



## Case Report

## A successful diagnostic case of Varicella zoster virus pneumonia by a Film Array assay for meningitis/encephalitis

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## ARTICLE INFO

## Keywords:

Varicella zoster virus  
Viral pneumonia  
Herpes zoster  
Shingles  
FilmArray  
ME panel

## ABSTRACT

**Introduction:** Although varicella zoster virus (VZV) infection is generally considered self-limiting and shows a favorable outcome, herpes zoster (HZ) can cause several complications such as neurological pain or meningitis, which lowers the patients' quality of life. HZ rarely manifests VZV pneumonia, resulting in a poor prognosis with a high mortality rate of 10–30 % if requiring a mechanical ventilation. Here, we present a rare successfully managed case of VZV pneumonia.

**Case presentation:** A 90-year-old man with a medical history of angina pectoris, prostate cancer, dementia, and brain infarction was diagnosed with pneumonia and was admitted to our institute. Four days before the admission, he had visited our outpatient clinic, where he had received anti-herpes therapy due to HZ on the right limb. Although TAZ/PIPC was started empirically, his respiratory status deteriorated. On day 3, we performed a Film Array Meningitis/Encephalitis (ME) PCR panel on a sputum specimen and VZV was identified. Thus, he was diagnosed as having VZV pneumonia and antiviral therapy with acyclovir was started. Since the patient's condition was improved, the antiviral therapy was ended on day 18. Despite that his VZV pneumonia was successfully cured, he passed away due to old age on day 63.

**Conclusion:** Due to poor medical conditions, some elderly patients cannot tolerate bronchoalveolar lavage fluid for diagnosing VZV pneumonia. Film Array ME panel on sputum specimen is a useful method to the diagnosis of VZV pneumonia.

## 1. Introduction

Generally, the reactivation of varicella-zoster virus (VZV) can cause herpes zoster (HZ), also known as shingles [1,2]. By 2050, the number of persons over 60 in the Asia-Pacific region is expected to reach 1.3 billion, representing approximately 25 % of the population [3]. The healthcare and economic burden of HZ and its complications are expected to increase in the aging population worldwide. Although VZV infection is generally considered self-limiting and shows a favorable outcome, HZ can cause several

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<https://doi.org/10.1016/j.rmcr.2025.102180>

Received 1 October 2024; Received in revised form 10 February 2025; Accepted 12 February 2025

Available online 14 February 2025

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complications, such as neurological pain and meningitis, which lowers the quality of life of patients. VZV pneumonia occurs in one in 400 cases of adult HZ and that the mortality rate can be as high as 10–30 % in untreated cases [4,5]. It is hard to diagnose viral pneumonia because there is not enough reliable testing to identify it. Some reported that polymerase chain reaction (PCR) using bronchoalveolar lavage fluid (BALF) is helpful in diagnosing viral pneumonia. However, some patients cannot tolerate the procedure due to their poor general condition. The Film Array ME panel covers 14 different pathogens including viruses, bacteria, and fungi, and has been implemented worldwide [6]. Here, we present a successful diagnosis and a successfully managed case of VZV pneumonia with a sputum sample using the Film Array Meningitis/Encephalitis (ME) panel.

## 2. Case presentation

A 90-year-old man had presented with high fever and dyspnea lasting for two days. He had a prior medical history of **angina pectoris**, prostate cancer, dementia, and brain infarction without any paralysis. Four days prior to the visit, he was diagnosed with shingles in the right lower limb and Amenamevir was administered. The skin had already crusted on admission, as shown in Fig. 1. He also had an acute respiratory failure (SpO<sub>2</sub> 89 % on 10 L/min O<sub>2</sub> mask) with inflammatory reactions (WBC 9200/μL, CRP 14.74 mg/dL). Chest radiography and computed tomography (CT) revealed diffuse ground-glass opacities (GGOs), suggesting viral pneumonia (Fig. 2). Rapid antigens for influenza and SARS-CoV-2 showed negative results. Following the admission with a clinical diagnosis of pneumonia, the empirical antibiotic therapy with Tazobactam/Piperacillin 4.5g three times daily was started but his respiratory failure worsened. On day 3, sputum culture showed no positive result. We performed a FilmArray assay of the ME PCR panel using sputum. The result displayed that the VZV was positive: the definite diagnosis was VZV pneumonia. Antiviral treatment with acyclovir (ACV) was started, and VZV pneumonia improved on day 17. Eventually, he did not require O<sub>2</sub> supplementation therapy. On day 63, he passed away due to old age.

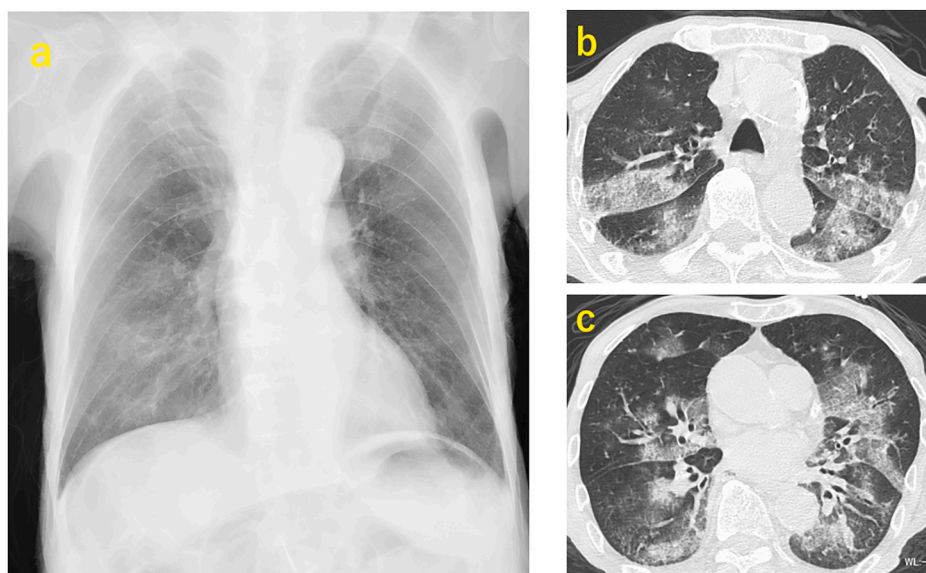
## 3. Discussion

The Film Array ME panel, which is the first multiplex PCR panel to detect different pathogens in the central nervous system (CNS), was approved by the US Food and Drug Administration in 2015 [7]. This diagnostic method can identify 14 different viral, bacterial, and fungal pathogens in CSF. It includes *Escherichia coli* K1, *Hemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, Cytomegalovirus (CMV), Enterovirus (EV), Herpes Simplex Virus 1 (HSV-1), HSV-2, Human Herpes Virus 6 (HHV-6), Human Parechovirus (HPeV), VZV, and *Cryptococcus neoformans* [8]. The test requires a small amount of CSF and a recent meta-analysis reported that the diagnostic accuracy of the Film Array ME panel showed a moderate sensitivity and high specificity at (as) 90 % and 97 %, respectively [9]. In Japan, since the Film Array ME panel was covered by the national health insurance in Sep 2022, it has been used widely (nationwide).

VZV is a neurotropic *alphaherpesvirus* exclusively infecting humans, in whom it causes two distinct pathologies: varicella (chickenpox) upon primary infection and herpes zoster (shingles) following reactivation [2,10]. VZV spreads via inhalation of infectious droplets and infects mononuclear cells in the tonsils, leading to viremia through infected T cells and dissemination to the skin to replicate and cause the characteristic vesicular eruptions known as varicella [2]. Importantly, VZV establishes latency in sensory neuronal ganglia, from which it can reactivate and spread to the skin as zoster or to the CNS, manifesting as meningitis, encephalitis, cerebellitis, or vasculopathy with stroke [1,2,11,12]. About 20 % of patients hospitalized with chickenpox experience neurological complications [2,12], suggesting a correlation between impaired systemic control of the infection and the development of severe



Fig. 1. Shows a picture of skin lesion crusted on the right lower limb.



**Fig. 2.** Shows bilateral shadows in both lungs by chest X-ray (a) and diffuse lung alveolar shadows in both lungs by chest computed tomography (b, c).

varicella with dissemination to the CNS. Although the VZV infection is fundamentally self-limiting and shows a favorable outcome, VZV pneumonia is quite rare and can cause a severe respiratory failure, requiring mechanical ventilation with a high mortality rate of about 10–30 %. The gold standard for diagnosis of VZV pneumonia is PCR using BALF specimen, however, some patients are not able to tolerate the invasive procedure such as bronchoscopy. In a multicenter cohort from France, Mirouse et al. analyzed 102 VZV pneumonia cases and 28 % of the patients received BALF [13]. More VZV pneumonia cases have might be underdiagnosed due to poor patients' conditions. As Film Array using sputum sample is not an invasive diagnostic method, the technical method would be tolerable for the elderly or those with comorbidity.

Regarding risk factors of VZV pneumonia, such as smoking history, chronic respiratory failure, immunosuppressant drugs, pregnancy and old age were reported [14]. These risk factors are similar to those of HZ. Currently, immunization against HZ is recommended for adults aged  $\geq 50$  years. Two vaccines, a live attenuated and an adjuvant recombinant subunit are available in Japan. To prevent VZV pneumonia, patients with risk factors of HZ should receive a vaccination against HZ.

VZV pneumonia shows specific radiological findings on chest CT. Previous reports documented that multiple 5–10 mm small nodules with surrounding GGOs [15], and diffuse shadows are consistent with VZV pneumonia. Mirouse et al. reported 50 % of the VZV patients had small nodules on chest CT [13]. These specific signs in radiological findings were seen in our case, which were helpful to differentiate from COVID-19 pneumonia. Chest CT should be performed in HZ Patients with respiratory symptoms.

In conclusion, physicians should be aware of the utility of Film Array ME PCR panel use for the early diagnosis of VZV pneumonia. Thus, it may contribute to the improvement of the prognosis of the patients with VZV pneumonia.

#### CRediT authorship contribution statement

**Nobuhiro Asai:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Atsuko Yamada:** Writing – review & editing, Methodology, Formal analysis. **Akiko Nakamura:** Writing – review & editing, Formal analysis, Data curation. **Tomoko Ohno:** Writing – review & editing, Formal analysis, Data curation. **Narimi Miyazaki:** Writing – review & editing, Formal analysis, Data curation. **Yuzuka Kawamoto:** Writing – review & editing, Formal analysis, Data curation. **Mina Takayama:** Writing – review & editing, Formal analysis, Data curation. **Daisuke Sakanashi:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Toshihiro Ohta:** Writing – review & editing, Formal analysis, Data curation. **Yuichi Shibata:** Writing – review & editing, Data curation. **Hideo Kato:** Writing – review & editing, Formal analysis, Data curation. **Mao Hagihara:** Writing – review & editing, Formal analysis, Data curation. **Nobuaki Mori:** Writing – review & editing, Formal analysis, Data curation. **Hiroshige Mikamo:** Writing – review & editing, Visualization.

#### Compliance with ethical standards

Informed consent was obtained from the patients for the publication of this case report and any accompanying images.

## Funding

This article did not receive any specific grants from public, commercial, or non-for-profit funding agencies.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

We are grateful for the diligent and thorough critical reading of our manuscript by Yoshihiro Ohkuni, Chief Physician, Taiyo and John Wocher, Advisor, Kameda Medical Center (Japan). Additionally, we thank all medical staff for helping us care for these patients.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmcr.2025.102180>.

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