Case Report: Cavity Forming Pneumonia due to *Staphylococcus aureus* following Dengue Fever

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Abstract. While visiting Malaysia, a 22-year-old previously healthy Japanese man developed myalgia, headache, and fever, leading to a diagnosis of classical dengue fever. After improvement and returning to Japan after a five day hospitalization, he developed productive cough several days after defervescing from dengue. Computed tomography (CT) thorax scan showed multiple lung cavities. A sputum smear revealed leukocytes with phagocytized gram-positive cocci in clusters, and grew an isolate *Staphylococcus aureus* sensitive to semi-synthetic penicillin; he was treated successfully with ceftriaxone and cephalexin. This second reported case of pneumonia due to *S. aureus* occurring after dengue fever, was associated both with nosocomial exposure and might have been associated with dengue-associated immunosuppression. Clinicians should pay systematic attention to bacterial pneumonia following dengue fever to establish whether such a connection is causally associated.

INTRODUCTION

Dengue virus (DENV) infection is one of the most important vector-borne infectious diseases. The incidence of dengue fever has grown dramatically worldwide in recent decades. World Health Organization (WHO) currently estimates that there may be 50–100 million dengue infections worldwide every year.¹ Only one case of staphylococcal pneumonia following dengue fever was previously reported,² although a tremendous number of people have been infected with DENV. We have reported the second case and have discussed the characteristics and mechanism of the disease.

A written informed consent was obtained from the patient and this study was approved by the Yokohama Municipal Citizen's Hospital Ethics Committee.

CASE REPORT

A 22-year-old healthy Japanese male with no significant previous medical history had been to Kuala Lumpur, Malaysia to study for 4 months. He visited a hospital there on May 5th reporting 5 days of myalgia and headaches and 4 days of fever. He was diagnosed with dengue fever with serum IgM positive and was given intravenous fluid through peripheral line and was not intubated with 5 days of hospitalization. He recovered and returned to Japan where he developed pink sputum and a cough on May 12. The symptoms progressively worsened, and he was referred to our clinic on May 19. His temperature and other vital signs and physical findings including a chest examination were normal with no signs of endocarditis such as cardiac murmurs, conjunctival splinter hemorrhages, and cutaneous lesions on the palms. A chest X-ray showed a cavity in the left middle lung field (Figure 1). A computed tomography (CT) scan showed four cavities in the left lung and one cavity in the right lung (Figure 2). Hematological tests showed a white blood cell (WBC) count of 11,450 cells/ μ L and a neutrophil count of 8,700 cells/ μ L. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were 50 IU/L (8–38) and 152 IU/L (4–44), respectively. C-reactive protein (CRP)

was 5.1 mg/dL (0–0.5). A sputum smear revealed gram-positive cocci in clusters and leukocytes with phagocytized bacteria (Figure 3). Three sputum cultures for *Mycobacterium* were negative. We started ceftriaxone 2 g/day and his symptoms rapidly subsided. The sputum culture revealed *Staphylococcus aureus*, which was susceptible to oxacillin, cefazolin, erythromycin, co-trimoxazole, levofloxacin, clindamycin, and minocycline, but resistant to gentamicin. He was discharged after 4 days of ceftriaxone with 10 days of oral cephalexin 500 mg four times a day. He recovered fully and the subsequent chest X-ray showed a decrease in the size of the cavities.

DISCUSSION

This is the second case report of *S. aureus* pneumonia associated with DENV infection. Lee³ reported that among 127 dengue hemorrhagic fever/dengue shock syndrome patients, seven cases (5.5%) presented with complications due to bacteremia. Eight cases of concurrent *S. aureus* infection were reported and one of them was pneumonia.^{2,4–6} Authors of the first case report wrote that staphylococcal pneumonia may be thought of as simply coincidental in 2012.² However, in this case, we speculate that DENV infection caused the pneumonia due to *S. aureus*. Some viruses such as measles, cytomegalovirus, and influenza are known to induce transient in vitro and in vivo immunosuppression.^{7,8} DENV is also thought to induce immunosuppression leading to concurrent bacterial infections. The mechanism has been investigated, supported by reports from literature, and proposed as follows: 1) DENV infects and replicates in human dendritic cells and has been shown to block interferon (IFN)- α/β signaling in infected dendritic cells.⁹ Antigen-presenting cells isolated from patients with acute DENV infection exhibit defects in T cell priming.¹⁰ 2) Leukopenia, particularly affecting neutrophil and monocyte lineages, is well described and is thought to be related with bone marrow suppression.¹¹ Early blast cells are abortively infected, killed, and eliminated by phagocytosis by dendritic cells; infected adventitial reticular cells cause stromal failure of supporting hematopoiesis.¹² 3) Epithelial damage helps bacteria invade the tissue. Lung epithelial cells are possible targets of DENVs,¹³ and DENV infection induces apoptotic death of lung cells.¹⁴

Incidence of health care-associated pneumonia due to *S. aureus* is low and the main risk factor of it is the ventilation with endotracheal tube, which was not provided to this

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FIGURE 1. A chest X-ray. One cavity in the left middle lung field (arrow).

case.^{15,16} Therefore, the main risk of this case is considered to be dengue infection.

This patient was a healthy young male and did not have any past medical history or immunosuppressed conditions. The symptoms of pneumonia appeared several days after remission of dengue fever symptoms. His pneumonia was not severe and he made a full and quick recovery, although the pneumonia is severe with 51% of cases due to *S. aureus* reporting mortality.¹⁷ The differences in clinical courses between reported cases of staphylococcal pneumonia and this case are apparent. These facts suggest that dengue infection has the possibility to cause staphylococcal pneumonia but it may be less severe than pneumonia associated with influenza. The lack of severity is possibly one of the reasons why so few cases have been reported so far. The more widely DENV expands due to global warming, the more immunosuppressed people susceptible to dengue will be infected with DENV and may develop severe staphylococcal pneumonia.

In summary, we experienced a case of cavity-forming pneumonia due to *S. aureus* following dengue fever. Clinicians

FIGURE 2. A computed tomography (CT) scan. Cavities in the bilateral lung (arrows).

FIGURE 3. A sputum smear result. Gram-positive cocci in clusters and leukocytes with phagocytized bacteria are seen (arrow).

should pay attention to complications such as bacterial pneumonia following dengue fever.

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