J Infect Chemother 22 (2016) 633–637

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic

Case report

Severe fever with thrombocytopenia syndrome with myocardial dysfunction and encephalopathy: A case report

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ARTICLE INFO

Article history:
Received 17 November 2015
Received in revised form
23 January 2016
Accepted 27 January 2016
Available online 2 March 2016

Keywords:
Severe fever with thrombocytopenia syndrome
Myocardial dysfunction
Encephalopathy

ABSTRACT

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging infectious disease in China, Korea and Japan caused by a novel bunyavirus, SFTS virus (SFTSV). Although central nervous system manifestations are common in SFTS patients, the pathogenesis has not been elucidated; and there are few reports of myocardial dysfunction. Here we report an elderly Japanese patient with reversible myocardial dysfunction and encephalopathy. A previously healthy 65-year-old male engaged in forestry got a tick bite and developed fever and fatigue in 3 days. Three days after onset, he presented to a local hospital where the diagnosis of SFTS with hemophagocytotic syndrome was made. The blood test showed leukopenia and thrombocytopenia as well as elevated levels of alanine aminotransferase and aspartate aminotransferase. Marked hemophagocytosis was found on bone marrow smear. Peripheral blood was positive for SFTSV gene by reverse-transcription polymerase chain reaction. On day 7, the patient was transferred to our hospital. We observed disturbance of consciousness, Kernig sign and myoclonus to face and limbs. Decreased blood flow of whole cerebral cortex was detected by single photon emission computed tomography (SPECT). Chest X-ray revealed cardiomegaly and electrocardiography (ECG) showed abnormal T waves. These data suggested acute encephalopathy and myocardial dysfunction. We treated him with corticosteroid and blood transfusion, which resulted in the complete recovery of the above abnormal symptoms and laboratory data including the findings in SPECT and ECG in about a month. This case demonstrated transient myocardial dysfunction and encephalopathy can occur in addition to typical clinical manifestation of SFTS.

1. Introduction

Severe fever with thrombocytopenia syndrome (SFTS) is caused by SFTS virus (SFTSV), a novel bunyavirus which was first described in 2011 in China [1]. In Japan, SFTS was firstly reported in 2013 [2]. Subsequently, the number of SFTS cases has been increasing in western Japan, especially in the Shikoku and Kyushu regions; and the mortality rate is approximately 30% [3]. The common clinical manifestations observed in SFTS patients are fever, gastrointestinal tract symptoms and central nervous system (CNS) symptoms. Hemorrhagic manifestation, severe CNS symptoms such as coma and convulsion, and substantial elevation of aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase

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http://dx.doi.org/10.1016/j.jiac.2016.01.022
1341-321X/

(CK), and creatine kinase-MB isozyme (CK-MB) have been reported as major clinical indicators of poor prognosis [4]. Thus far, there have been few reports of myocardial dysfunction caused by SFTS. Here we report an elderly Japanese patient with typical presentation of SFTS and reversible myocardial dysfunction and encephalopathy.

2. Case report

A previously healthy 65-year-old male engaging in forestry in a hilly rural area recieved a tick bite to the left chest in May, 2013. The patient developed fever and fatigue 3 days later. The patient was seen at a local clinic and given oral antibiotic. On day 3, fever continued and he was admitted to the local hospital. Erythema around the tick bite lesion on the left chest was observed (Fig. 1). The tick was later identified as an *Amblyomma testudinarium*. Blood test showed leukopenia, thrombocytopenia and elevation of AST, alanine aminotransferase (ALT), and CK. Rickettsial infection was suspected and minocycline and levofloxacin were administered intravenously. On day 5, the patient had diarrhea. Because SFTS was included in the differential diagnosis, peripheral blood was sent to the Miyazaki Prefectural Institute for Public Health and Environment for analysis. The SFTSV gene was detected in blood by reverse-transcription polymerase chain reaction (RT-PCR). Symptoms and laboratory data prompted a diagnosis of SFTS. Bone marrow aspiration revealed hemophagocytosis (Fig. 2). On day 7, the patient's condition deteriorated and he was transferred to our hospital.

On admission to our hospital, the patient had slight fever and disturbance of consciousness (Glasgow coma scale, GCS: E3V4M6). Nuchal rigidity and Kernig sign, myoclonus to the face and limbs was observed. Deep tendon reflex was increased systemically. Leukocytopenia and thrombocytopenia were evident (Table 1). Urinalysis showed hematuria and proteinuria. He had an elevation of AST, ALT, LDH, CK, ferritin, soluble Interleukin-2 receptor (sIL-2R) and abnormality of blood coagulation. Interleukin-6 and tumor necrosis factor-α were high; however, C-reactive protein and CK-MB did not increase (Table 1). The current patient had four clinical findings of the eight diagnostic criteria in HLH (Hemophagocytic lymphohistiocytosis)-2004, which were fever, cytopenias, hemophagocytosis seen in bone marrow and increased level of serum ferritin [5]. In addition, this patient had increased levels of transaminase, elevation of sIL-2R, hypertriglyceridemia, hypofibrinogenemia, and hyponatremia (Table 1). Therefore, clinical findings of this patient matched proposed HLH diagnostic criteria, 2009 [6]. Taken together, these findings strongly suggested the diagnosis of virus-associated hemophagocytic syndrome (VAHS) associated with SFTS.

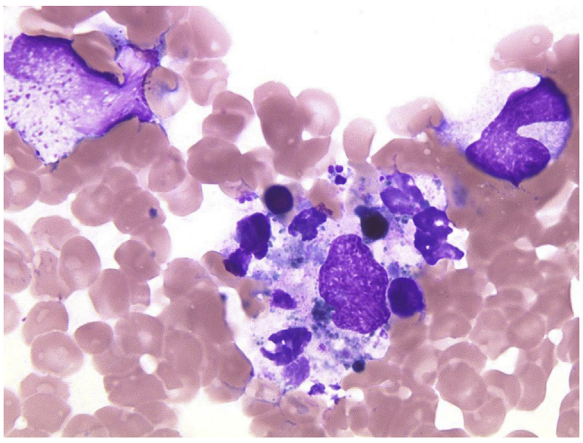

Fig. 2. A hemophagocytotic cell in bone marrow (hematoxylin-eosin stain, magnification: ×400).

Chest radiograph in sitting position revealed cardiac dilatation and a small amount of pleural effusion on the left side (Fig. 3). Electrocardiogram (ECG) showed negative T waves in $V_{3,4}$ and flat T waves in $V_{5,6}$ (Fig. 4). Brain natriuretic peptide (BNP) was high at 116 pg/ml. Echocardiogram demonstrated mild mitral valve regurgitation, mitral E to A ratio 1.6 (pseudo normal pattern) and no pericardial effusion. Because he had CNS symptoms, cerebrospinal fluid (CSF) was analyzed. Results revealed a normal cell count, but slightly increased protein. SFTSV in CSF was negative by RT-PCR. These data suggested myocardial dysfunction and encephalopathy in addition to VAHS due to SFTS. The patient was treated with methylprednisolone (1 g for 3days) followed by prednisolone (60 mg for 3 days) for VAHS. Transfusion of platelet and fresh frozen plasma was administered. On day 8, fever had disappeared; however, melena persisted 2 days. Laboratory data improved gradually and antibody for SFTSV converted to positive on day 12 (Table 2).

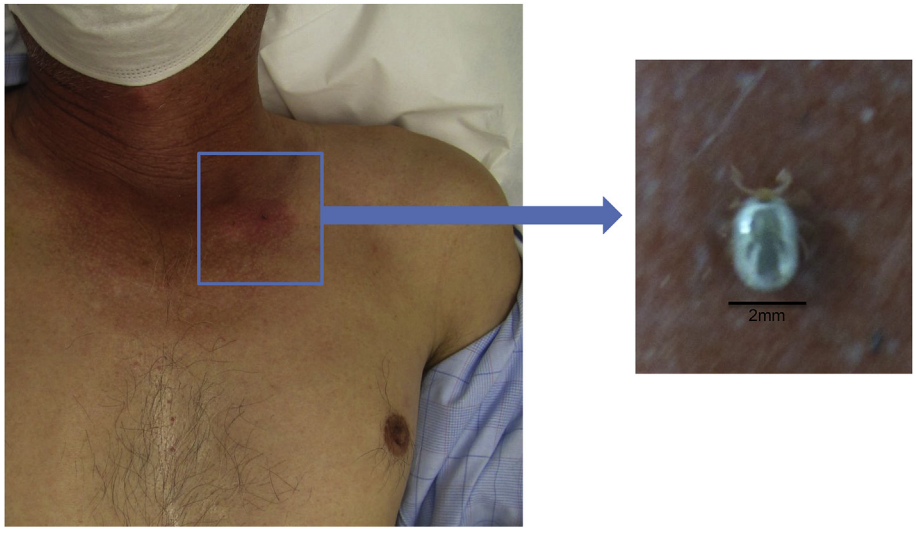

Fig. 1. Erythema with tick bite to the patient's chest.