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CASE REPORT
Other

Pericardial effusion and tamponade in the context of herpes zoster: a novel occurrence

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Background Pericarditis and pericardial effusion are relatively common hospital presentations, which rarely result in cardiac tamponade. The aetiology is often undetermined and presumed idiopathic or viral. This article reviews varicella zoster virus (VZV)–associated pericardial effusion and peri/myopericarditis and constitutes the first report of VZV-associated cardiac tamponade in the adult population.

Case summary We report the case of a 59-year-old woman who presented to hospital with pleuritic chest pain, haemodynamic instability, and a recent herpes zoster rash in the left T1 distribution. Computed tomography revealed a large pericardial effusion, and echocardiography showed features of cardiac tamponade. The patient was treated with pericardial drainage. Aspirate analysis revealed abundant polynuclear cells and histocytes with no organism. Polymerase chain reaction did not determine a cause.

Discussion There are 13 reported cases of VZV-associated peri/myopericarditis in adults in the literature published in the English language. Of these, only three patients had a pericardial effusion. Aetiological diagnosis of an effusion is challenging and rarely made on virological grounds but rather on clinical features. Varicella zoster virus–associated pericardial effusion should be considered in patients presenting with haemodynamic instability and a dermatomal rash affecting the C3–C5 and T1–T4 distributions.

Keywords Case report • Varicella zoster • Shingles • Tamponade • Pericardial effusion

ESC curriculum 2.2 Echocardiography • 6.6 Pericardial disease • 7.1 Haemodynamic instability

Learning points

- Varicella zoster virus (VZV) infection is associated with peri/myopericarditis and pericardial effusion in both its primary and secondary forms.
- This is the first documented case of herpes zoster–associated cardiac tamponade.
- In patients presenting with herpes zoster affecting the C3–C5 and T1–T4 distributions, the diagnosis of peri/myopericarditis should be considered.
- The most common management strategy for VZV-related myopericarditis is a combination of anti-virals and broad-spectrum antibiotics.

Introduction

Pericardial effusion can be caused by any condition affecting the myopericardium.[1] An increase in pericardial fluid most commonly occurs as a result of pericarditis, but a variety of systemic disorders, including malignancy, autoimmune, renal failure, and aortic dissection, have been identified as underlying causes.[1] The normal pericardium is a fibroelastic sac with a small amount of fluid separating the visceral and parietal

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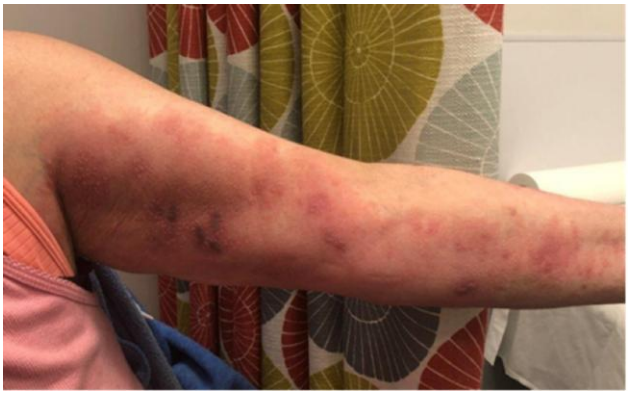


Figure 1 Photograph of the patient's left arm taken 2 weeks prior to her emergency admission showing a vesicular rash in the T1 and T2 dermatomal distributions.

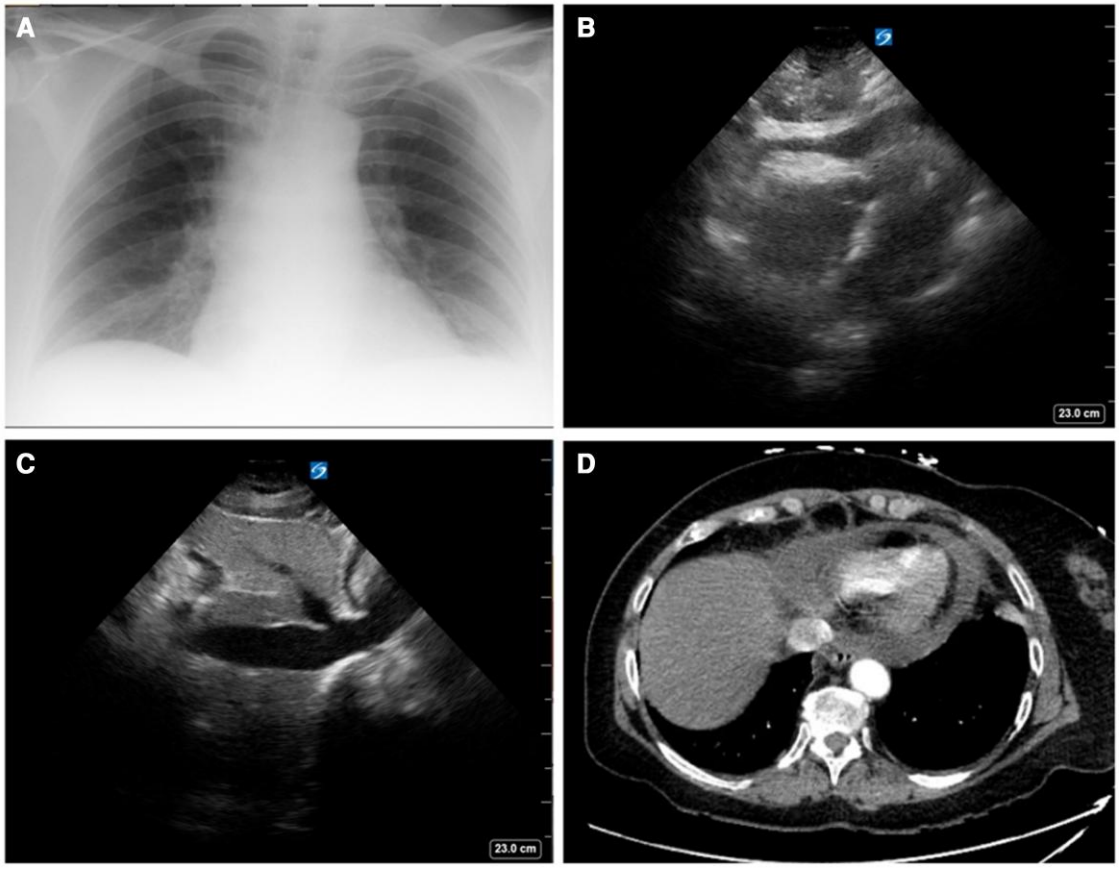


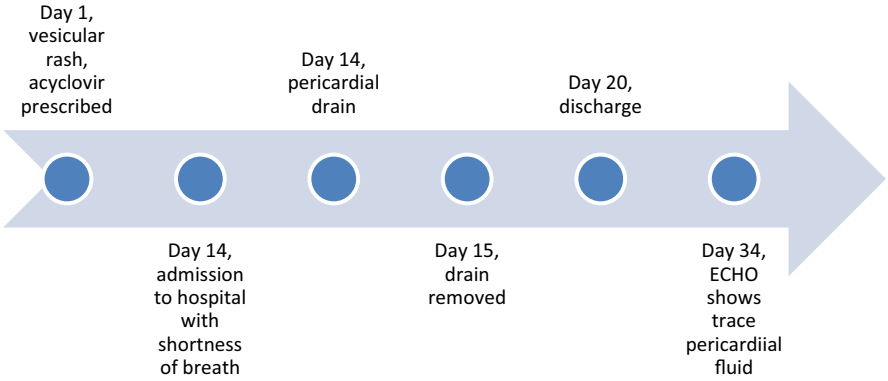
Figure 2 Photomontage of representative images from radiologic studies displaying the patient's anteroposterior chest X-ray at the time of admission (*A*), echocardiographic subxiphoid view of the heart demonstrating the pericardial effusion and right ventricular collapse (*B*) (supplementary file), echocardiographic sagittal view of the inferior vena cava (IVC) demonstrating a non-collapsed IVC in mid inspiration (*C*), and an axial slice of the patient's computed tomography showing a large pericardial effusion.

layers. An increase in fluid volume can lead to a rapid increase in intrapericardial pressure. When this exceeds intracardiac pressure, cardiac filling is impeded, and tamponade occurs. Pericardial effusions are most commonly deemed to be idiopathic, with infective and malignant aetiologies being the most common when a cause can be identified.[1] Pericardial aspiration is diagnostic in only 20–25% of cases.[2,3]

Varicella zoster virus (VZV) infection, in the form of chicken pox or herpes zoster (HZ), has been documented to be associated with acute myopericarditis.[4]

In this article, we present a unique case of cardiac tamponade in a patient who bore physical stigmata of a recent VZV infection and review the literature relevant to this rare clinical scenario.

Timeline



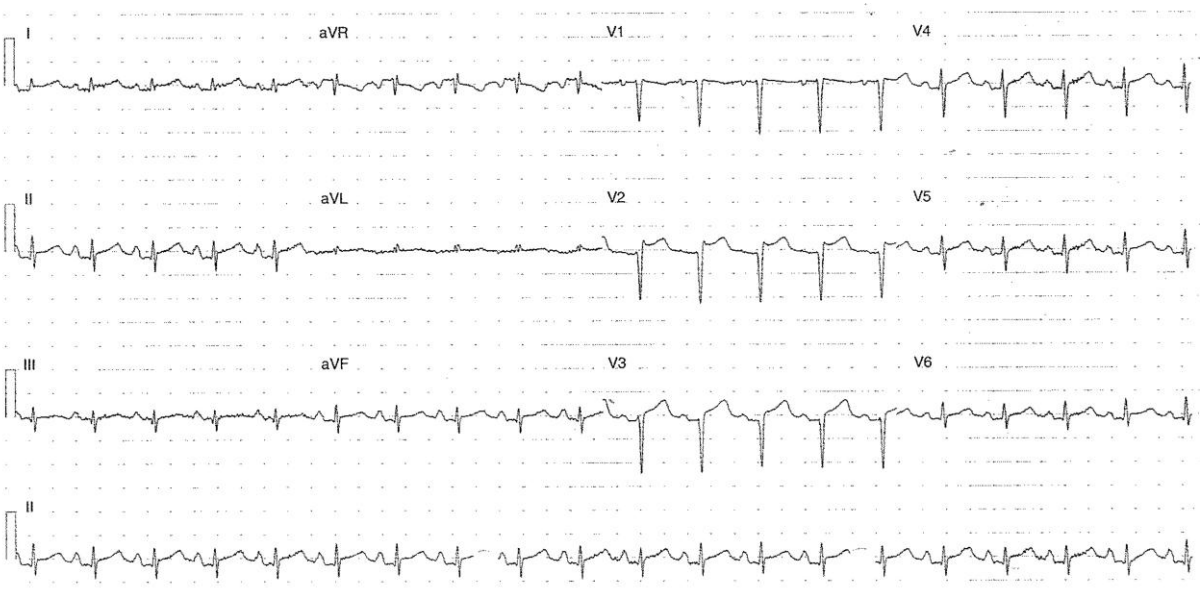


Figure 3 Electrocardiogram taken at the time of the patient's emergency admission displaying subtle widespread ST elevation and PR depression most notable in lead II.

Case presentation

A 59-year-old immunocompetent woman presented to our emergency department with a 4-day history of central pleuritic chest pain, productive cough, and subjective fevers.

Two weeks prior to her presentation, she had developed a painful vesicular rash following a T1 dermatomal distribution on the left (*Figure 1*) and completed a course of acyclovir. Her medical background was notable for bilateral scleromalacia, paroxysmal atrial fibrillation, lifelong smoking, childhood chickenpox, and intolerance to non-steroidal anti-inflammatory drugs (NSAIDs). A transthoracic echocardiogram 1 year prior showed regional wall motion abnormalities in the left anterior descending territory. No angiogram had been performed.

On examination, the patient was peripherally shut down with a blood pressure of 90/60 mmHg and a heart rate of 120 b.p.m.; her tympanic temperature was 36.3°C. Her heart sounds were muffled with no murmurs, and both respiratory and abdominal examinations were non-contributory.

A chest radiograph revealed a cardio-thoracic ratio of 0.60 with clear lung fields (*Figure 2A*). An electrocardiogram showed sinus tachycardia,

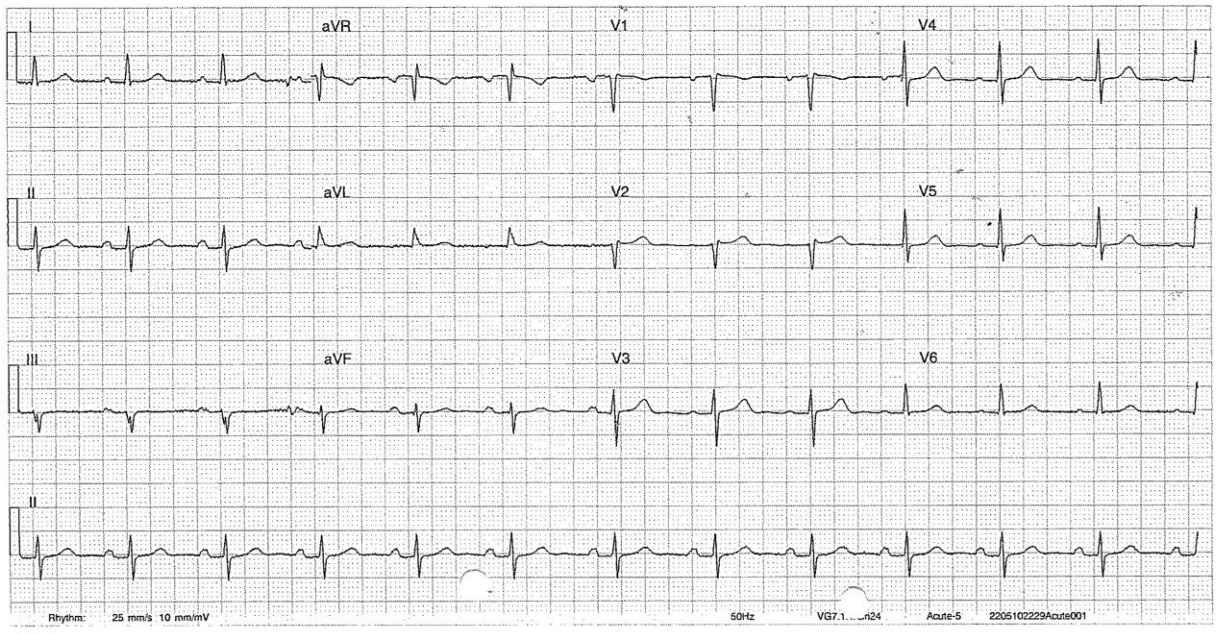


Figure 4 Follow-up electrocardiogram taken 3 months after our patient's discharge from hospital showing complete resolution of ST and PR segment changes.

Q waves (V1–3) and widespread ST-segment elevation, and PR interval depression most notable in Lead II (*Figure 3*). A full blood count revealed an elevated white cell (18.5 × E9/L reference value 4–11) and neutrophil count (15.2 × E9/L reference value 1.9–7.5) with a normal haemoglobin (131 g/L reference value 115–155). Her electrolytes and liver function tests were normal. She had an acutely elevated creatinine (95 µmol/L, estimated glomerular filtration rate 57 mL/min reference value 45–90) and a C-reactive protein titre of 100 mg/L (reference value <5). Serial cardiac troponin T was not elevated (9.8 ng/L reference value <13).

Fluid resuscitation and empiric broad-spectrum antibiotic therapy were initiated in the emergency department. An urgent computed tomography scan of the chest abdomen and pelvis revealed a large pericardial effusion, mild periportal oedema, and the absence of overt mass lesions, suspicious lymph nodes, or infection (*Figure 2D*).

A metaraminol infusion was initiated due to ongoing haemodynamic compromise despite initial volume resuscitation, and the patient was transferred to the intensive care unit where an urgent bedside echocardiogram was performed. The clinical diagnosis of cardiac tamponade was supported by right ventricular collapse during diastole (*Figure 2B*) and an inferior vena cava that did not collapse on inspiration (*Figure 2C*). A pericardial drain was placed, and 320 mL of straw-coloured turbid fluid was drained. The analysis of the aspirate revealed elevated white cells [27 800 × 10(6)/L] with polymorphonuclear cell predominance (88%). No organism was cultured. Cytology showed abundant neutrophils, modest number of histiocytes, and no malignant cells. A polymerase chain reaction (PCR) was performed and did not detect any viral nucleic acids.

Outcome and follow-up

Following the placement of the pericardial drain, the patient's haemodynamics was rapidly normalized. Due to historic drug intolerances and patient preference, a 5-day course of prednisone was initiated. A subsequent transthoracic echocardiogram the following day showed a small pericardial effusion, normal valves, and well-preserved right and left ventricular function. The pericardial drain was removed after 24 h, and the patient was transferred to the ward whence she was discharged 5 days later. The follow-up of transthoracic echocardiogram at 2 weeks showed trace amounts of pericardial fluid and the ST and PR segment changes on the electrocardiogram had resolved (*Figure 4*). At the time of writing (6 months later), this had not reoccurred.

Discussion

Varicella zoster virus is a highly contagious double-stranded DNA virus belonging to the alphaherpesvirinae subfamily.[5] Varicella zoster virus spreads from skin and mucosal lesions along the sensory nerves where it reaches the dorsal ganglion cells and enters a latent phase.[5] It commonly causes primary infection in childhood and re-activates in late adulthood causing the clinical syndrome known as HZ or shingles.

A review of all reported cases associating VZV infections (primary or secondary) with peri/myopericarditis in the English language is detailed in *Table 1*. Prior to this report, 13 cases of VZV-associated pericarditis or myopericarditis had been described in adults, in addition to five in the paediatric population. Amongst the adults, eight patients had primary VZV infection and five had secondary HZ. An effusion was present in three of the adult patients with HZ and two with primary VZV. None of the described pericardial effusions caused clinically significant tamponade. In the paediatric population, all patients had primary VZV infections, and all had an effusion with clinically significant tamponade.

To our knowledge, this present report constitutes the first description of pericardial tamponade temporally associated with HZ.

The innervation to the parietal pericardium stems from branches of the phrenic nerves (C3–C5). The visceral pericardium receives visceral sensory innervation from sympathetic (T1–T4) and vagus nerves. Previous authors propose that re-activation of neurotropic latent VZV affecting the dermatomes described here-above may affect the pericardium, cause pericarditis, and result in an effusion.[4]

Table 1 Literature review of all varicella zoster virus–associated pericardial effusions published in the English language

Study	Age, sex	VZV	Location of rash	Viral testing	Type of cardiac involvement	Onset of rash in relation to cardiac event	Effusion	Aspirate	Treatment
Franken *et al.* 2001[11]	68 F	HZ	Right shoulder	No	Pericarditis	1 day after	No	NA	None specified
Nasreddine *et al.* 2015[12]	87 M	HZ	Right C2	No	Pericarditis	5 days prior	Yes	Yes—VZV DNA microarray positive	Valacyclovir + colchicine
Elikowski *et al.* 2016 [13]	23 M	HZ	Left T1–T4	Serum VZV PCR negative	Myopericarditis	1 week prior	Yes	No	Acyclovir + ceftriaxone
Yamanaka *et al.*[4]	53 M	HZ	Right T4	Serum VZV IgG elevated	Pericarditis	3 days after	Yes	No	Ceftriaxone
Winfield *et al.* 1980 [14]	22 M	HZ	Mouth ulcers only	VZV complement fixing antibodies elevated	Pericarditis	1 day after	No	NA	None specified
Chaudhuri *et al.* 2015 [15]	27 M	CP	Trunk and face	Serum VZV Immunoglobulin M elevated	Myopericarditis	Concurrent	Yes	No	Acyclovir + broad-spectrum antibiotics
Biocic *et al.* 2009 [16]	27 M	CP	Generalized	Serum VZV ELISA positive	Myopericarditis	Concurrent	No	NA	None specified
Cohen *et al.* 2007 [17]	29 M	CP	Generalized	Blister fluid immunofluorescence positive	Pericarditis	Concurrent	No	NA	Acyclovir
Mandelbaum *et al.* 1956 [18]	33 M	CP	Generalized	No	Pericarditis	3 weeks prior	No	NA	None specified
Helmly *et al.* 1963 [19]	25 M	CP	Generalized	No	Pericarditis	4 days prior	No	NA	Penicillin
Ioannou *et al.* 2017 [20]	46 M	CP	Generalized	No	Myocarditis	Concurrent	No	NA	Acyclovir
De *et al.* 2011 [21]	17 M	CP	Generalized	Varicella titre elevated	Myocarditis	Concurrent	No	NA	Acyclovir + broad-spectrum antibiotics
Seddon *et al.* 1986 [22]	16 F	CP	Generalized	Positive immunofluorescence pustule fluid	Pericarditis	Concurrent	Yes	No	None specified
Azak and Cetin[6]	15 M	CP	Trunk	Elevated VZV IgG + IgM	Myocarditis	Weeks	No	NA	Immunoglobulin
Kirk *et al.* 1987 [23]	18 m F	CP	Generalized	Serology confirmed recent infection	Effusion	5 weeks	Tamponade	Yes—complement fixation VZV tires elevate	Prednisone
Shefler *et al.* 1998 [24]	4.5 m M	CP	Generalized	Serum complement fixation, serum IgG	Effusion	2 weeks	Tamponade	Yes—Streptococcus species cultured	Broad-spectrum antibiotics
Masood *et al.* 2008 [25]	8 mM	CP	Not specified	No	Effusion	4 days	Tamponade	Yes—Staphylococcus cultured	Broad-spectrum antibiotics
Bilici *et al.* 2014 [26]	5 F	CP	Scalp and trunk	Serum VZV IGM	Effusion	Concurrent	Tamponade	Yes—culture and cytology only—negative	Acyclovir + broad-spectrum antibiotics

CP, chicken pox; HZ, herpes zoster/shingles; NA, not applicable; ELISA, enzyme-linked immunosorbent assay.

The pathophysiology of primary VZV-induced myopericarditis is not well understood. It is postulated that VZV is directly cytotoxic and causes the release of inflammatory cytokines, which leads to T-cell-mediated lysis of cardiac myocytes.[7]

Clinically significant tamponade in the context of VZV infections was only described in paediatric patients prior to our report. Animal studies suggest that neonatal fibrous pericardium has higher tensile strength compared with adult tissue.[8] This, combined with smaller pericardial volumes, could explain why a pericardial effusion may result in higher cardiac functional impairment in children. Furthermore, as described in four reports included in the present review (*Table 1*), secondary bacterial infection of the pericardial fluid could further contribute to the occurrence of haemodynamic compromise in this group.

In most reported cases, the diagnosis of VZV infection is made clinically on the basis of a typical rash and in the absence of confirmatory biological tests. When performed, biologic testing most commonly consists of serological testing of VZV immunoglobulins. Interestingly, serological analysis, when performed, always concords with positive clinical features of VZV infection. Pericardial fluid analysis and pustule fluid analysis are only very seldomly performed.

Determining the aetiology of pericardial effusions is often challenging. A large prospective study analysing the usefulness of different diagnostic methods in identifying the underlying aetiology of pericarditis in 1162 patients shows that only 5% of pericardial aspirates return positive PCR results.[9] This study included one patient who had VZV-induced pericarditis based on positive serology, and this patient did not have an aspirate. Unfortunately, the study did not correlate the PCR results with the patients' clinically suspected underlying diagnosis.

In our case, the aspirate revealed no viral, malignant, or bacterial cause. It is possible that our PCR was negative as a course of acyclovir had already been completed and because the test was performed 2 weeks after the onset of the rash. The recent advent and relative democratization of molecular analyses and epicardial biopsy have enabled the identification of a group of autoreactive pericarditis patients bearing evidence of active autoimmune processes in the absence of viral and bacterial agents.[10] Such investigations unfortunately remain poorly accessible in our clinical practice. We believe that the temporal association of our patient's presentation with their VZV re-activation and the polymorphonuclear predominance in their pericardial aspirate does not support the diagnosis of autoreactive pericarditis. In retrospect, serial serological analysis of VZV immunoglobulin may have been useful. These were unfortunately not performed at the time of the patient's presentation.

The European Society of Cardiology recommends that aspirin or ibuprofen be used in combination with colchicine as the first-line treatment of acute pericarditis. Given our patient's historic intolerance to NSAIDs and her preference not to trial them under close monitoring, we opted to treat her with prednisone as the recommended second-line treatment.

Current guidelines on the management of pericarditis and myopericarditis do not provide specific advice for the management of varicella-associated disease. Reported management of the adult patients with VZV-associated peri/myopericarditis varies from author to author, but most patients received anti-viral and broad-spectrum antibiotic therapies. In the presence of an effusion without features of tamponade, drainage can be performed but may not necessarily aid diagnosis. The prescription of broad-spectrum antibiotics may be more important in the paediatric population where secondary bacterial infections have been reported.

Pericardial effusions in the context of HZ are rare. In the paediatric population, few reports of cardiac tamponade in the context of an acute primary VZV infection exist.

Here, we report the first case of cardiac tamponade associated with a secondary VZV infection. This case highlights the importance of considering the possibility of cardiac tamponade in patients presenting with pleuritic chest pain, haemodynamic compromise, and a dermatomal rash affecting the neck, upper limbs, or upper chest wall.

Lead author biography

Aleisha Easton is currently an advanced trainee in internal medicine at Taranaki Base Hospital. She has completed 5 years of postgraduation training as well as her Royal Australasian College of Physician exams. She is passionate about cardiology and plans to continue her training as a dual trainee in cardiology next year.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports*.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: Patient consent for this publication has been obtained in accordance with COPE guidelines.

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