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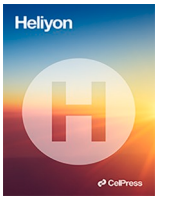

Case report

Case report: Multiple organ failure caused by Japanese spotted fever

Pei Zhou [1], Yinhui Zhu [1], Qian Cai, Zhe Li, Yuyang Yu, Yingqun Zhu [*], Lan Guan

Department of Respiratory Medicine, The Third Hospital of Changsha, Hunan, 410015, China

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ABSTRACT

A 71-year-old male had disseminated multiple organ dysfunction syndrome (MODS). Following treatment with cefotaxime and piperacillin-tazobactam, his symptoms have worsened instead. Multiple organ failure caused by Japanese Spotted Fever (JSF) was diagnosed based on metagenomic next-generation sequencing (mNGS), we rapidly treated the patient with doxycycline. Thereafter, his symptoms gradually improved. In this report, we emphasized the importance of rapid microbial diagnostic tools and the early use of tetracyclines for the treatment of JSF.

1. Introduction

Japanese spotted fever (JSF) is a tick-borne infectious disease caused by the Rickettsia japonica, the classic triad of JSF symptoms are high fever, erythema, and eschar formation. JSF is predominantly endemic in Asia, most of which occur in Korea, the Philippines and Thailand. The typical signs and symptoms of JSF and scrub typhus are similar, thus leading to a high rate of misdiagnosis. Although the overall prognosis for the disease is favorable, there have been reports showing the risk of serious complications and even death. In this case, we reported a patient with JSF combined with multiple organ dysfunction syndrome (MODS) caused by Rickettsia japonica. This case report provides certain clinical evidence for the treatment of MODS caused by JSF and reminds medical workers of the importance of early diagnosis and treatment of JSF in its prognosis. Metagenomic next-generation sequencing (mNGS), as an emerging pathogen test, can be an important addition to the diagnosis of the disease.

2. Case presentation

A 71-year-old male farmer was admitted to our hospital after experiencing fever and rash for 7 days, and oliguria for 2 days. The patient had a normal past medical history and family history. He presented with a fever 7 days after fieldwork with a maximum temperature of 40 °C, with generalized soreness and red macular rashes on both lower extremities. However, he still had a fever after cefotaxime treatment at a local clinic. Moreover, 2 days before treatment in our hospital, the patient developed decreased urine output. Physical examination revealed a drowsy status, a body temperature of 39 °C, a pulse rate of 106 beats/minute, a respiratory rate of 30 breaths/minute, a blood pressure of 149/89 mmHg, and a blood oxygen saturation of 88 % (without oxygen). He also had axillary lymphadenopathies and erythematous rashes were scattered all over the body. An eschar measuring 3 mm in diameter was noticed on the medial aspect of the left ankle. Clinical biochemistry results suggested abnormal heart, liver and kidney function (creatine kinase:

* Corresponding author.
E-mail address: 1104633835@qq.com (Y. Zhu).
[1] These authors contributed equally to this work and should be considered co-first authors.

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358 U/L, lactate dehydrogenase: 398 U/L; alanine aminotransferase: 169.9 U/L; aspartate aminotransferase: 217.5 U/L; and blood creatinine: 129 μmol/L), elevated infection index (C-reactive protein: 204.3mg/L; procalcitonin: 2.83ng/ml; and erythrocyte sedimentation rate: 21mm/h), hematological abnormality (white blood cell count: 8.30 × 109/L; eosinophil granulocyte count:0 × 109/L, and platelet count: 76 × 109/L), and increased urinary protein (2g/L). Arterial blood gas analysis indicated type I respiratory failure, with PH 7.38, PaO2 59.34 mmHg, and PaCO2 41.11 mmHg on ambient air. High-resolution computed tomography of chest suggested bilateral oligoinflammation. There were no significantly abnormal conditions in the Wiel-Felix reaction. Based on the above symptoms and laboratory tests, the patient was diagnosed with multiple organ failure, but no cause has been found. The patient was treated with piperacillin-tazobactam (4.5g/8 hours), albumin infusion, hepatoprotective, platelet-boosting and non-invasive ventilator-assisted ventilation therapy. After 3 days of treatment, the patient's symptoms were not relieved, as well as a persistent hematological abnormality, and he even developed atrial fibrillation. On day 4, the presence of Rickettsia japonica was detected by mNGS from the peripheral blood. Therefore, the patient was thought to have a diagnosis of MODS after JSF, and he was treated with a combination of anti-infective therapy (doxycycline and piperacillin-tazobactam). On day 5 the patient's temperature returned to normal and the atrial fibrillation changed to a sinus rhythm. After treatment with doxycycline (0.2g once daily) and piperacillin-tazobactam (4.5g/8 hours) for two weeks, the patient's symptoms resolved completely.

3. Discussion

JSF was first reported in 1984 in Tokushima Prefecture, Japan, and in 1992 the pathogen was identified as being caused by Rickettsia japonica [1,2]. Although JSF is usually characterized by a triad of high fever, rash and eschar formation, other symptoms of JSF are often vague and nonspecific, including headache, nausea, vomiting, abdominal pain and chills, which easily leads to clinical misdiagnosis and delayed treatment. Currently, there are no clear diagnostic criteria for JSF, serological diagnosis is still the main method of diagnosing rickettsial infections. Due to the early use of antimicrobial drugs and immunocompromise, it is not suitable for early diagnosis of the disease and may be false-negative [3]. Immunohistochemical detection of rickettsiae in skin biopsy specimens (from eschar or rash lesions) has been shown to be a technique capable of confirming infection in the acute phase [4], but not all patients develop a rash or eschar [5]. As for polymerase chain reaction (PCR) and mNGS, although it is easier to diagnose by PCR, it requires clinicians to have a directional diagnosis of the disease. It is more difficult to diagnose by this method due to the fact that JSF has been disseminated everywhere in China. On the other hand, mNGS can rapidly detect a large number of pathogenic microorganisms (including viruses, bacteria, fungi and parasites) in the samples. Clinicians should not rely too much on laboratory diagnosis and need to understand the disease manifestations of Rickettsia japonica infection, pay attention to the epidemiological history, carefully examine the body, use mNGS to assist in the diagnosis when appropriate, and comprehensively analyze the clinical data in an effort to achieve early diagnosis.

Rickettsia japonica infection may cause an unregulated state of hyperinflammation, which may lead to cytokine release syndrome and subsequent multiple organ failure [6], Therefore, early treatment with doxycycline can be used in highly suspected patients to reduce the morbidity and mortality of JSF. At the same time, our case shows that tetracyclines in combination with broad-spectrum, semi-synthetic penicillins are clinically useful in the treatment of severe cases of JSF, which provides certain clinical evidence for the treatment of MODS caused by JSF.

3.1. Limitation

β-lactam antibiotics and aminoglycosides, are commonly used in the empirical treatment of febrile disease, in our case β-lactam antibiotics and tetracycline were used to treat MODS after JSF, whether tetracycline alone will be effective as well as reduce the adverse effects of the drug needs to be further investigated.

4. Conclusion

Early diagnosis and treatment of JSF are crucial for the patient's prognosis. It is easy to misdiagnose or delay the diagnosis of JSF in the early stages because of the lack of specific clinical manifestations, so the early use of mNGS is essential. When patients with JSF develop MODS, they should be given appropriate interventions as soon as possible to reverse multiple organ failure. This case report provides certain clinical evidence for the treatment of MODS caused by JSF and reminds clinicians of the importance of mNGS and treatment of doxycycline in its prognosis.

Ethical statement

We hereby confirm that we have read and complied with the policy on ethical conduct.

The patient (or his proxies/legal guardians) provided written informed consent for the publication of all clinical data and other data included in the main manuscript.

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Data availability statement

The datasets for this article are not publicly available due to concerns regarding participant/patient anonymity. Requests to access the datasets should be directed to the corresponding authors.

CRediT authorship contribution statement

Pei Zhou: Writing – review & editing, Writing – original draft, Conceptualization. **Yinhui Zhu:** Writing – review & editing, Writing – original draft, Conceptualization. **Qian Cai:** Writing – review & editing. **Zhe Li:** Writing – review & editing. **Yuyang Yu:** Writing – review & editing. **Yingqun Zhu:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Lan Guan:** Writing – review & editing.

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.

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