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Case report

Community-acquired, hospital-acquired, and healthcare-associated pneumonia caused by *Pseudomonas aeruginosa*Ayumi Fujii^{a,b,1}, Masafumi Seki^{a,*,1}, Masachika Higashiguchi^b, Isao Tachibana^b, Atsushi Kumanogoh^b, Kazunori Tomono^a^a Division of Infection Control and Prevention, Osaka University, Suita City, Osaka, Japan^b Department of Respiratory Medicine, Allergy and Rheumatic Diseases, Osaka University, Suita City, Osaka, Japan

A B S T R A C T

Keywords:

Lung abscess
Drug resistance
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Nosocomial pathogenWe describe three types of *Pseudomonas aeruginosa* pneumonia.

Case 1. *P. aeruginosa* was isolated from the blood and sputum of a 29-year-old male non-smoker who developed severe community-acquired pneumonia (CAP). Piperacillin was initially effective, but fever and lobular pneumonia with cavities developed seven days after discharge. Intravenous piperacillin/tazobactam and tobramycin were administered for four weeks, followed by oral ciprofloxacin for two weeks. He finally recovered, but developed recurrent CAP due to *P. aeruginosa* despite appropriate antibiotic therapy and immunocompetent status.

Case 2. *P. aeruginosa* was isolated from the blood and sputum of a 57-year-old woman with renal cancer who developed hospital-acquired pneumonia (HAP) after surgical treatment. She recovered after meropenem administration for four weeks.

Case 3. A 67-year-old woman with systemic sclerosis and malignant lymphoma who was followed up on an outpatient basis underwent immunosuppressive therapy. Thereafter, she developed pneumonia and was admitted to our institution where *P. aeruginosa* was isolated from blood and sputum samples. Healthcare-associated pneumonia (HCAP) was diagnosed and effectively treated with tobramycin and ciprofloxacin.

P. aeruginosa is not only a causative pathogen of HAP and HCAP, but possibly also of CAP.

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Introduction

Pseudomonas aeruginosa is a common nosocomial pathogen that often causes pneumonia in hospitalized patients [1,2], most of whom have underlying medical conditions or risk factors for *Pseudomonas* infection. Although rare, case reports and reviews have described healthy individuals who have developed community-acquired pneumonia (CAP) caused by *P. aeruginosa* [3–8] that is often rapidly progressive and fatal.

Here, we compared hospital-acquired (HAP) and healthcare-associated (HCAP) pneumonia caused by *P. aeruginosa*, with

rapidly progressive *P. aeruginosa* CAP in a previously healthy 29-year-old man.

Case report

Case 1

A previously healthy 29-year-old man presented at the emergency room in June 2012 with acute pain around the right shoulder and high fever accompanied by extreme fatigue that had persisted for nine days. He had a medical history of mild sinusitis, but had never smoked.

A physical examination indicated the following: temperature, 39.5 °C; blood pressure, 111/50 mmHg and a respiratory rate of 28 breaths/min. A physical examination revealed crackles (rhonchi) at the upper right lung and chest radiography indicated bilateral opacities (Fig. 1(A) and (B)). His initial WBC count was 26,400/L, and C-reactive protein (CRP) was 20.0 mg/dL. *P. aeruginosa* was identified in blood cultures and respiratory specimens and the minimum

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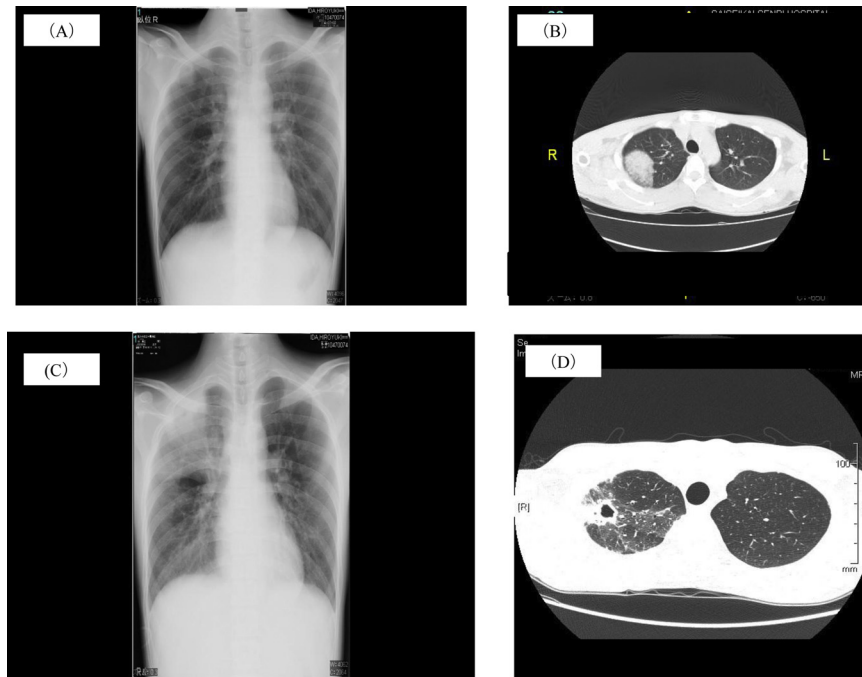


Fig. 1. Chest radiography and computed tomography images of a 29-year-old patient admitted with CAP in June 2012 and August 2012. Chest radiography and computed tomography images in June 2012 (A and B, respectively) show patchy airspace opacity in right upper lung lobe. Those acquired in August 2012 (C and D, respectively) show right upper lobular pneumonia with cavity.

inhibitory concentration (MIC) test according to Clinical and Laboratory Standards Institute criteria revealed susceptibility to levofloxacin, piperacillin, ciprofloxacin and gentamicin. Rapid antigen tests for influenza A and B virus were negative. Intravenous piperacillin (4×3 g/day) for 19 days improved the chest X-ray findings and the inflammatory markers, WBC (8900/L) and CRP (0.9 mg/dL). Blood cultures also became negative. He was discharged from hospital after completing the course of treatment.

However, he returned to the hospital two days later with high fever. Chest radiography and CT revealed lobular pneumonia with cavities and *P. aeruginosa* that was susceptible to most of the same antibiotics as before was isolated from sputum once again. The WBC count and CRP concentration at this point were 10,800/L and 11.6 mg/dL, respectively. Oral levofloxacin (500 mg/day) for one week improved chest radiography findings, WBC (7500/L) and CRP (2.8 mg/dL).

One month thereafter, a chest X-ray and CT during August 2012 revealed worsened infiltration shadows around cavities (Fig. 1(C) and (D)). Therefore, he was admitted for a third time, and treated with intravenous piperacillin/tazobactam (3×4.5 g/day) and tobramycin (300 mg/day) for four weeks followed by 300 mg/day of oral ciprofloxacin for two weeks. The patient has since remained free of further recurrence.

Case 2

A 57-year-old woman with current renal cancer and a history of smoking developed pneumonia seven days after a nephrectomy in October 2012.

A physical examination revealed a temperature of 37.1 °C, blood pressure of 120/80 mmHg and crackles (rhonchi) in the left lung. Chest radiography indicated infiltration shadows in the left lung field (Fig. 2(A) and (B)). Her initial WBC count was 720/L because she was under chemotherapy, and CRP was 16.4 mg/dL. *P.*

aeruginosa determined in blood cultures and respiratory specimens was susceptible to meropenem, ciprofloxacin and gentamicin but resistant to piperacillin. Intravenous meropenem (3×1 g/day) for 14 days followed by cefepime (3×1 g/day) for 10 days improved the chest X-ray findings and the pneumonia.

Case 3

A 67-year-old woman with systemic sclerosis and malignant lymphoma was admitted to the emergency room in March 2013 with dyspnea and disturbed consciousness. She was followed up as an outpatient, and had recently been treated with rituximab and oral prednisolone.

A physical examination indicated a temperature of 39.1 °C and blood pressure of 88/56 mmHg. A physical examination revealed crackles (rhonchi) at the left lung. Chest radiography indicated infiltration shadows mainly in the left lower field (Fig. 2(C) and (D)). Saturated pulse oxygen was 90% under an O₂ 10 L/min mask and the patient was therefore placed on a respirator. Her initial WBC count was 4900/L, and CRP was 27.8 mg/dL. *P. aeruginosa* determined in blood cultures and respiratory specimens was susceptible to levofloxacin, piperacillin, ciprofloxacin and gentamicin. Intravenous piperacillin/tazobactam (3×4.5 g/day) improved her status after 17 days.

Discussion

P. aeruginosa is an established causative pathogen of HAP and HCA P [1], but CAP caused by this organism in previously healthy individuals is rare. However, over ten occurrences of CAP have been documented [3,8]. Rose [8] described chronic pneumonia due to *P. aeruginosa* that developed in a 43-year-old man who had been previously considered healthy, in contrast to the HAP and HCAP caused by *P. aeruginosa* that develops in patients and which might

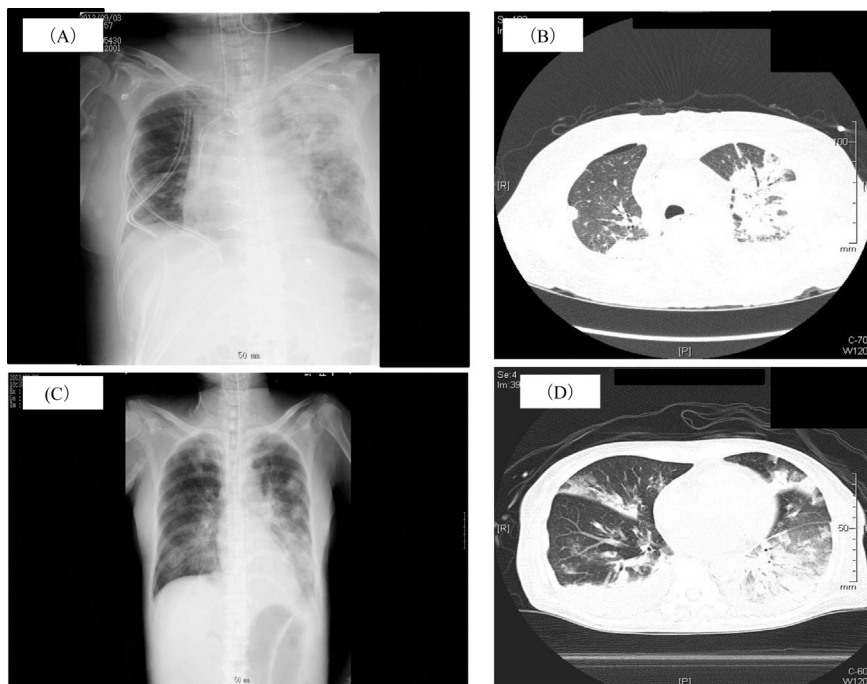


Fig. 2. Chest radiography and computed tomography images of a 57-year-old patient with HAP and a 67-year-old patient with HCAP. Chest radiography (A) and computed tomography (B) images of 57-year-old patient with HAP show infiltration shadow mainly in left upper lung field. Those (C and D) of 67-year-old with HCAP show infiltration shadow mainly in left lower lung field.

be more common. The comparison of CAP with HAP and HCAP caused by *P. aeruginosa* (Table 1) indicated that the features of CAP caused by this pathogen differ from those of HAP and HCAP.

Huhulescu et al. also reported that community-acquired *P. aeruginosa* infections are rare, tend to be mild and superficial, and tend to arise in middle-aged patients. Five patients described in the literature were smokers [4]. The presentation can be variable, with cough, pleuritic chest pain, fever and sputum production. Half of all reported patients with sputum production had hemoptysis.

The 29-year-old patient described herein had chest pain and fever, but no apparent underlying diseases and no history of smoking. He was negative for HIV antibodies. CD4 and CD8 counts and neutrophil functions such as phagocytosis and sterilizing

functions were normal (data not shown). The cause of *P. aeruginosa* CAP remained unclear, but we considered that chronic sinusitis might be involved. However, an otorhinolaryngeal specialist evaluated the sinusitis as mild and *P. aeruginosa* was not isolated from nasal specimens.

One report suggests that *P. aeruginosa* CAP should be suspected in patients with environmental risk factors and gram-negative bacilli in sputum samples, and in those who present with pneumonia accompanied by overwhelming sepsis [9]. Pneumonia caused by *P. aeruginosa* has been associated with exposure to contaminated aerosolized water. Examples include otitis externa, varicose ulcers and folliculitis associated with Jacuzzis [10]. Our patient with CAP was a clerk, he had not been exposed to aerosolized water and none of his family and colleagues had similar symptoms.

Over 92% of CAP caused by *P. aeruginosa* patients have bacteremia, and 83% of them have *P. aeruginosa* in sputum specimens. Although the mortality rate in one series was 33%, patients died within a median of 11 h from admission [3]. Of those who survived, only one was treated empirically upon admission with an antibiotic effective against *Pseudomonas* spp [3]. Therapy for the remaining survivors was directed by positive culture results obtained at 1–3 days after admission.

The infections in our patients were not fatal, but pneumonia with lung abscesses recurred despite the absence of underlying diseases or immunocompromising factors in the patient with CAP. He was then treated with levofloxacin, which does not affect anaerobes that are major pathogens involved in abscesses [1,11]. He might have been co-infected with anaerobes during the first episode, although anaerobes were not detected in any specimens, including sputum and blood at the first and subsequent admissions in June and August (data not shown). Co-infection with *P. aeruginosa* and anaerobes has been suggested in diabetic foot infections, Fournier gangrene and paranasal sinus fungus balls [12–14]. Fungi were also undetectable in all specimens from our patient.

P. aeruginosa pneumonia can be difficult to treat because it tends to resist the usual antibiotics recommended for treating CAP. Torres

Table 1
Comparison of three types of *Pseudomonas aeruginosa* pneumonia.

	Patient 1	Patient 2	Patient 3
Category	CAP	HAP	HCAP
Age	29	57	67
Comorbidity	None	Renal cancer	Systemic sclerosis, Malignant lymphoma
Severity			
CURB65	Mild	Moderate	Severe
PSI	29	107	167
Chest X-ray	<1/3	>2/3	Middle range
Cavity	Yes	Yes	Yes
Shock	No	No	Yes
Respirator	No	No	Yes
WBC (cells/L)	26,000	720	4900
CRP (mg/dL)	20.0	16.4	27.8
Culture			
Sputum	Positive	Positive	Positive
Blood	Positive	Positive	Positive
30-day Survival	Survived	Survived	Survived
Drug resistance	No	Yes	No

CAP, community-acquired pneumonia; HAP, hospital-acquired pneumonia; HCAP, healthcare-associated pneumonia; PSI, pneumonia severity index.

et al. described that all of five patients who presented with severe CAP due to *P. aeruginosa* also had bronchiectasis, suggesting that patients with structural lung diseases should receive broader therapy [15]. Both the American Thoracic Society and Canadian guidelines for treating CAP recommend that patients with structural lung diseases who present with CAP should be given antibiotics that are effective against *P. aeruginosa* [11]. However, our patient and others with *P. aeruginosa* CAP did not have underlying diseases, including structural lung diseases. Kunimasa et al. isolated *P. aeruginosa* from a patient with CAP who was similar to ours and analyzed the organism *in vivo* using a mouse pneumonia model and *in vitro* using biofilm production, but they could not explain how such severe CAP developed in an otherwise healthy young man [6]. Further immunological and microbiological analyses of CAP caused by *P. aeruginosa* are required.

In conclusion, we described three patients with *P. aeruginosa* pneumonia including a 29-year-old man with CAP who had otherwise been healthy except for a history of mild sinusitis. Although he recovered with appropriate therapy, *P. aeruginosa* CAP recurred with a lung abscess. Co-infection with anaerobes might have been associated with this pathogenesis. Further studies of host status and microbiological characteristics are required and *P. aeruginosa* CAP should be carefully distinguished from HAP and HCAP and appropriately treated.

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