Disseminated Aspergillosis Associated With Tsunami Lung

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Many survivors of the tsunami that occurred following the Great East Japan Earthquake on March 11, 2011, contracted a systemic disorder called "tsunami lung," a series of severe systemic infections following aspiration pneumonia caused by near drowning in the tsunami. Generally, the cause of aspiration pneumonia is polymicrobial, including fungi and aerobic and anaerobic bacteria, but *Aspergillus* infection is rarely reported. Here we report a case of tsunami lung complicated by disseminated aspergillosis, as diagnosed during autopsy. *Key words: ARDS; autopsy; cardiomyopathy; disasters; disseminated aspergillosis; extravascular lung water.* [Respir Care 2012;57(10):1674–1678. © 2012 Daedalus Enterprises]

Introduction

The Great East Japan Earthquake that occurred on March 11, 2011, was one of the most serious disasters affecting the people living on the Pacific coast of Japan. The government of Japan (http://www.cao.go.jp/index-e.html) reported that approximately 20,000 people were killed or missing and that more than 90% of the victims died from drowning in the ensuing tsunami. In general, major complications of near drowning in seawater include trauma, hypothermia, skin abscess, and aspiration pneumonia.[1] Although accurate numbers of near-drowning incidents are unknown, many survivors of near drowning subsequently contracted a systemic disorder called "tsunami lung."

The pathophysiology of tsunami lung is thought to involve not only chemical or mechanically induced inflammation, but also bacterial infection, the chief pathogens of which include *Aeromonas* species, *Burkholderia pseudomallei*, *Chromobacterium violaceum*, and *Pseudomonas aeruginosa*, among Gram-negative rods; *Streptococcus pneumoniae* among Gram-positive cocci; and *Pseudallescheria boydii* among fungi.[2] Interestingly, several types of infections caused by *Aspergillus* were reported in the aftermath of the 2004 Indian Ocean earthquake and tsunami.[3,4] However, no cases of disseminated aspergillosis in a tsunami survivor have been reported thus far. Here we report a case of an immunocompetent female patient with tsunami lung, contracted as a consequence of the Great East Japan Earthquake and tsunami. She was transported to our hospital and provided with intensive care treatment, and was diagnosed with disseminated aspergillosis at autopsy.

Case Report

A 68-year-old woman experienced an episode of near drowning during the tsunami following the Great East Japan Earthquake on March 11, 2011. She was admitted to a nearby hospital and diagnosed with tsunami lung at around 11:00 PM on March 11, approximately 7 hours after the near-drowning experience. She was previously healthy and had no particularly noteworthy medical history. On admission, her consciousness was clear, and she was able to walk by herself. She gradually developed dyspnea and mental deterioration after admission, which was followed by sudden cardiac arrest at 7:00 AM on March 12. After

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The authors have disclosed no conflicts of interest.

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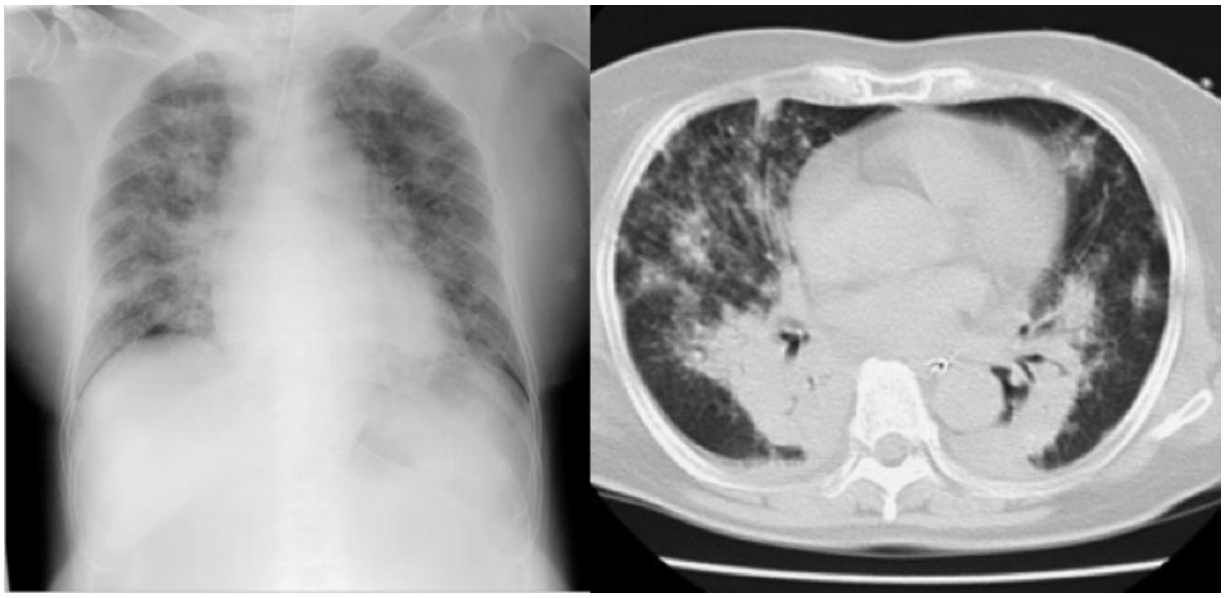

Fig. 1. The chest radiograph (left) showing bilateral diffuse infiltration in all lung zones on admission. The computed tomography scan (right) showing moderate atelectasis in the bilateral inferior lobe.

cardiopulmonary resuscitation for 3 min, with 1 mg of epinephrine infusion, performed by the doctors in charge, spontaneous circulation was achieved. She was immediately transferred to our hospital by helicopter for further intensive treatment.

On admission to our hospital she was intubated and well sedated with midazolam (40 μg/min). Her body temperature was 37.3°C, and her hemodynamic status was stabilized with a dopamine infusion (5 μg/kg/min). Blood gas analysis showed a P_{aO_2} of 131.5 mm Hg, a P_{aCO_2} of 79.3 mm Hg, and a base excess of −3.7 mEq/L, under 100% oxygen. Laboratory data showed an elevated white-blood-cell count and increased levels of procalcitonin (13.8 ng/mL, normal range $<$ 0.05 ng/mL), lactate dehydrogenase, and creatinine phosphokinase. We did not assess the (1,3)-beta-D-glucan levels at this point, as we did not suspect fungi as the pathogen responsible for respiratory failure, since she was not an immunosuppressed patient.

Chest radiography and computed tomography showed diffuse bilateral infiltrates and posterior atelectasis (Fig. 1). Computed tomography of the head showed no abnormal change. Cardiovascular monitoring, using a pulse contour cardiac output system (PiCCO, Pulsion Medical Systems, Munich, Germany), showed markedly elevated levels of extravascular lung water[5] (18 mL/kg, normal range 7.4 $\pm$ 3 mL/kg) and an increased pulmonary vascular permeability index[6] of 4.8, indicating noncardiogenic pulmonary edema caused by ARDS.[7]

We started an infusion of cefotiam (2 g/d), according to the guidelines for the treatment of aspiration pneumonia and near drowning in seawater.[2,8] We did not perform therapeutic hypothermia. During intensive care we strictly followed the guidelines for the prevention of nosocomial pneumonia.[9]

Although a fair amount of discolored mucus was discharged from the intubation tube during treatment, bronchoscopy performed on days 7 and 18 revealed no abnormal change in the tracheal mucosa. Blood culture tests on days 1 and 7 were negative for bacterial and fungal infections. Because her respiratory function did not improve, despite treatment, we tested for the presence of elevated (1,3)-beta-D-glucan levels as evidence of fungal infection and repeated the assessment of sputum culture. On the basis of the sputum culture results, we changed the intravenous antibiotic to piperacillin/tazobactam (18 g/d) on day 6, and subsequently to ciprofloxacin (900 mg/d) on day 18. Pneumonia due to *Aspergillus fumigatus* was diagnosed on day 13, on the basis of the results of a sputum culture performed on day 6 and the slightly elevated (1,3)-beta-D-glucan levels (31.4 pg/mL, normal range $<$ 20.0 pg/mL) measured on day 10. Her procalcitonin levels decreased on day 10 (1.8 pg/mL). Therefore, intravenous micafungin treatment (300 mg/d) was started immediately; however, the patient's condition, including her hemodynamic status, continued to worsen due to septic shock, as assessed by the PiCCO parameters.

Because of the general confusion and interrupted transportation available after the earthquake, acquisition of the results of the blood and culture tests was delayed. We also could not perform whole-body computed tomography for further evaluation because of her unstable hemodynamic status. Therefore, we assessed her respiratory condition using the PiCCO system and portable chest radiography,

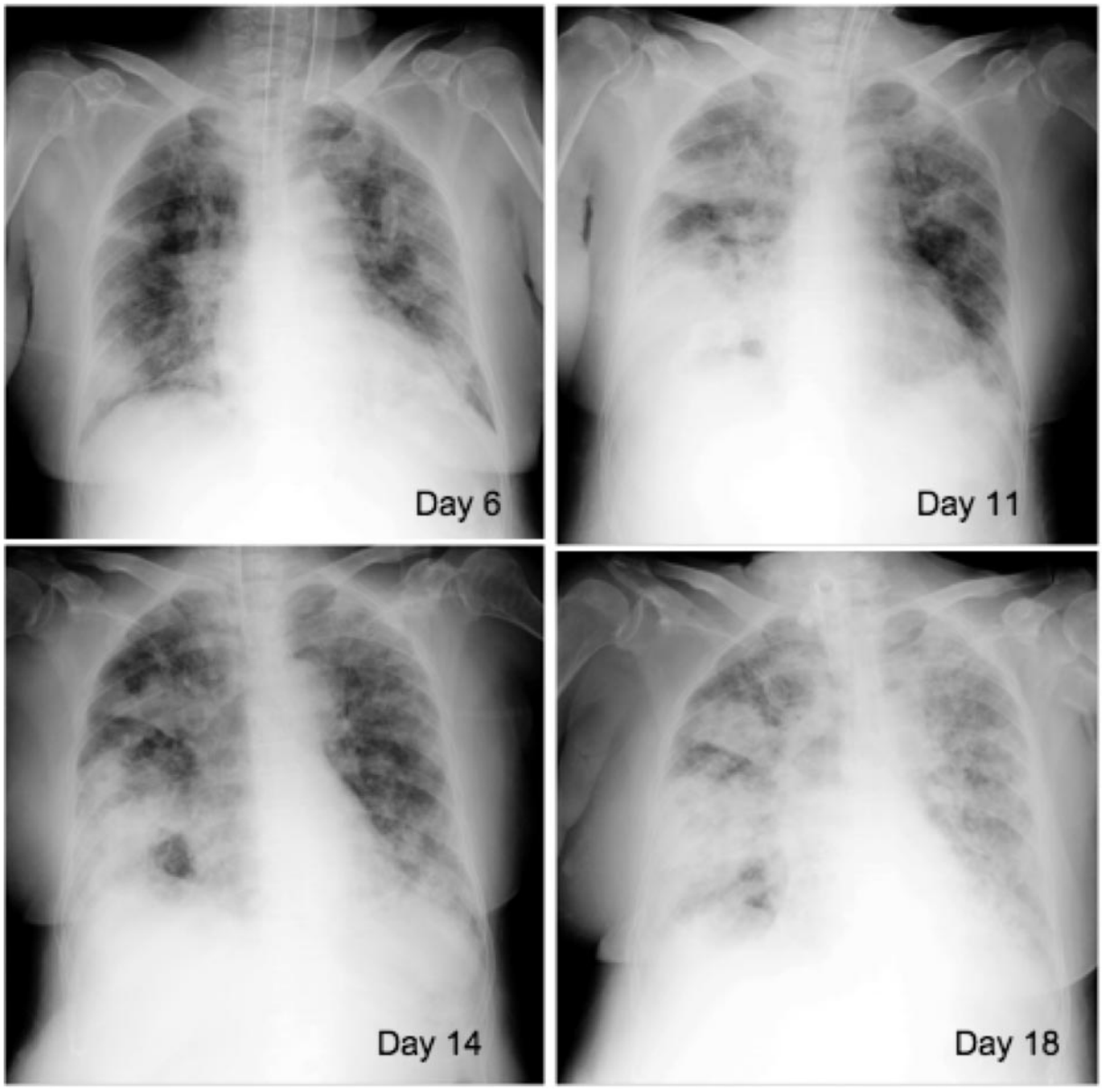

Fig. 2. Serial chest radiograph showing a rounded opacity in the right lower zone on day 6, which gradually increased in size (day 11), with additional involvement of the right upper zone, giving an appearance of a fungus ball (day 14) in the lower zone, and finally involving the bilateral lung fields on day 18.

which showed a rounded opacity in the right lower zone on day 6. This infiltrate grew bigger and seemed separated from other lung fields, like a fungus ball, on day 14; additionally, other gradually expanding, diffuse infiltrates were noted bilaterally (Fig. 2). Ultrasonography was also performed, which showed no evidence of a massive cavity or cardiomyopathy. She died on day 18, despite the intensive care provided, due to multiple organ dysfunction syndrome.

Autopsy revealed degenerative empyema, with multiple cavities and abscesses, and massive *Aspergillus* invasion (Fig. 3). Microabscesses were also found in the heart (Fig. 4), kidneys, stomach, gallbladder, mandibular gland, iliopsoas muscle, tongue, and adrenal glands. All the abscesses contained large amounts of *Aspergillus* hyphae, which had invaded the surrounding vessels.

Discussion

This report suggests that, with regard to severity of outcome, disseminated aspergillosis is one of the most important complications of tsunami lung. Tsunami lung occurs when individuals, swept away by a tsunami, aspirate seawater containing contaminated mud and bacteria.[10] In general, pneumonia that follows near drowning results

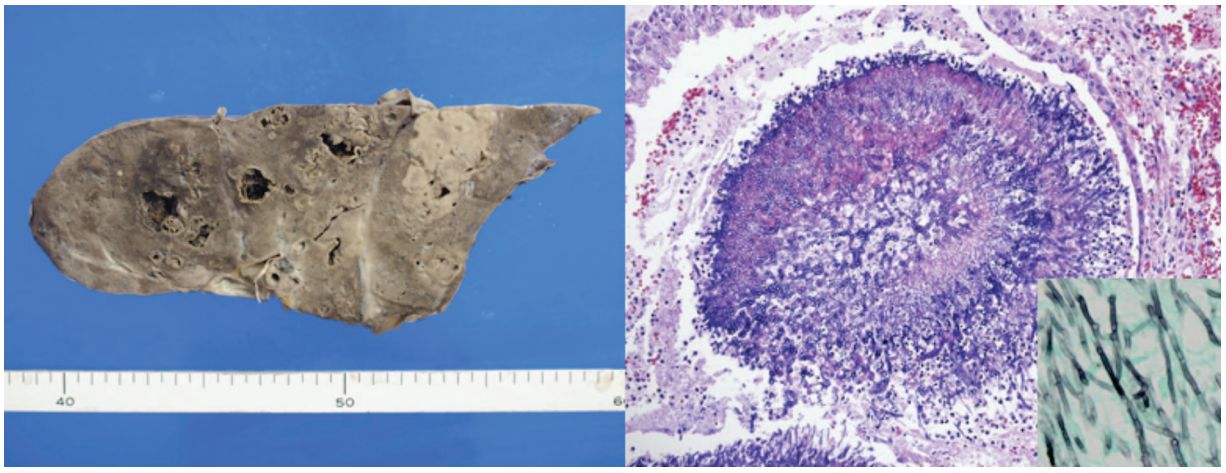

Fig. 3. Grossly, the lung shows multiple cavitary lesions, which on microscopy showed necrotizing pneumonia, with colonization of the cavities and acutely branching *Aspergillus* hyphae. There is invasion of the blood vessels and parenchyma (right × 200, hematoxylin and eosin stain). Grocott staining shows dichotomously branching and septate hyphae (inset × 400).

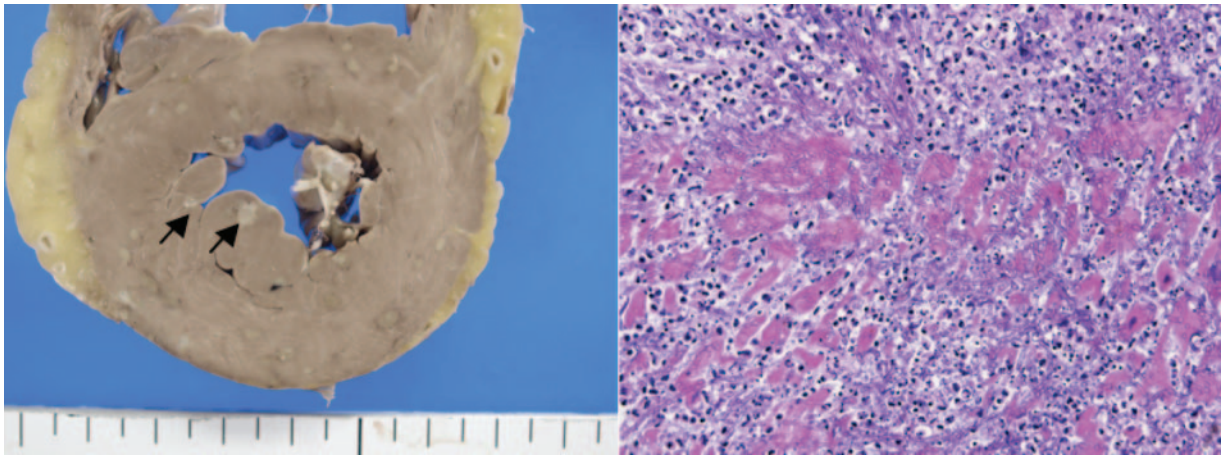

Fig. 4. Gross specimen of the heart shows several abscesses (arrows) in the left ventricle (left). *Aspergillus* hyphae can be seen growing in the abscess cavity, with extensive myocardial destruction and neutrophilic infiltration (right × 200, hematoxylin and eosin stain).

from polymicrobial infection. However, interestingly, reports of the Indian Ocean earthquake and tsunami in 2004, such as those on meningitis in a 17-year-old girl with neurological symptoms after near drowning during the tsunami,[3] and meningitis of pregnant women receiving anesthesia for Caesarean section at the hospitals affected by the tsunami, have suggested an association between tsunamis and *Aspergillus* infections.[4] Further epidemiological investigations are needed to determine whether this association is a true post-tsunami effect.

The present case indicates that even healthy individuals can contract refractory systemic *Aspergillus* infections after tsunami lung. However, it is possible that the patient had aspirated vast amounts of *Aspergillus* in a short time during the near-drowning experience. After *Aspergillus* pneumonia is acquired, it is difficult to treat the patient effectively, despite the use of appropriate antibiotics, respiratory aids, and hemodynamic management, and this condition often results in death or severe neurological defects, even in immunocompetent patients.[11-14]

Another possible explanation for this patient's outcome is that post-cardiac arrest conditions could have detrimentally affected the immune system of the patient. Patients resuscitated from cardiac arrest are known to contract pulmonary complications and show increased pulmonary vascular permeability.[15,16] In addition, pneumonia after cardiac arrest is a common phenomenon.[17] However, *Aspergillus* pneumonia has not yet been reported as a major complication of post-cardiac arrest syndrome.[17] Further studies are required for elucidating the influence of post-cardiac arrest syndrome on the immune system.

In the case described here, the diagnosis and treatment of disseminated aspergillosis was delayed for several reasons. As the diagnosis of *Aspergillus* infection was not

considered at presentation and the patient was not immunocompromised, we had not evaluated the presence of (1,3)-beta-D-glucan as evidence of fungal infection, which might have delayed the initiation of antifungal treatment. A normal bronchoscopic appearance of the tracheobronchial tree, with delayed acquisition of sputum culture and (1,3)-beta-D-glucan test results, due to the interrupted transportation caused by the earthquake, further delayed the diagnosis. Moreover, we also could not measure the galactomannan levels, which might have been helpful in supporting the diagnosis.

In conclusion, aspergillosis should be considered when treating tsunami survivors, and an effective antifungal agent should be considered for empirical treatment in the early phase, even in immunocompetent patients.

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