

A Case of Scrub Typhus with Multiple Eschars and New-Onset Atrial Fibrillation

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Abstract We report a case of scrub typhus with multiple eschars and acute myocarditis with a new onset atrial fibrillation in a 53 year-old man. Eschar and cardiovascular complications of scrub typhus were discussed.

Keywords: *eschar, myocarditis, atrial fibrillation*

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1. Introduction

Scrub typhus, also called tsutsugamushi disease in Japan, is an acute febrile disease caused by *orientia tsutsugamushi*, an obligate intracellular gram-negative bacteria. Human are infected accidentally by the bite of the larva (chigger) harboring this bacteria. It is a serious health problem especially in the endemic regions known as tsutsugamushi triangle.

The World Health Organization (WHO) in 1999 stated that scrub typhus is probably one of the most underdiagnosed and an underreported disease that often required hospitalization.

Fever, skin eruption and eschar are three major clinical symptoms of scrub typhus. The percentage of eschar varies among areas of endemicity, races, and the researchers (reporters), high in individuals of Japanese and Korean ancestries, low in Southeast Asians with dark skin. The number of eschar is usually one, but may be more than one in very rare cases.

Serious cardiovascular complications of scrub typhus were reported in the second-third week of the clinical course, as a result of delayed or untreated cases (mostly, in the pre-antibiotic era) complicated with fatal disseminated multiple organ failure.

2. Case Presentation

A 53 year-old male with a medical history of well controlled hypertension presented with chief complaint of a fever and malaise for three days. Physical examination revealed that his body temperature was 38.20C (axillary), blood pressure, 72/48mmHg. irregular heart beat. ECG

showed atrial fibrillation with rapid heart beat (Figure 1, Figure 2). Morbiliform skin eruption over his chest and proximal aspects of the extremities were observed (Figure 3). Typical eschars at his right lower extremity and left leg were found via a thorough skin check (Figure 4, Figure 5). Routine blood tests showed a high white blood cell count (WBC), 11700/ μ L 4% atypical lymphocytes, elevated C-reactive Protein 6,3mg/dl, impaired liver function test; aspartate transaminase (AST), 54/ μ L alanine transaminase (ALT). 50/ μ L gammaglutamyl transpeptidase (γ -GTP) 61 / μ L, lactate dehydrogenase (LDH) 537/ μ L creatine and platelet count were within normal range, Creatine-Kinase-MB (CK-MB) was 8.58ng/ml (normal <2.2 ng/ml), cardiac troponin T was 0.033 ng/ml (normal <0.014 ng/ml), and BNP was 178 pg/ml (normal<118.4 pg/ml).

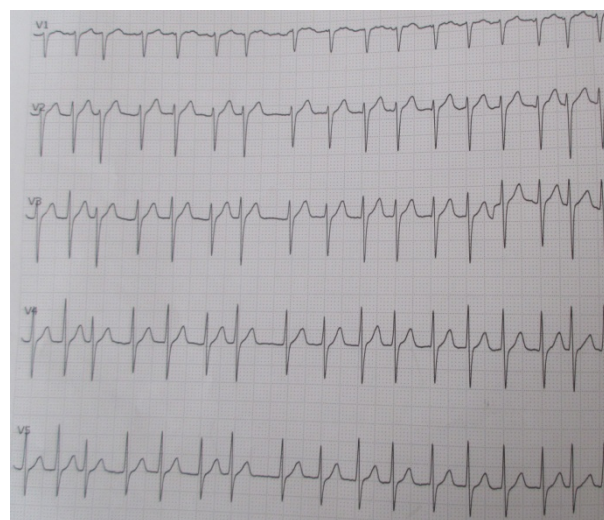


Figure 1. EKG taken on the day of his first visit showed atrial fibrillation with rapid ventricular rate (V1-V6).

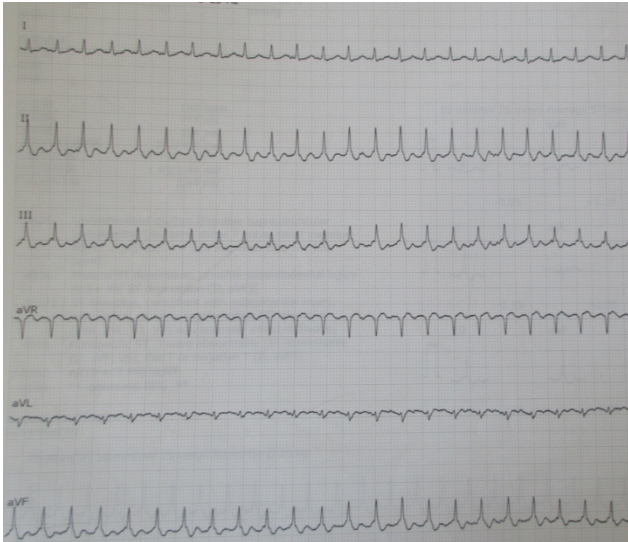


Figure 2. Atrial fibrillation with rapid ventricular response 141/min (limb leads)



Figure 3. Morbiliform skin rash over chest and proximal parts of extremities

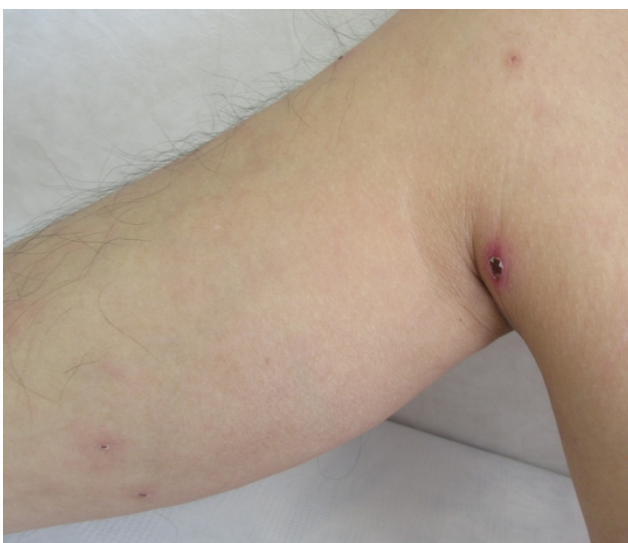


Figure 4. Multiple eschars over his right lower extremity with a typical one at medial aspect of knee joint



Figure 5. A typical eschar at left leg of the patient

Echocardiography showed absence of kinetic A wave in left ventricular inflow. Pleural or pericardial effusion were not observed. Global hypokinesia with a left ventricular ejection fraction 48% was detected.

Orientia tsutsugamushi infection (Kawasaki serotype) was proved by Nested Polymerase Reaction (PCR) with patient’s eschar before antibiotic therapy. Immunofluorescent Antibody (IFA) performed ten days after his first visit showed a highest titer of Kawasaki serotype among six strains of scrub typhus (Table 1).

Table 1. Serological data of Immunofluorescent Antibody (IFA)

Serotype	IgG/IgM
Kato	320/1280
Gilliam	640/1280
Karp	320/320
Kawasaki	1280/5120
Kuroki	320/640
Shimokoshi	80/80

Intravenous infusion of 500ml normal saline with one ampule digoxin(0.25 mg) was initiated immediately for hemodynamic support. Minocycline 200mg/day orally for one week was prescribed. His fever was subsided within 24 hours after the initiation of antibiotic treatment. In the morning of the next day, his blood pressure was 126/70 mmHg, ECG was reverted to ordinary sinus rhythm, 81/min (Figure 6, Figure 7). Recurrence of atrial fibrillation did not occur at follow-up visits. Dosage of his hypertension medications (calcium antagonist, angiotensio II receptor blocker) were cautiously adjusted.

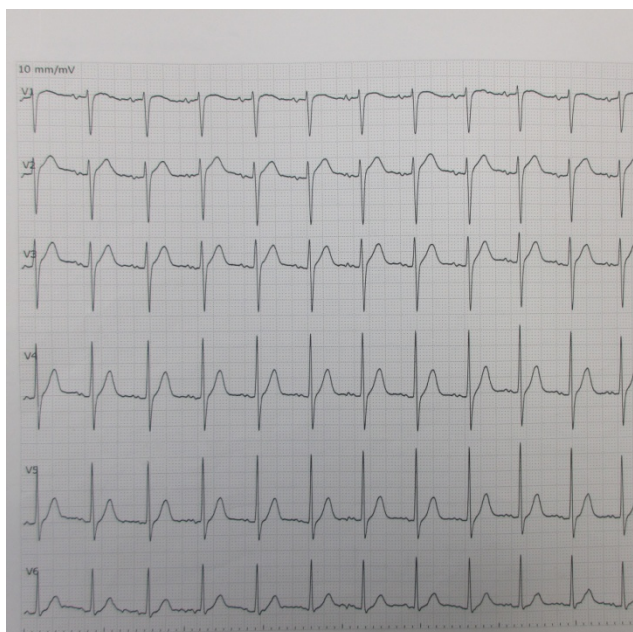


Figure 6. ECG taken in the morning of day 2, showed ordinary sinus rhythm (V1-V6) with a regular heart beat 81/min

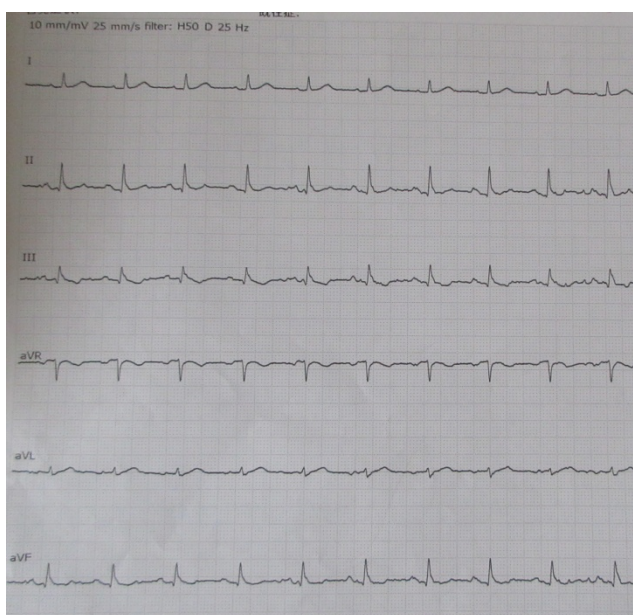


Figure 7. ECG (limb leads) taken in the morning of day 2, showed ordinary sinus rhythm with a regular heart beat 81/min

3. Discussion

Scrub typhus (ST) and Japanese Spotted Fever (JSF) are two main rickettsial infectious diseases in Japan and were classified as Category IV infectious diseases designated by the government ordinance in 1999.

Fever, skin eruption and eschar are three main clinical symptoms of scrub typhus. Eschar, the location where the chigger feeds, pathognomonic of scrub typhus can occur at any part of the body, including head, ear canals, axillary fossa, umbilicus, genital and anal areas. Eschar is usually painless and not pruritic. In classical type of scrub typhus, patients may remember a pain during being stabbed by akamushi larva. The percentage of skin eruption and eschar vary among races, areas of endemicity and

serotypes of ST, high in individuals of Japanese and Korean ancestries and low in Southeast Asians who contracted the disease. Thorough check of skin, including genital areas in females, increased the percentage of eschar from 82.6% to 100% of scrub typhus cases, was reported by a Japanese researcher Dr. Araiyou. [1]. We experienced some cases of scrub typhus, the eschars were found when hypernemia of patients' skin were resolved and the rashes faded.

In scrub typhus, dissemination of the bacteria via vasculitis and perivasculitis may involve lung, heart, liver, spleen, kidney, pancreas and central nervous system. Cardiovascular complications of scrub typhus is rare and is usually subclinical. Cardiomyocardial lesions in untreated patients were more frequent in the pre-antibiotic era, usually during the second to third week of illness. The use of effective antibiotics has reduced the complications of scrub typhus. ECG abnormalities were usually nonspecific; sinus tachycardia, non-specific ST-T changes, T wave abnormality, atrial and ventricular premature beats, AV block, prolongation of QTc interval. However, patients of scrub typhus with paroxysmal atrial fibrillation and torades de pointes need special attention [2]. In South Korea, a total of 233473 patients diagnosed with scrub typhus from 2006 to 2016, 2402 cases (1%) case were reported to have new-onset atrial fibrillation. New-onset atrial fibrillation was significantly associated with three month mortality rate and concurrent cardiac adverse outcomes, acute heart failure (AHF) and ischemic heart disease (IHD) [3].

Antibiotics such as Tetracycline, doxycycline, minocycline, azithromycin, rifampicin are effective for treatment of scrub typhus. Minocycline 200mg/D for 7 days is the standard treatment of scrub typhus for adult in Japan. Chloramphenicol is also effective (often used, in Southeast Asia). Rifampicin is effective in areas where doxycycline resistance is present. Different schemes (treatment options) have been evaluated by many researchers. For instance, doxycycline, 100mg twice daily for 7 days, orally or intravenously, chloramphenicol 500mg, four times daily, azithromycin 500mg/D for 3-5 days, rifampicin 600-900mg daily for 7 days [4].

Azithromycin, is classified in category B by the US Food and Drug Administration (US FDA) Pregnancy Category and is the suggested alternative drug in these patients and young children under 8 years-old [5]. Routine ECG, serum level of electrolytes, liver and renal function should be carefully checked in the patients of ST treated with azithromycin that prolong QT intervals.

Pathophysiology of atrial fibrillation is not yet completely understood. Inflammatory biomarkers such as cytokines, IL-1 beta, IL-6, IL-8, IL-10, TNF-alpha (tumor necrosis factor), Interferon (IFN- gamma), transforming growth factor (TGF-beta) and high-sensitivity C-reactive protein (hs-CRP) has received increasing attention recently. High sensitivity C-reactive protein and interleukins (IL-1, IL-2) have been associated with the occurrence of AF and its prognosis. Inflammation and oxidative stress may be the key mechanism underling the initiation and maintenance of atrial fibrillation. Atrial electrical remodeling begin within a few hours after the onset of atrial fibrillation resulting in decreased atrial refractory period conduction heterogeneity, abnormal

calcium ionic handling, increased P wave dispersion and atrial ectopy [6].

Acute myocarditis in scrub typhus can present with a wide range of clinical manifestations, from nonspecific symptoms, such as fever, palpitation, malaise, dyspnea, to cardiac arrhythmia syndrome, cardiogenic shock or sudden cardiac death. Endocardial biopsy are essential in confirming the diagnosis of myocarditis. Yet, some limitations restrict its application. The inflammation may be focal and this technique is invasive in hemodynamically unstable patients. Cardiac magnetic resonance (Cardiac MRI) enables clinicians to access cardiac function indirectly, and also provide assistance in directing myocardial biopsy to appropriate locations [7].

Three types of troponins exists, troponin T (cTnT), troponin I(cTnI) and troponin C(cTnC). Each subunit has a unique function; cTnT binds the troponin components to tropomyosin, cTn I inhibits the interaction of myosin with actin, and cTnC contains the binding sites for Ca²⁺ that helps initiating contraction. Troponin T is released into the blood stream when damage to heart muscle occur [8].

Scrub typhus with multiple eschars complicated with acute myocarditis with a new onset atrial fibrillation on the third day of illness highlights this interesting case. Scrub typhus with such complication is potentially fatal. Early diagnosis, prompt effective antibiotics and haemodynamic support resulted in good cardiac recovery in this patient.

Follow-up echocardiography of the patient revealed no clinically significant stenosis or regurgitation of heart valves (aortic, mitral, tricuspid and pulmonary). Respiratory collapse of inferior vena was complete. Left ventricular inflow pattern; E/A, 60.5/58.4cm/s, deceleration time, 170msec. Left ventricular ejection fraction was 63%. Mitral annulus velocity on tissue Doppler; e/a', 14.7/12 cm/s and E/e', 60.5/14.7 cm/s.

WBC count, liver function and cardiac biomarkers of the patient were within normal limit at follow-up visits.

Cover Letter

This manuscript (A Case of Scrub Typhus with Multiple Eschars and New-onset Atrial Fibrillation) is original and has not already been published elsewhere.

Competing Interest

The authors declare that there have no competing interest exist.

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