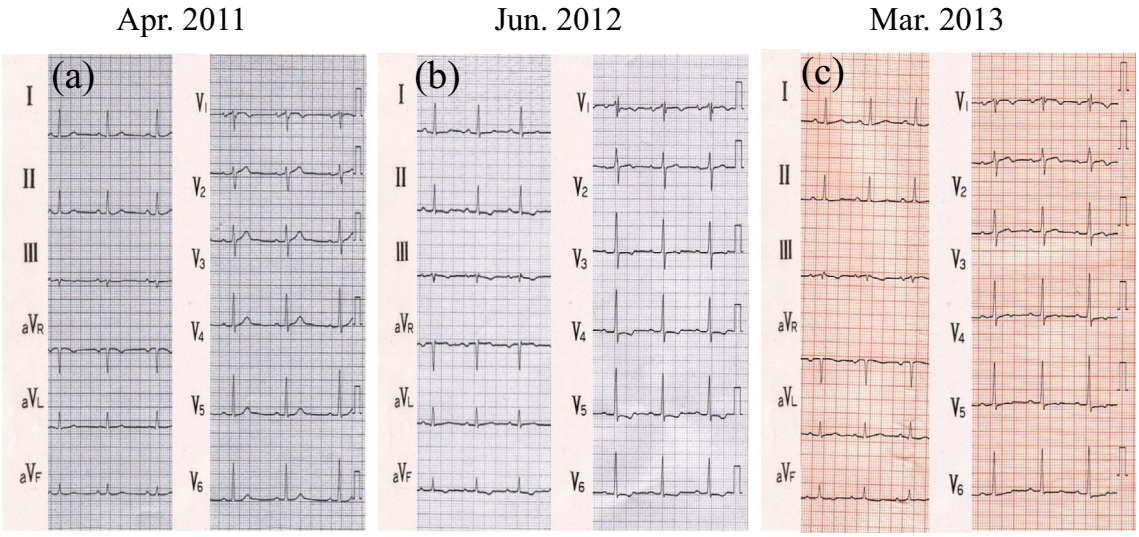

Figure 1. (a) Electrocardiogram (ECG) showing no abnormalities of the ST segment or T waves. (b) ECG recorded after one year showing ST depression and T wave inversion in leads II, III, aVF and V3-6. (c) ECG recorded after two years showing reversion of the ST segment and T wave changes to nearly normal.

lower limbs. Laboratory examinations yielded the following results: C-reactive protein, 0.50 mg/dL (normal, 0.00-0.40 mg/dL); aspartate aminotransferase, 284 IU/L (8-38 IU/L); alanine aminotransferase, 529 IU/L (4-44 IU/L); alkaline phosphatase, 1,194 IU/L (104-338 IU/L); lactic acid dehydrogenase, 240 IU/L (106-211 IU/L); amylase, 263 IU/L (41-112 IU/L); total bilirubin, 8.0 mg/dL (0.2-1.2 mg/dL); direct bilirubin, 6.8 mg/dL (0.0-0.4 mg/dL); antinuclear antibodies, ×80 (<×40); IgG4, 637 mg/dL (4.8-105 mg/dL); and IgE, 483 IU/mL (<173 IU/mL). Other results are shown in Table 1. An electrocardiogram (ECG) revealed a normal sinus rhythm without changes in the ST segment or T waves (Fig. 1a). Chest radiography demonstrated a normal cardiac silhouette without pulmonary congestion. Echocardiography disclosed a normal left ventricular function (ejection fraction, 62%) and normal left ventricular wall thickness. No pericardial effusion was detectable, although the pericardial thickness could not be evaluated. The Doppler transmitral inflow showed a pseudonormal pattern (E wave velocity, 75 cm/s; A wave velocity, 57 cm/s; E/A=1.3; and E/E'=12). Dynamic contrast-enhanced computed tomography (CT) from the chest to the pelvis revealed enlargement of the pancreatic parenchyma in the body and tail in addition to wall thickening of the common bile duct, resulting in dilatation of the intrahepatic bile duct (Fig. 2a). The enlarged pancreatic parenchyma displayed decreased enhancement compared with the normal adjacent pancreatic parenchyma in the pancreatic phase on CT, with no dilatation of the main pancreatic duct. These imaging findings were considered typical of AIP (6). Due to the detection of an obstructive pattern on a liver function test, as well as an elevated serum IgG4 level, positive serum antinuclear antibodies and the CT imaging findings, the patient met the Clinical Diagnostic Criteria for Autoimmune Pancreatitis 2011 (6, 7) and

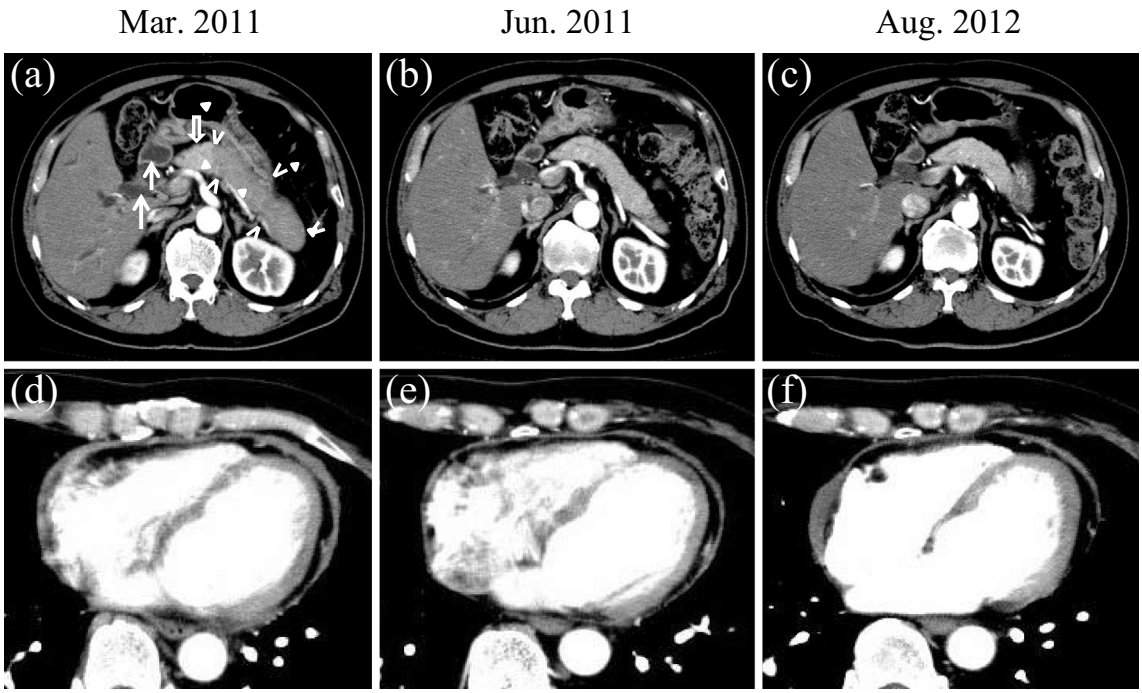

Figure 2. **Sequential abdominal and chest computed tomography. (a) Extra/intrahepatic biliary tract dilatation, lower bile duct stricture and wall thickening (arrows) with an enlarged pancreas (arrowheads) are shown. The enlarged pancreatic parenchyma exhibited decreased enhancement compared with the normal adjacent pancreatic parenchyma (open arrow). (b, c) After corticosteroid therapy, the bile duct thickening and pancreatic swelling gradually resolved. (d) Pericardial thickening was observed on admission. The maximum pericardial thickness over the anterior surface of the heart was 6.3mm. (e, f) Following corticosteroid therapy, the pericardial thickening gradually decreased. The maximum pericardial thickness was 3.8 and 3.6 mm, respectively.**

Figure 3. **Clinical course of the patient.**

was diagnosed with IgG4-RD. Contrast-enhanced CT of the chest revealed thickening of the pericardium, suggesting fibrous thickening (Fig. 2d). The administration of 30 mg of prednisolone ameliorated his nausea and abdominal discomfort, and the serum levels of amylase and other liver enzymes gradually returned to normal (Fig. 3). In addition, the serum IgG4 level decreased to 205 mg/dL after three months. Follow-up CT images of the abdomen obtained after the completion of corticosteroid therapy showed gradual regression of enlargement of the pancreas, which was enhanced homogeneously, in addition to improvements in the intrahepatic and extrahepatic bile duct dilatation and thickening of the common bile duct wall (Fig. 2b, c). Although the pericardial thickening improved after the steroid therapy, slight thickening remained on the latest CT examination (Fig. 2e, f). The initial dose of prednisolone was administered for four weeks, then tapered by 5 mg every two weeks to a maintenance dose of 2.5 mg/day. An ECG recorded one year after disease onset showed ST segment depression and T wave inversion in both the limb and precordial leads

Table 2. Summary of Published Reports and the Present Case of Immunoglobulin G4-related Disease Complicated by Pericardial Involvement.

Case	Age	Sex	Diagnosis	Basis for diagnosis	Reference
1	68	M	Constrictive pericarditis Pleural fibrosis	Pericardiectomy Serum IgG4 level	3
2	83	M	Idiopathic retroperitoneal fibrosis Autoimmune pancreatitis Constrictive pericarditis Mediastinal fibrosis	Autopsy	4
3	29	F	Chronic pleuritis Constrictive pericarditis	Biopsy Serum IgG4 level	5
Present case	65	M	Autoimmune pancreatitis Acute pericarditis	CT Serum IgG4 level	

(Fig. 1b). An ECG recorded after two years showed that the ST segments and T waves had returned to near control values (Fig. 1c). No recurrence was noted two years after the initial treatment.

Discussion

Although IgG4-RD was initially recognized as AIP by a Japanese group (1), it is known to involve one or multiple organs (8-10). Commonly shared features include tumor-like swelling of the involved organs, lymphoplasmacytic infiltrates enriched in IgG4-positive plasma cells, an elevated serum IgG4 concentration and a positive response to corticosteroid therapy (11). In the present case, AIP was diagnosed based on the patient's laboratory data and CT imaging findings (6, 7), and chest CT revealed pericardial disease complications. Multiple organs are affected in 60-90% of patients with IgG4-RD (6, 12, 13), including the pancreatobiliary tract, liver, salivary glands, lacrimal glands, nasopharynx, extraocular muscles and retrobulbar space, thyroid gland, breasts, lungs, kidneys, lymph nodes, aorta, arteries, retroperitoneal space, skin, bone marrow and prostate (8-11), accompanied by pericarditis, a complication rarely associated with IgG4-RD. Pericardial involvement is not uncommon in many connective tissue diseases (i.e., rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis and mixed connective tissue disease) (14); however, the clinical features and laboratory findings in this case suggested that these diseases were absent in our patient. To the best of our knowledge, there have been only three reported cases of IgG4-related constrictive pericarditis, all of which were histologically diagnosed on pericardiectomy or at autopsy (Table 2). Although a histopathological assessment of the biopsied pericardium was not performed in this case, chest CT imaging revealed fibrous thickening of the pericardium, despite the absence of electrocardiographic and echocardiographic evidence of pericardial involvement, indicating the possible utility of CT imaging for detecting pericardial involvement in cases of IgG4-RD. Of note, overt ST-T segment abnormalities suggestive of pericardial injury appeared when the pericardial thickness decreased after the initiation of corticosteroid therapy. Hence, patients with IgG4-RD and pericardial involvement may show paradoxical findings on ECG and chest CT, which should be noted when making the diagnosis and monitoring the disease. The mechanisms underlying the ST-T-wave changes observed after corticosteroid therapy in this case remain unclear. In patients with acute pericarditis, ECG changes can be dynamic, while ST elevation is uncommonly absent during the acute phase (15). Subsequent ECG changes are also variable; in some cases, the ECG findings revert to normal over the course of days or weeks, while in others, ST segment depression and T wave inversion persist for weeks or even months. Similarly, ECG changes indicative of pericardial involvement in patients with IgG4-RD may be variable, a topic that should be investigated in future studies.

The main treatment for IgG4-RD is corticosteroid therapy, and, in most reports, one-half to two-thirds of patients respond to this approach. The response time is variable, usually within two weeks or four months (16). The present patient responded to corticosteroid therapy within several days; at three months, there were improvements in symptoms and the hepatobiliary function, a decrease in the serum IgG4 level and reductions in the size of the pancreas and amount of pericardial thickening. Most patients with IgG4-RD initially respond to corticosteroid treatment, although relapse is common after the therapy is discontinued (17). Additional organs and tissues may become involved over time despite the apparent efficacy of treatment. Although corticosteroid therapy ameliorated the acute inflammatory pericardial involvement in this case, we will carefully monitor the patient for constrictive pericarditis or the involvement of other organs. Long-term follow-up is needed to determine his prognosis over time.

In summary, we herein reported the case of a patient with IgG4-RD with combined AIP and pericardial involvement. This case report indicates that recognizing pericardial complications in AIP patients is important and that CT imaging may be useful for obtaining the diagnosis and providing follow-up of pericardial lesions in cases of IgG4-RD.

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

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