


# Viral-Induced Erythema Multiforme Complicated by Secondary Bacterial Infection with Hyperpyrexia Following Cervical Spine Surgery: A Rare Case of Dual Infection

Junhong He<sup>1,2</sup>, Yang Wang<sup>2,3</sup>, Qiong Yang<sup>1,2</sup> 

<sup>1</sup>Department of Pharmacy, Ningbo No.6 Hospital, Ningbo, Zhejiang, People's Republic of China; <sup>2</sup>Ningbo Clinical Research Center for Orthopedics, Sports Medicine & Rehabilitation, Ningbo, Zhejiang, People's Republic of China; <sup>3</sup>Department of Spinal Surgery, Ningbo No.6 Hospital, Ningbo, Zhejiang, People's Republic of China

Correspondence: Qiong Yang, Email yangqiong02164516@163.com

**Abstract:** Erythema multiforme, an inflammatory skin and mucosal condition, is mainly caused by a viral infection and presents as plaques of various morphologies. We present the case of a 59-year-old man who developed a pruritic rash all over his body seven days after posterior cervical single-open-door spinal decompression surgery. He had no history of a viral rash. He received antibiotics and anti-allergic treatment without relief of symptoms. Suspecting a viral infection, antivirals were started. While the rash subsided, the inflammatory markers continued to increase, accompanied by hyperpyrexia, leading to the suspicion of secondary bacterial infection. Meropenem was started, and the patient's vital signs returned to normal. This is a rare case of erythema multiforme and secondary bacterial infection following cervical spine surgery. Based on our findings, antimicrobial therapy is recommended for patients with viral infection after cervical spine surgery in the following situations: bacterial infection was not confirmed by the blood cultures obtained, and was suspected by the patients' course and elevated infection indices.

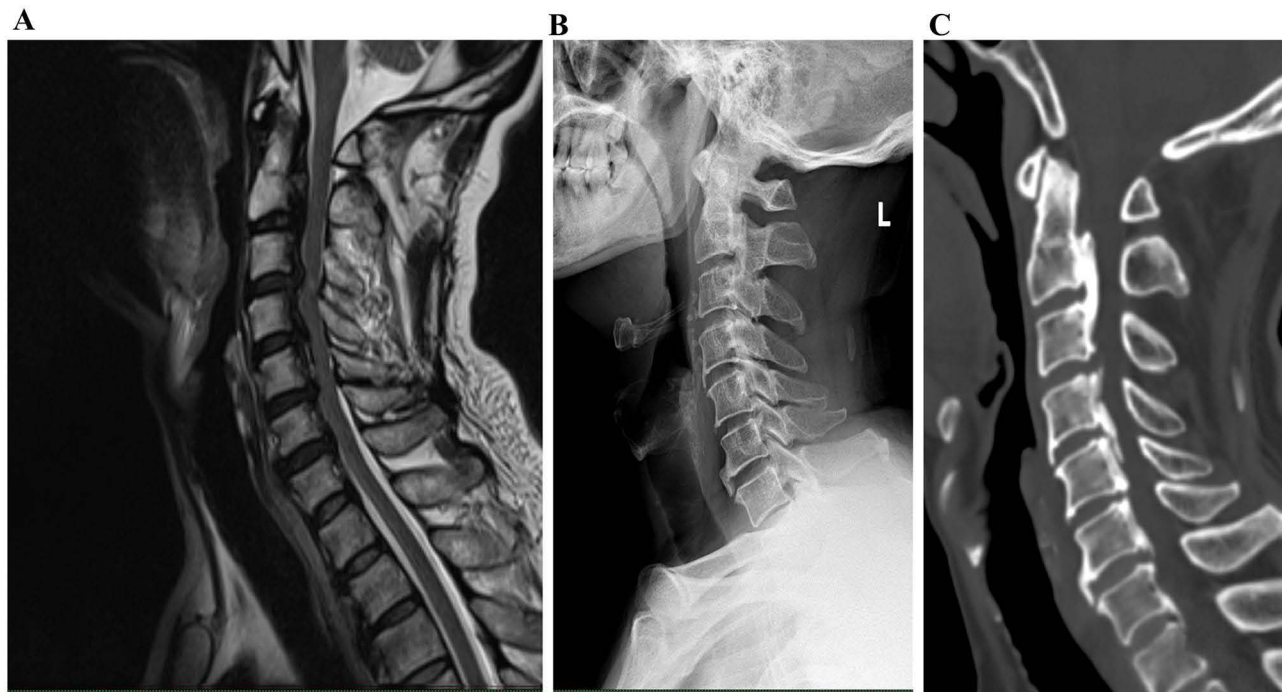
**Keywords:** cervical spine surgery, erythema multiforme, secondary bacterial infection, hyperpyrexia

## Introduction

Erythema multiforme (EM) is a rare skin disease characterized by a variety of lesions, including targetoid plaques. With an annual incidence of less than 1%, it is common in adults under 40 years. The lesions mainly appear on the limbs and are less common on the trunk.<sup>1</sup> EM is considered to have a unique etiology, pathophysiology, and clinical course. It is mainly associated with infections, with herpes simplex virus (HSV) being the most common causative agent.<sup>2,3</sup> Some drugs and vaccines have also been reported to induce EM.<sup>4,5</sup> There are currently no reports of EM occurring after spinal surgery. Postoperative spinal infection is primarily caused by bacteria, with *Staphylococcus aureus* being the most common pathogen.<sup>6</sup> However, due to reduced immune function after surgery, the patients are at a rare risk of viral infection or viral reactivation, and persistent viral infection can easily induce bacterial infection.<sup>7,8</sup> We describe a rare case of EM following cervical spine surgery caused by a viral infection and a secondary bacterial superinfection marked with hyperpyrexia. We believe our findings will provide valuable insight into diagnostic and therapeutic strategies in similar cases.

## Case Presentation

A 59-year-old man who presented with numbness in both upper limbs for more than a month was admitted to our hospital on November 12, 2024. The patient had previously taken vitamin B1, B6, and methylcobalamin for one month without relief of symptoms. Magnetic resonance imaging (MRI) showed multiple ossifications of the posterior longitudinal ligament of the cervical spine, spinal cord compression, and cervical spinal cord deformation (Figure 1). The patient had a history of penicillin



**Figure 1** Images of the cervical spine. (A) Magnetic resonance, (B) X-ray, and (C) Computed tomography images.

allergy but denied any history of viral rash and familial, genetic, neurological, or mental diseases. After admission, the patient had a body temperature of 36.8 °C, white blood cell count (WBC) of  $5 \times 10^9/L$ , and erythrocyte sedimentation rate (ESR) of 25 mm/h. Based on these findings, he was diagnosed with spondylotic myelopathy and ossification of the posterior longitudinal ligament of the cervical spine.

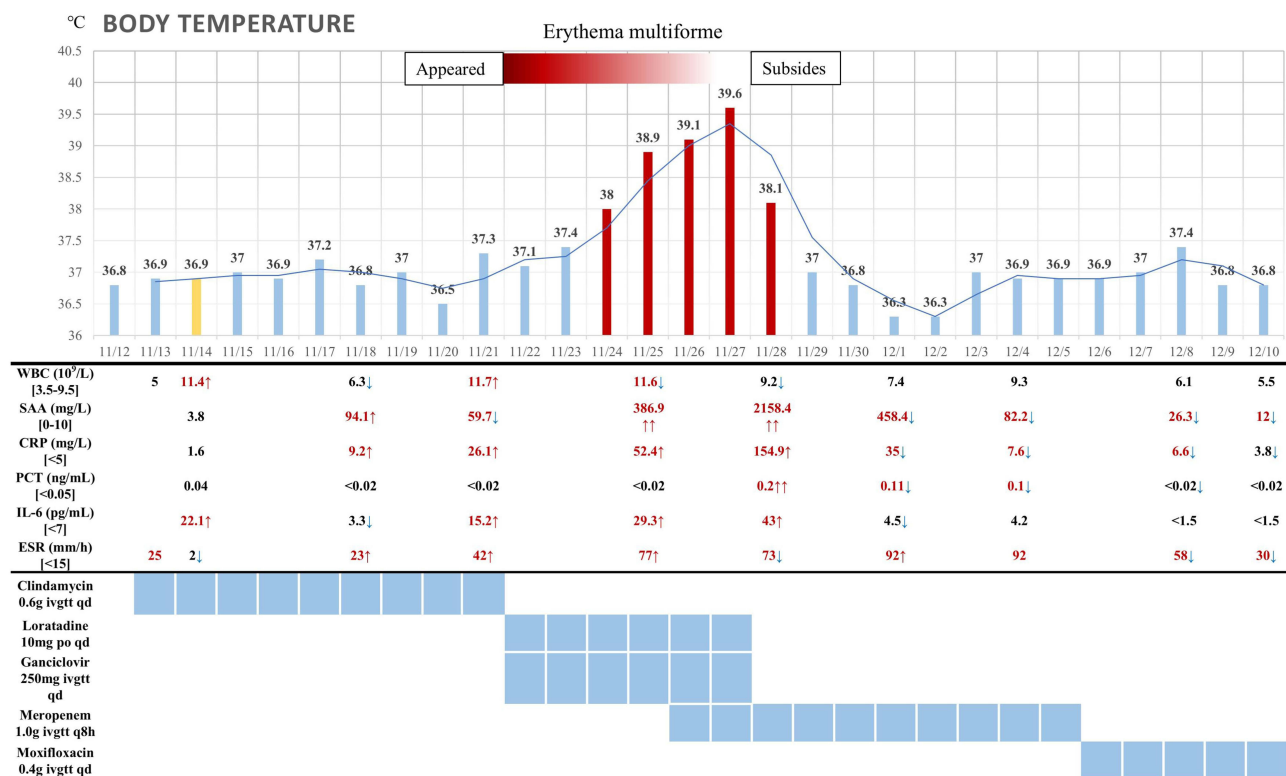
After ruling out surgical contraindications, the patient underwent single posterior cervical open-door spinal decompression on November 14. During the operation, the left lamina of the cervical vertebrae C2 to C7 were opened to expand the cross-sectional area of the spinal canal, relieve spinal cord compression, and fixed with a micro steel plate. Following the operation, the patient was conscious and had a normal body temperature. However, he had a WBC count of  $11.4 \times 10^9/L$  and an interleukin 6 (IL-6) level of 22.1 pg/mL. Considering the risk of infection owing to internal fixation, the patient was administered clindamycin (0.6, IVGTT, BID) on November 14. Subsequently, although the surgical incision morphology remained normal, multiple infection indicators gradually increased. On November 21, the following parameters were noted in the patient: WBC count,  $11.7 \times 10^9/L$ ; serum amyloid A (SAA), 59.7 mg/L; C-reactive protein (CRP), 26.1 mg/L; ESR, 42 mm/h. On the morning of November 22, the patient suddenly developed large, itchy red rashes and target-like plaques throughout the body (Figure 2). All medications were discontinued, and he was administered loratadine (10 mg PO, once) and dexamethasone sodium phosphate (5mg, IVGTT, once) for anti-allergic treatment; however, there was no improvement. After consulting dermatologists, viral infection-induced EM was suspected. The viral antigen test of nasal secretions was negative for all types of viral infections. After treatment with ganciclovir (250 mg IVGTT QD) and loratadine (10 mg PO QD), the rash gradually subsided. By November 27, the rash had completely subsided, and ganciclovir and loratadine were discontinued.

However, as the rash began to subside, the patient's body temperature began to rise again on November 24, 2024. On November 25, he had a body temperature of 38.9 °C, WBC count of  $11.6 \times 10^9/L$ , SAA 386.9 mg/L, CRP 52.4 mg/L, IL-6 29.3 pg/mL, and ESR 77 mm/h. On November 26, the body temperature further rose to 39.1 °C. Two sets of blood culture samples were collected from each arm that day, with each set comprising both aerobic and anaerobic bacterial cultures. However, no aerobic or anaerobic bacteria were detected in the blood cultures. After consultation with infection experts and clinical pharmacists, secondary bacterial infection was considered, and meropenem (1.0 g IVGTT Q8H) was administered as an anti-infection treatment. On November 28, although the patient's infection indicators continued to



**Figure 2** Erythema multiforme lesions. The red mark indicates the typical target lesion of EM.

increase, the body temperature dropped. Eventually, the body temperature returned to normal, and the infection indicators also gradually decreased. On December 6, after evaluation by clinical pharmacists, meropenem was discontinued, and moxifloxacin hydrochloride was initiated (0.4 g IVGTT QD) (Figure 3 and Table S1). On December 10, the patient was discharged in stable condition. One month later, the physician confirmed that the patient’s upper limb numbness had



**Figure 3** Changes in the patient’s body temperature and infection indicators over time. The yellow bars indicate surgery, and the red bars indicate abnormal body temperature. The red values are outside the normal range, and the blue squares indicate that medication was used. The red arrow indicates that the indicator has increased compared to the previous measurement, while the blue arrow indicates a decrease. Double red arrows indicate that the indicator has increased fivefold compared to the previous value.

subsided, the skin lesions had completely healed, and there were no signs of recurrent infection. The patient experienced no recurrence of fever or rash for six months after discharge.

## Discussion

Spinal surgical site infections (SSIs), especially those occurring after internal fixation, are postoperative complications that require special attention and are often associated with gram-positive bacteria.<sup>9</sup> Therefore, after surgery, when the patient showed an abnormal increase in WBC count and IL-6 levels, an infection at the surgical site was suspected, and he was given clindamycin as an empirical antibiotic. However, several factors argued against a typical SSI: the patient was the first case in the operating room that day, making the possibility of environmental infection low; the surgical incision appeared normal; and, crucially, clindamycin failed to alleviate symptoms or reduce rising infection indicators. The rarity of postoperative viral infection initially delayed consideration of this etiology until the characteristic EM rash emerged. Pathogenic factors that cause EM include infections, drug allergies, and vaccines.<sup>10–12</sup> Allergy was systematically excluded: the patient had not received any recent vaccinations, and the rash persisted despite the immediate discontinuation of all medications and the administration of loratadine and dexamethasone. Concurrently, there was no elevation in procalcitonin, a sensitive marker for bacterial infection,<sup>13</sup> further ruling out the possibility of a bacterial cause and shifting the focus toward a viral etiology. Nasal secretions and nasopharyngeal swabs were negative for all tested viral infections. HSV is the most common cause of EM.<sup>1</sup> Surgery is known to be a precipitating factor for HSV reactivation, and patients with no known history of HSV infection can contract it and develop encephalitis after surgery. This might be caused by the early lack of immunity in postoperative patients. In most (71.4%) previously reported cases of postoperative herpes virus infection, obvious symptoms appeared 2–7 days after surgery. The occurrence, symptoms and postoperative time course of vesicular rash are related to inflammatory response, which is consistent with our patient characteristics. Based on the above evidence, we speculated that the patient had postoperative HSV infection-induced EM. We opted for ganciclovir antiviral treatment instead of escalating the antibiotics, and its effectiveness confirmed our speculation.

Interestingly, following the resolution of EM and effective antiviral treatment, the patient developed a new episode of hyperpyrexia (peaking at 39.6°C), accompanied by joint pain and myalgia, symptoms atypical for EM.<sup>14</sup> Concurrently, previously stable infection indicators, including procalcitonin, rose significantly. This clinical shift suggested a secondary bacterial superinfection. Persistent viral infections can induce bacterial superinfections.<sup>15–17</sup> For example, immune-mediated damage caused by the influenza virus leads to the destruction of airway epithelium and its barrier function, induces cytokine production, and disrupts macrophage and regulatory T-cell function, which is believed to promote the colonization of multiple bacteria. In this case, the patient's postoperative immunocompromised state, combined with extensive EM-related skin barrier disruption on the back, likely created an environment conducive to secondary bacterial invasion. Because the infecting bacteria could not be identified and the patient continued to have a high fever after surgery, the broad-spectrum antibiotic meropenem was administered.<sup>18</sup> Subsequently, the fever and systemic symptoms resolved, supporting the diagnosis of bacterial superinfection.

This is the first reported case of a rare dual infection of virus-induced EM complicated by secondary bacterial infection and hyperpyrexia after cervical spine surgery. A limitation of this study is that the HSV diagnosis was not confirmed because our laboratory does not have the required serological or polymerase chain reaction tests. In addition, because of the low positivity rate of routine blood culture, the nature of the secondary bacterial infection could not be clarified. However, the changes in the patient's skin manifestations, body temperature, and infection indicators over time, as well as the response to antiviral and antimicrobial treatment, support our speculation.

## Conclusion

Based on our findings, antimicrobial therapy is recommended for patients with viral infection after cervical spine surgery in the following situations: bacterial infection was not confirmed by the blood cultures obtained, and was suspected by the patients' course and elevated infection indices. Preventive antiviral treatment before surgery may be beneficial for patients with a history of HSV infection, while for those without such a history, it is necessary to remain vigilant for the activation of latent viruses.

## Abbreviations

COVID-19, coronavirus disease 2019; CRP, C-reactive protein; EM, erythema multiforme; ESR, erythrocyte sedimentation rate; HSV, herpes simplex virus; IL-6, interleukin 6; MRI, magnetic resonance imaging; SAA, serum amyloid A; WBC, white blood cell count; SSIs, spinal surgical site infections; PO, take orally; QD, once a day; BID, twice a day; Q8H, once every 8 hours; IVGTT, intravenous drip.

## Ethical Approval and Informed Consent

The study was approved by the Ethics Committee of the Ningbo No.6 Hospital. The patient provided consent for the participate of the study.

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## Consent for Publication

The patient gave written informed consent for his personal or clinical details along with any identifying images to be published in this study. The publication of the case details requires approval from the Ethics Committee of Ningbo No.6 Hospital. The approval number was [2025(L)004].

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## Disclosure

The authors report no conflicts of interest in this work.

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