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Correspondence

Metagenomic next-generation sequencing to diagnose atypical severe scrub typhus

KEYWORDS
Scrub typhus;
Metagenomic next-generation sequencing;
Orientia tsutsugamushi;
Multiorgan dysfunction

Dear Editor,

We report a 24-year-old Chinese men with scrub typhus, presented with fever and multiple organ dysfunction. Hallmark features of scrub typhus are absent and the patient went through lengthy diagnostic procedures. Finally, the diagnosis was confirmed by metagenomic next-generation sequencing (mNGS) of alveolar lavage fluid and peripheral venous blood.

The patient was an employee of a company who lived in Fujian Province, He was normally in good health and was admitted to our hospital due to fever for 8 days, with dry cough, muscle aches and fatigue. He was given anti-infective treatment in the primary hospital for 7 days (the specific regimen was not available), but his symptoms did not improve. Physical examination at the hospital revealed that the body temperature was 39.6 °C; the blood pressure was 90/51 mmHg; no eschar was observed on the skin of the whole body. The laboratory tests indicated the following: white cell count 10.58 × 10^9/L (3.5—9.5 × 10^9); platelet count 46 × 10^9/L (125—350 × 10^9); C-reactive protein 130.47 mg/L (0—8); procalcitonin 6.08 ng/mL (0—0.5); alanine aminotransferase 159.8 U/L (9—50); aspartate transaminase 325.4 U/L (15—40); creatinine 181.3 μmol/L (57—97); epidemic hemorrhagic fever virus antibody (hantavirus IgM/IgG) was negative. On admission, we gave moxifloxacin hydrochloride (0.4 g qd) as anti-infective therapy. The next day, the patient developed dyspnea, the blood oxygen saturation decreased to 85%, and the chest CT scan showed increasingly patchy density images in both lungs and bilateral pleural effusion (Fig. 1A,B). The patient was transferred to ICU for ventilator-assisted ventilation. Two days later, mNGS of alveolar lavage fluid identified 6 DNA sequence reads (out of 16,422,429) corresponding to *Orientia tsutsugamushi*; four days later, mNGS of peripheral blood identified 22 DNA sequence reads (out of 15,608,629) corresponding to *O. tsutsugamushi* (the processes of mNGS were similar to those in published literatures[1]). The Weil—Felix testing performed in Shanghai Xinpei Jing Medical Laboratory was negative. All bacterial cultures of alveolar lavage fluid, peripheral blood were negative. Given the low sensitivity of the Weil—Felix testing[2] and the lack of other serum or molecular biological tests for scrub typhus in our hospital, the patient was diagnosed with scrub typhus, and administered doxycycline hydrochloride tablets (0.1 g, q12 h) for oral anti-infective therapy. Six days later, the patient was discharged without fever and other symptoms. Twenty days later, all abnormal blood tests and chest CT scan (Fig. 1C,D) returned to normal.

Scrub typhus is a mite-borne infectious disease caused by *O. tsutsugamushi*. In China, scrub typhus mainly occurs in rural and jungle areas in the southern provinces. Skin eschar is the most typical clinical manifestation and the most useful diagnostic clue of scrub typhus.[3,4]

In recent years, mNGS has been widely used in medical microbiology, especially for the detection of special pathogens of unknown causes and new microorganisms. Due to the lack of reliable diagnostic tests, Scrub typhus are prone to misdiagnosis. Therefore, we determined that mNGS provides a convenient way to diagnose atypical scrub typhus.

Statement

The patient and his father had agreed to report the case anonymously before submitting the report.

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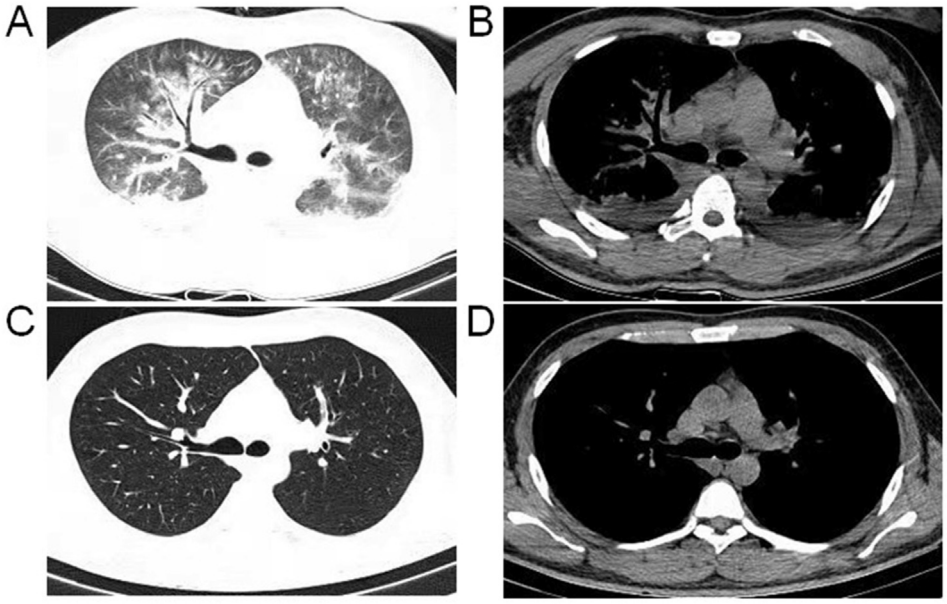

Figure 1. (A) and (B) Chest CT showed multiple patchy shadows with blurred margins scattered in both lungs, aerated bronchial shadows in some lesions, and a small pleural effusion on both sides. The above CT imaging features were consistent with pneumonia. (C) and (D) Chest CT reexaminations after the hospital which showed that the previous lesions had completely returned to normal.

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None declared.

Declaration of competing interest

None declared.

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