



## Case Report

## Pericarditis caused by herpes zoster



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## ABSTRACT

A 53-year-old immunocompetent male visited our hospital complaining of chest pain which persisted for 6 h. After detailed examination, the patient was diagnosed with viral pericarditis and treated with aspirin. On day 3 after admission, rash with blisters appeared on the right side of chest. Paired serum evaluation on the day of admission and 3 weeks later revealed that varicella zoster virus (VZV) titer had significantly increased, and the patient was diagnosed with pericarditis caused by herpes zoster. Although VZV is known to cause various complications, there are few reports of pericarditis associated with VZV. We should consider the possibility of concomitant pericarditis with herpes zoster.

**<Learning objective:** Although varicella zoster virus may cause various complications, the occurrence of myopericarditis is rare. Based on this case, it is suggested that pericarditis may develop concurrently with herpes zoster. Therefore, we should consider this possibility in patients exhibiting herpes zoster on the chest.>

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## Introduction

Infection with the varicella zoster virus (VZV) causes two distinct clinical syndromes, varicella and herpes zoster. Primary infection with VZV results in varicella, characterized by viremia with a diffuse rash and seeding of multiple sensory ganglia, where the virus establishes lifelong latency. Endogenous reactivation of latent VZV typically results in a localized skin infection known as herpes zoster. VZV may cause various complications such as secondary bacterial infection, pneumonia, acute cerebellar ataxia, meningitis, encephalitis, and Reye syndrome [1,2]. In contrast, the occurrence of myopericarditis is extremely rare [2]. The occurrence of concurrent myopericarditis with herpes zoster, as in the present case, is extremely rare [3–5]. This article describes a case of pericarditis caused by herpes zoster.

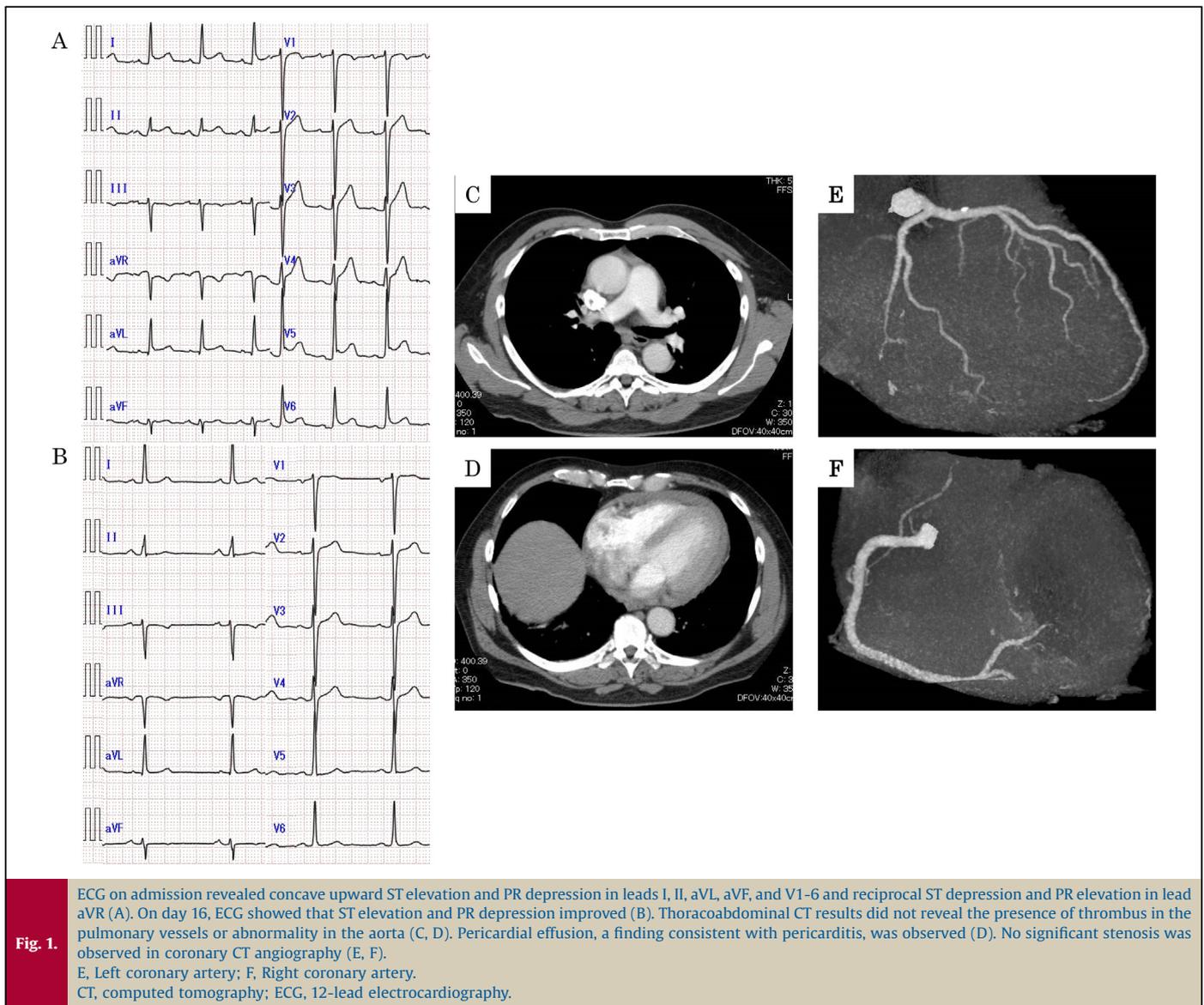
## Case report

We report the case of a 53-year-old immunocompetent male who developed pericarditis caused by herpes zoster.

The patient had no particular past history except for varicella in his childhood. Six hours prior to consultation, the patient suddenly noticed chest pain at rest without physical disorders before chest pain developed. At the time of consultation, the patient had a blood pressure of 134/92 mmHg, heart rate of 110 beats per minute, and body temperature of 37.6 °C. There was no paradoxical pulse observed. Heart sounds were slightly distant and muffled with no sound of pericardial friction. The jugular venous distension was not observed, and there was no edema of the legs. No rash was observed on the body surface. However, the chest pain persisted. The 12-lead electrocardiography (ECG) revealed concave upward ST segment elevation in the leads of I, II, aVL, aVF, and V1–6 without mirror-image changes and PR segment depression (Fig. 1A). Blood tests revealed a white blood cell count of  $11.5 \times 10^3/\mu\text{L}$  [normal range (NR),  $3.6\text{--}8.7 \times 10^3/\mu\text{L}$ ] and C-reactive protein (CRP) of 1.27 mg/dL (NR, 0.00–0.17 mg/dL) both of which were slightly elevated. Myocardial enzyme was normal with the creatine kinase/creatinine level of 158/80 IU/L (NR, 110–318/0–12 IU/L) and troponin I level of 0.02 ng/mL (NR, 0.00–0.04 ng/mL). Renal function was normal with a creatinine level of 0.78 mg/dL (NR, 0.65–1.07 mg/dL). The human immunodeficiency virus antibody (types 1, 2) and antigen (type p24) evaluated by chemiluminescent enzyme immunoassay test were negative (NR, negative). Transthoracic echocardiography (TTE) revealed left ventricular ejection fraction of 67%, indicating normal left

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ventricular function. Parasternal long-axis view of the left ventricle in the end-diastole phase revealed anterior/posterior echo free space of 12/10 mm, indicating moderate pericardial effusion around the entire heart (Fig. 2A). No sign of right ventricle collapse was observed. Thoracoabdominal computed tomography (CT) results did not reveal the presence of thrombus in the pulmonary vessels (Fig. 1C) or abnormality in the aorta (Fig. 1C, D). Pericardial effusion, a finding consistent with pericarditis, was observed (Fig. 1D). There were no neoplastic lesions found that could have been a metastasis to the pericardium. No significant stenosis was observed in coronary CT angiography (Fig. 1E, F). Based on these findings, the patient was diagnosed with pericarditis and hospitalized on the consultation day for close examination and treatment.

On the day of admission, in order to investigate the cause of pericarditis, we evaluated  $\beta$ -D-glucan: 5.9 pg/mL (NR,  $\leq 20$  pg/mL), antinuclear antibodies:  $<40$  (NR,  $<40$ ), T-SPOT<sup>®</sup> TB: negative (Oxford Immunotec, Oxford, United Kingdom), and thyroid function [thyroid stimulating hormone: 0.76  $\mu$ IU/mL (NR, 0.30–4.50  $\mu$ IU/mL)/Free T4: 0.84 ng/dL (NR, 0.70–1.80 ng/dL)/Free T3: 2.6 pg/mL (NR, 2.0–4.5 pg/mL)]. The first virological tests to evaluate infection with various viruses were done at this point

(Table 1). Aspirin (3 g/day) along with ceftriaxone (1 g/day) was started after blood culture in view of possible bacterial pericarditis. On day 3, the levels of CRP reached a peak at 23.33 mg/dL, and subsequently declined. On day 3, painful vesicular rashes appeared on the right side of the chest (Fig. 2D). On day 8, the chest pain almost resolved. On day 9, at the end of diastolic phase in the parasternal left ventricular long-axis view, pericardial effusion was 13 mm in the anterior side and 12 mm in the posterior side, respectively (Fig. 2B). Although the amount of pericardial effusion at that time was the maximum amount in the clinical course, this did not lead to cardiac tamponade. Tzanck test was also performed on day 9 to examine the possibility of herpes zoster virus infection, which proved negative. On day 11, ceftriaxone was discontinued because it turned out that the blood culture was negative, and procalcitonin was not elevated (0.04 ng/mL; NR  $<0.05$  ng/mL). On day 16, ECG showed improvement of ST elevation and PR depression (Fig. 1B). Inflammatory response and pericardial effusion gradually decreased thereafter, and the patient was discharged on day 17.

On day 24, the second virological test was performed for evaluation of paired serum. VZV (EIA test: IgG) titer increased considerably from 15.6 on day 1 to 540 on day 24, while no significant

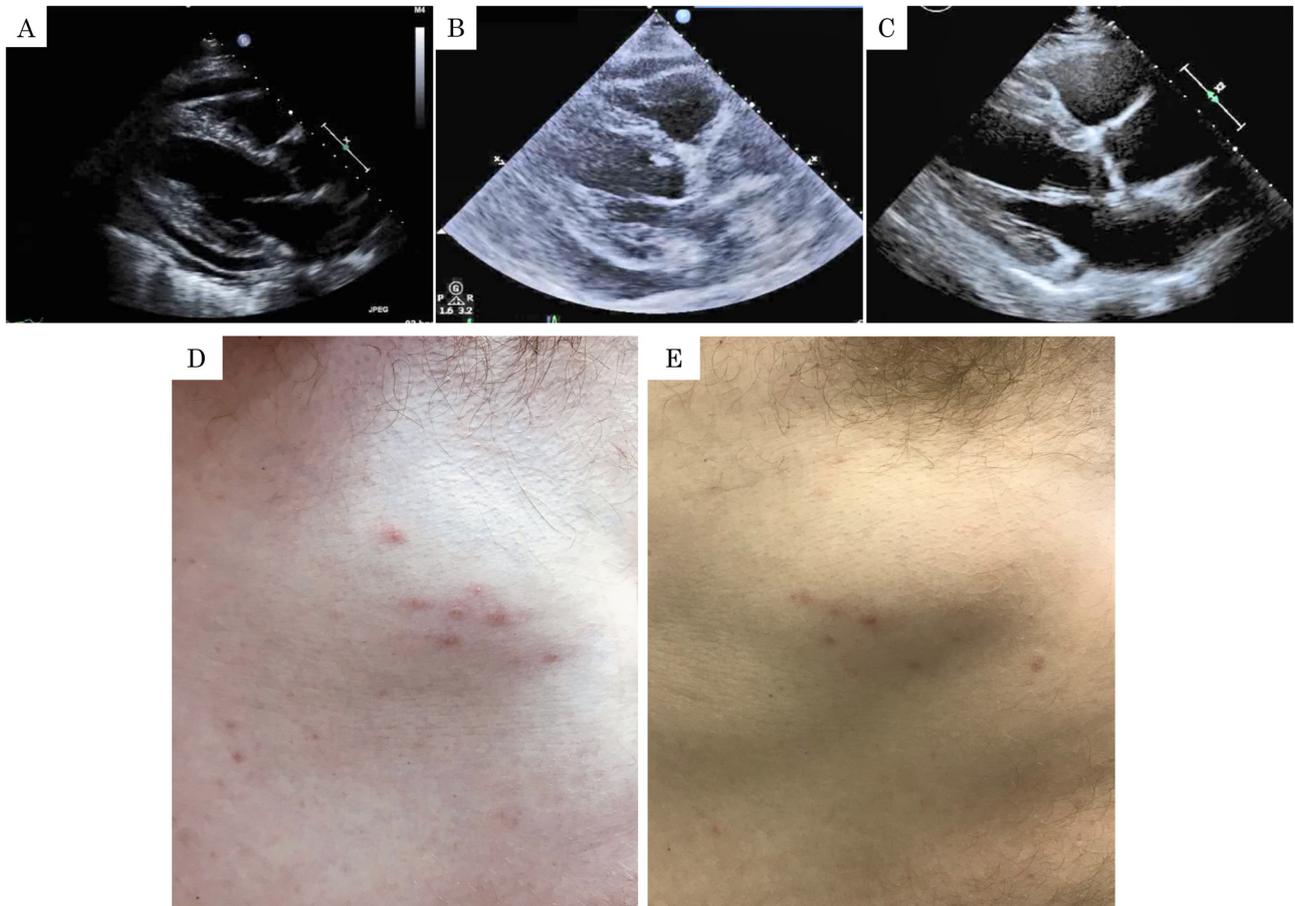


Fig. 2.

TTE on admission revealed LVEF of 67%, indicating normal left ventricular function. Parasternal long axis view of the left ventricle in the end-diastole phase revealed anterior/posterior echo free space of 12/10 mm, indicating moderate pericardial effusion around the entire heart (A). On day 9, at the end of diastolic phase in the parasternal left ventricular long-axis view, pericardial effusion was 13 mm on the anterior side and 12 mm on the posterior side, respectively. Although the amount of pericardial effusion at that time was maximum, this did not lead to cardiac tamponade (B). On day 38, TTE confirmed that the pericardial effusion had improved to within the physiological range (C). On day 3, painful vesicular rashes appeared on the right side of the chest (D). On day 55, the rash with blisters had almost disappeared and only pigmentation remained (E). TTE, transthoracic echocardiography; LVEF, left ventricular ejection fraction.

increase was observed in antibody titers of any other viruses (Table 1). Therefore, we diagnosed that the patient had pericarditis caused by herpes zoster. Anti-herpes viral therapy was not administered because the clinical symptoms of the patient had markedly improved by the time the diagnosis was made. On day 38, TTE confirmed that the pericardial effusion had decreased to within the physiological range (Fig. 2C). On day 55, the rash with blisters had almost disappeared and only pigmentation remained (Fig. 2E). Administration of aspirin was gradually reduced and discontinued on day 87. Follow-up observation was performed on an outpatient basis for 3 months and the patient remained stable without relapse.

## Discussion

As a cause of pericarditis, the possibility of viral infection, bacterial infection, tuberculosis, mycotic disease, autoimmune disease, metabolic disease, and neoplasm were considered. Therefore, we evaluated virus paired serum, blood culture, procalcitonin, T-SPOT<sup>®</sup> TB,  $\beta$ -D-glucan, antinuclear antibodies, thyroid function (thyroid stimulating hormone, free T4 and free T3), serum creatinine and thoracoabdominal CT. From these examination results, the possibility other than the viral infection was negative. As a result of virus paired serum evaluated three weeks after admission, VZV IgG considerably increased from

15.6 to 540, and thus, VZV infection was diagnosed as the cause. The levels of VZV IgM did not increase. It has been reported that the levels of IgM do not increase at the time of VZV reactivation, unlike those of IgG [6,7]. Therefore, based on the results of the paired serum analysis, it was inferred that this patient presented with pericarditis caused by VZV reactivation.

Pericarditis caused by VZV was diagnosed by paired serum evaluated 3 weeks after admission. Since the clinical findings were markedly improved at the time when the herpes zoster virus was found to be the cause, antiviral drugs were not used. Although all cases using acyclovir for myopericarditis by herpes zoster have recovered without sequelae [3,4], a limited number of studies have been reported and the effectiveness is not clear on these cases. Therefore, further examination is thought to be necessary to confirm the effectiveness of the agent.

Tzanck test conducted on day 9 upon suspicion of herpes zoster proved negative. Tzanck test is reported to have sensitivity of 76.9% and specificity of 100%, but the sensitivity decreases with lapse of time since onset [8]. In the present case, Tzanck test was performed as late as on day 9, 6 days after the appearance of rash, which probably caused the false negative results. Considering the result of the paired serum analysis, we believe that the rash with blisters was caused by herpes zoster despite the negative Tzanck test result.

**Table 1** The results of paired serum.

Virus	Method	Type		Titer on admission	Titer on day 24
Adenovirus	CF			4<	4<
Parainfluenza virus	HI	1, 2, 3		10, <10, 80	10, 10, 160
Influenza virus	CF	A, B		16, 16	16, 8
Parvovirus	EIA	B19	IgM	0.28	0.25
Echovirus	HI	3, 7, 11, 12		<8, <8, <8, <8	<8, <8, <8, <8
Coxsackie virus	CF	A-9, B-1, -2, -3, -4, -5, -6.		<4, <4, 4, <4, 4, <4, <4	<4, <4, 4, <4, 4, <4, 4
Mumps virus	EIA		IgM	0.09	0.09
			IgG	4.6	6.2
Paramyxovirus	EIA		IgM	0.08	0.04
			IgG	18.3	21.0
Rubella virus	EIA		IgM	0.18	0.19
			IgG	45.0	72.1
Varicella zoster virus	EIA		IgM	0.29	0.29
			IgG	15.6	540
Herpes simplex virus	EIA		IgM	0.11	0.15
			IgG	43.2	30.7
Cytomegalovirus	EIA		IgM	0.37	0.44
			IgG	35.2	30.7
Epstein-Barr virus	FA	EA-DR	IgG	10<	10<
		VCA	IgM	10<	10<
			IgG	160	320
		EBNA		40	20
Chlamydomphila pneumonia	ELISA		IgG	13	18
			IgM	0.0	0.0

CF, complement fixation test; EA-DR, early antigen, diffuse type and restricted type antibody; EBNA, Epstein–Barr virus–nuclear antibody; EIA, enzyme immunoassay; ELISA, enzyme-linked immuno-sorbent assay; FA, direct immunofluorescence assay; HI, hemagglutination inhibition test; VCA, capsid antigen antibody; VZV, varicella zoster virus.

The fibrous pericardium and the parietal layer of the serous pericardium are supplied by the right and left phrenic nerves which arise from the cervical segment (C3–C5) of the spinal cord. The visceral layer of the serous pericardium is innervated by the right and left branches of the sympathetic trunks and the vagus nerves, via the cardiac plexus which arises from thoracic segment (T1–T4) of the spinal cord and brainstem. In three reported cases of pericarditis associated with herpes zoster, sites of rash were the upper left part of the thorax [3], left thorax [4], and right shoulder [5] respectively, and all of them are consistent with the innervation level of pericardium. Rash with blisters in our patient appeared at T4 level, which is also consistent with the innervation level of pericardium. Therefore, when herpes zoster is observed at these levels, we believe that concurrent pericarditis should be considered.

In general, pericarditis is associated with the risk of recurrence and secondary constrictive pericarditis [9]. Recurrence of herpes zoster has been also reported in 6.2% of cases followed up for more than 8 years [10]. However, there are no reports of patients with recurrent pericarditis caused by VZV or those who developed constrictive pericarditis. Therefore, we believe that it is advisable to observe this case carefully for a long period.

The reason why myopericarditis caused by herpes zoster has been scarcely reported may be that in the event of occurrence of a rash with blisters on the chest accompanied by chest pain, herpes zoster virus infection alone is considered the cause of chest pain; however, the presence of concurrent myopericarditis is rarely suspected. This may lead to this condition being underdiagnosed.

Based on the present findings, it is suggested that pericarditis may develop concurrently with herpes zoster.

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## Conflict of interest

None declared.

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