Elmer Press

Case Report J Clin Med Res. 2016;8(11):831-835

Bacterial Pneumonia Caused by *Streptococcus pyogenes* Infection: A Case Report and Review of the Literature

Nobuhiro Akuzawa[a, c], Masahiko Kurabayashi[b]

Abstract

A 78-year-old Japanese man was admitted to our hospital because of fever lasting for 4 days. His white blood cell count and C-reactive protein level were elevated and computed tomography of the chest showed bronchopneumonia in the right upper lobe of the lung. *Streptococcus pyogenes* was detected from sputum and blood culture samples on admission and administration of ampicillin/sulbactam was effective. Although our patient's clinical course was good, *S. pyogenes* pneumonia commonly shows a high rate of fatality and septicemia, and may affect a previously healthy population. Physicians should be aware of pernicious characteristics of *S. pyogenes* pneumonia.

Keywords: Community-acquired pneumonia; High fatality rate; Septicemia; *Streptococcus pyogenes*

Introduction

Streptococcus pyogenes (*S. pyogenes*), or group A streptococcus, is a pathogen which causes localized illness, such as pharyngitis and skin lesions [1]. *S. pyogenes* can asymptomatically colonize humans, and may cause invasive diseases, such as bacteremia, pneumonia, necrotizing fasciitis, and streptococcal toxic shock syndrome [1, 2].

S. pyogenes accounts for 2-5% of cases of bacterial pneumonia in the early 20th century [3]. Fatality of pneumonia due to *S. pyogenes* decreased to a low level after the advent of antibiotics [4]. Sporadic outbreaks of *S. pyogenes* infection have been reported mainly in military camps, and *S. pyogenes* rarely causes pneumonia in general [5]. However, an outbreak of *S. pyogenes* pneumonia occurred at a US military camp in 2002 [6]. This outbreak ended after intramuscular benzathine penicillin or oral azithromycin administration, suggesting that the potential for an epidemic of *S. pyogenes* infection cannot be ignored.

We present here a sporadic case of *S. pyogenes* pneumonia. A patient was admitted to our hospital to thoroughly investigate the cause of a persistent fever of unknown origin. Chest X-ray findings were unremarkable, and plain computed tomography (CT) of the chest showed bronchopneumonia in the right upper lobe of the lung. Notably, *S. pyogenes* was detected from sputum and blood culture samples on admission. Our patient was discharged from our hospital after 6 g/day of aminobenzylpenicillin administration for 10 days.

Case Report

A 78-year-old Japanese man was admitted to our hospital because of a fever lasting for 4 days. He had no relevant past history, except for lung tuberculosis in his 20s, and had no family history. He had taken no medications. He had smoked 10 cigarettes a day for approximately 60 years, but did not consume alcohol. Four days before admission, he suddenly had a fever (39.4 °C) with a sore throat and chills. He went to his home doctor for a check-up and underwent an influenza antigen test, but the result was negative. Oral acetaminophen was prescribed, but his fever persisted. He visited his home doctor again 2 days before admission and had a blood test, which showed that his white blood cell (WBC) count and C-reactive protein (CRP) level were elevated (12,400/mm^3 and 16.01 mg/dL, respectively.) Although oral cefcapene pivoxil (300 mg/day) was added, his fever did not improve, and he was then admitted to our hospital.

On admission, his height was 165 cm, weight was 65.8 kg, body temperature was 38.3 °C, and blood pressure was 150/75 mm Hg. His heart rate was 90 beats per minute and regular. A physical examination showed no major abnormalities, except for mild pharyngeal erythema due to pharyngitis, and mildly increased sputum excretion. His arterial blood O_2 saturation (98%) and partial O_2 pressure (92.1 Torr) in room air were normal. A chest X-ray film showed granular shadows that were predominantly distributed in the bilateral lower lung field (Fig.

Manuscript accepted for publication September 14, 2016

[a]Department of General Medicine, National Hospital Organization Shibukawa Medical Center, 383 Shiroi, Shibukawa, Gunma 377-0280, Japan
[b]Department of Medicine and Biological Science, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan
[c]Corresponding Author: Nobuhiro Akuzawa, Department of General Medicine, National Hospital Organization Shibukawa Medical Center, 383 Shiroi, Shibukawa, Gunma 377-0280, Japan. Email: akuzawa_nobuhiro@yahoo.co.jp

doi: http://dx.doi.org/10.14740/jocmr2737w

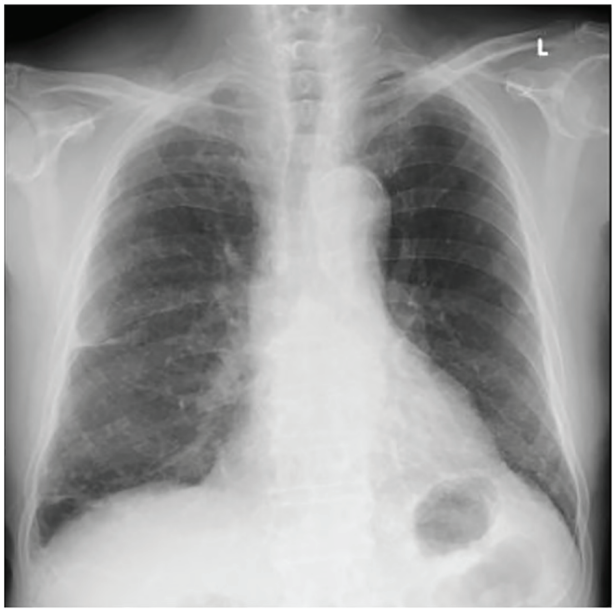

Figure 1. A chest X-ray film on admission. Multiple granular shadows predominantly distributed in the lower lung field, and thickening of the right interlobar pleura were observed. These findings had been pointed since the patient had had been infected with tuberculosis. No obvious findings suggesting pneumonia were observed.

1). An abdominal X-ray film and an electrocardiogram were normal. Laboratory tests showed a high WBC count of 11.6 $\times 10^9$ cells/L (normal: 3.5 - 9.0 $\times 10^9$ cells/L), lactate dehydrogenase concentration of 226 U/L (normal: 124 - 222 U/L), blood urea nitrogen concentration of 25.4 mg/dL (normal: 8 - 20 mg/dL), and CRP concentration of 16.33 mg/dL (normal: < 0.3 mg/dL). All of these variables were above the normal range. Urinary findings were normal. Rapid antigen tests for influenza, pneumococcus, and mycoplasma were negative. Therefore, ultrasonography of the abdomen was performed, but no major abnormalities were observed. Echocardiography also showed no abnormalities. Subsequently, plain CT of the chest and the abdomen was performed, and this showed bronchial wall thickening in an upper lobe of the right lung, which was not evident on a chest X-ray film (Fig. 2). Sputum culture samples for general and acid-fast bacteria and blood culture samples were collected soon after admission. He was initially diagnosed with bronchopneumonia. Intravenous administration of levofloxacin (LVFX, 500 mg/day) and ampicillin/sulbactam (ABPC/SBT, 6 g/day) was started.

On day 2, the patient's temperature started to fall. A sputum smear detected no obvious acid-fast bacteria. Notably, gram-positive cocci were detected in blood culture samples and these were identified as *S. pyogenes* on day 4. Moreover, *S. pyogenes* was detected from sputum culture samples. Streptococci that were detected from sputum and blood culture samples showed the same antibiotic susceptibility and were sensitive to LVFX and ABPC. On day 5, his temperature returned to normal and the WBC count was normalized (5.9 $\times 10^9$ cells/L). Therefore, administration of LVFX was terminated. With regard to sputum culture, species-specific polymerase chain reaction assays for acid-fast bacteria, including *Mycobacterium tuberculosis (M. tuberculosis), M. avium, M. intracellulare*, and *M. kansasii*, were negative. On day 9, his symptoms including fever, sore throat, and increased sputum excretion, completely resolved and the CRP level returned to normal (0.19 m/dL). Therefore, oral amoxicillin (750 mg/day) was substituted for intravenous administration of LVFX and ABPC/SBT on day 10. He was discharged from our hospital on day 10 and took oral amoxicillin for 10 days. No exacerbation was observed thereafter. Image findings of bronchopneumonia disappeared on plain chest CT 1 month after discharge. The patient was lost to follow-up after this time.

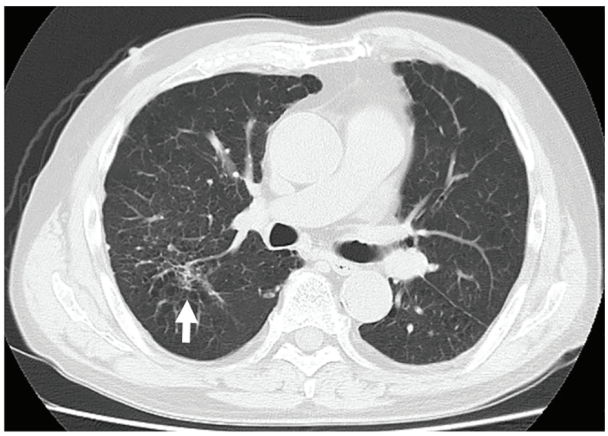

Figure 2. A plain computed tomography image of the lung on admission. Increased density around the lobar bronchi in the right upper lobe of the lung, which suggested bronchopneumonia (white arrow), and emphysematous changes in both lungs were observed.

Discussion

Pneumonia caused by *S. pyogenes* is an uncommon cause of community-acquired pneumonia, but it may show a high mortality rate. Barnham et al [7] reviewed 17 cases of *S. pyogenes* pneumonia and reported its high mortality rate (47%), as well as a high detection rate (88%) of *S. pyogenes* from blood culture samples. They reported that 63% of patients who did not survive died within 1 day after hospitalization [7]. A recent study also showed a high mortality rate (20%) of *S. pyogenes* pneumonia, with half of the patients dying within 24 h after admission, and the detection rate of *S. pyogenes* from blood culture was 43% (17/40 cases) [8]. *S. pyogenes* pneumonia commonly occurs in winter and spring [7, 8]. Hypertension, chronic obstructive pulmonary disease, and diabetes have been reported as frequent comorbidities in patients with *S. pyogenes* pneumonia [7, 8]. With regard to complications of *S. pyogenes* pneumonia, pleural effusion, cavity formation in the lungs, septicemia, and septic shock have been reported [7, 8]. Symptoms mimicking scarlet fever, including desquamating rash, may be observed in rare cases [7]. Despite these serious conditions, there have been few other studies on the clinical presentation, prognosis, and characteristics of *S. pyogenes* pneumonia. To the best of our knowledge, 16 case reports de-

Table 1. Sixteen Adult Cases of *S. pyogenes* Pneumonia Reported in the Past Three Decades

Author	Year	Age (years), sex	Comorbidity	Duration from onset to hospitalization	Blood pressure, pulse rate, and body temperature on admission	Administered antibiotics for initial treatment	Complication emerging after hospitalization	Blood culture-positive	Outcome
McMurray et al [9]	1987	33, female	-	72 h	80/50 mm Hg, 120 bpm, 39 °C	ABPC + EM + MFIPC + GM	Pleural effusion	-	Dead on the day of hospitalization
McIntyre et al [10]	1989	30, female	Bronchial asthma	2 days	95/65 mm Hg, 100 bpm, 38.7 °C	ABPC	Lung abscess	+	Alive
McWhinney et al [11]	1991	26, male	Intravenous drug misuser	2 days	60/40 mm Hg, 60 bpm, 35 °C	EM + MFIPC	Pleural effusion, lung abscess	+	Alive
Hamour et al [12]	1994	53, male	Herpes labialis, oral candidiasis	1 week	117/70 mm Hg, 120 bpm, 38 °C	CTX + EM + CPFX	Pleural effusion, atrial fibrillation and flutter, desquamating skin rash	-	Alive
Brusch et al [13]	1996	51, male	-	1 week	105/55 mm Hg, 130 bpm, 38.5 °C	VCM + EM + DOXY	Supraventricular tachycardia, multiple organ failure	-	Dead on the second hospital day
Kalima et al [14]	1998	35, female	Flu-A	1 week	Unknown	PC-G + CLDM	Pneumothorax, bronchopleural fistula	+	Alive
Birch and Gowardman [15]	2000	33, male	-	1 week	110/55 mm Hg, 130 bpm, 40.3 °C	CTX + EM	Pleural effusion, multiple organ failure, DIC	+	Alive
Taylor and Barkham [16]	2002	89, male	COPD, stroke	2 days	140/100 mm Hg, pulse rate unknown, 38 °C	CTRX	-	+	Dead on the day of hospitalization
Papadas et al [17]	2008	24, female	Tonsillitis	9 days	Blood pressure and pulse rate unknown, 40 °C	AMPC/CVA + CAM	-	+	Alive
Saldias et al [18]	2008	35, female	Thyroid cancer	Within 1 day	106/60 mm Hg, 90 bpm, 37.8 °C	CTRX + CLDM	Acute respiratory failure, septic shock	+	Alive
Izumiyama et al [19]	2008	30, female	-	1 week	70/40 mm Hg, 160 bpm, 37.6 °C	MEPM + MINO	Acute respiratory failure, septic shock	+	Dead 7 h after hospitalization
Weinblatt et al [20]	2009	54, female	Rheumatoid arthritis	1 week	110/70 mm Hg, 110 bpm, 38.9 °C	CTRX + CLDM + VCM	Acute respiratory failure, pneumothorax, septic shock	-	Dead 8 h after hospitalization
Abei et al [21]	2010	39, female	Flu-B	3 days	Unknown	PIPC/TAZ + CLDM	Acute respiratory failure, septic shock	+	Alive
Abei et al [21]	2010	27, female	Flu-B	3 days	Unknown	AMPC/CVA + CAM	Acute respiratory failure, septic shock, pulmonary hemorrhage	+	Dead 18 days after hospitalization
Lam et al [22]	2013	34, male	Flu-B	5 days	Unknown	MEPM + AZM + VCM	Septic shock, multiple organ failure	+	Alive
Akuzawa (our case)	2016	78, male	Obsolete pulmonary tuberculosis	4 days	124/72 mm Hg, 96 bpm, 39.4 °C	ABPC/SBT	-	+	Alive

ABPC: aminobenzylpenicillin; ABPC/SBT: aminobenzylpenicillin/sulbactam; AMPC/CVA: amoxicillin/clavulanic acid; CAM: clarithromycin; CLDM: clindamycin; COPD: chronic obstructive pulmonary disease; CPFX: ciprofloxacin; CTRX: ceftriaxone; AZM: azithromycin; CTX: cefotaxime; DIC: disseminated intravascular coagulation; DOXY: doxycycline; EM: erythromycin; GM: gentamycin; MEPM: meropenem; MFIPC: flucloxacillin; MINO: minocycline; PC-G: penicillin G; PIPC/TAZ: piperacillin/tazobactam; VCM: vancomycin.

scribing patients with *S. pyogenes* pneumonia, including our case, have been published in the past three decades (Table 1) [9-22]. The duration from onset of *S. pyogenes* pneumonia to hospitalization varied from 1 to 9 days, and the mean duration was 4.8 ± 2.4 days. Among these 16 cases, six (38%) patients died after hospitalization [9, 13, 16, 19-21] and four of the six patients who did not survive died within 1 day after hospitalization [9, 16, 19, 20]. Blood culture samples were positive for *S. pyogenes* in 12 (75%) patients. With regard to the background of these patients, three had a history of respiratory illness (asthma, chronic obstructive pulmonary disease, and obsolete pulmonary tuberculosis) [10, 16], one underwent anti-tumor necrosis factor therapy using adalimumab for rheumatoid arthritis [20], one was an intravenous drug abuser [11], and one underwent thyroidectomy for treatment of thyroid cancer 5 days before onset of *S. pyogenes* pneumonia [18]. However, apart from these six patients having underlying diseases or risk factors of immunodeficiency, the remaining 10 (63%) patients were previously healthy. Moreover, based on duration from onset to hospitalization, the patients could be divided into two groups: 1) ≤ 5-day group (shorter than average duration, nine patients) and 2) > 5-day group (longer than average duration, seven patients). In the ≤ 5-day group, three of nine (33%) patients died after hospitalization [9, 16, 21], while three of seven (43%) patients died in the > 5-day group [13, 19, 20]. Interestingly, in the ≤ 5-day group, three patients showed co-infection of influenza B virus and *S. pyogenes*, and one of these three patients died [21, 22]. However, in the > 5-day group, there was only one case of influenza A virus (IAV) infection. Acute viral tract infections can be associated with the occurrence of *S. pyogenes* pneumonia, reflecting virus-induced epithelial damage in the respiratory tract together with transient immune suppression [7]. Tamayo et al [8] also suggested the potential of influenza B virus for aggravation of *S. pyogenes* pneumonia. Therefore, physicians should be careful about preceding influenza virus infection in patients with *S. pyogenes* pneumonia.

Previous studies have shown that IAV infection facilitates *S. pyogenes* infection in the respiratory tract. IAV infection increases the abundance of fibrinogen 4 days after infection [1]. Fibrinogen is important for *S. pyogenes* adherence and internalization within epithelial cells via M protein, which is adhesion molecule on the streptococcal surface and triggers uptake of bacteria into the host cells [23]. Production of fibronectin, another important ligand for *S. pyogenes*, also increases during IAV infection [1]. On the other hand, viral hemagglutinin and neuraminidase also stimulate expression of adhesion molecules on the cell surface [1]. These findings suggest that IAV infection may promote *S. pyogenes* infection in the respiratory tract. The outcome of IAV and *S. pyogenes* co-infections in murine models varies depending on the specific viral and bacterial strains [1]. However, whether influenza B virus more rapidly deteriorates *S. pyogenes* infection than IAV is unclear because of a lack of adequate comparative studies. In addition, limitations of this report include our inability to determine the M protein serotype of the *S. pyogenes* strain detected from our patient. Additionally, we were unable to show the genetic identity of the *S. pyogenes* strains obtained from sputum and blood culture samples. Further research to determine other factors, including preceding viral infection other than influenza and mechanisms exacerbating *S. pyogenes* pneumonia, is required.

In conclusion, we present a case of *S. pyogenes* pneumonia. Although our patient's clinical course was good, our literature review showed a high mortality rate of *S. pyogenes* pneumonia (38%). Notably, 63% of the reviewed patients presenting with *S. pyogenes* pneumonia were previously healthy. A high detection rate (75%) of *S. pyogenes* from blood culture samples is also a characteristic in *S. pyogenes* pneumonia. Although *S. pyogenes* is not a major pathogen of community-acquired pneumonia, physicians should be aware of its characteristics.

Grant Support

No support was received specifically for this work.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Herrera AL, Huber VC, Chaussee MS. The Association between Invasive Group A Streptococcal Diseases and Viral Respiratory Tract Infections. Front Microbiol. 2016;7:342.
2. O'Loughlin RE, Roberson A, Cieslak PR, Lynfield R, Gershman K, Craig A, Albanese BA, et al. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000-2004. Clin Infect Dis. 2007;45(7):853-862.
3. Keefer CS, Rantz LA, Rammelkamp CH. Hemolytic Streptococcal Pneumonia and Empyema: A Study of 55 Cases with Special Reference to Treatment. Trans Am Clin Climatol Assoc. 1940;56:31-56.
4. Basiliere JL, Bistrong HW, Spence WF. Streptococcal pneumonia. Recent outbreaks in military recruit populations. Am J Med. 1968;44(4):580-589.
5. Welch CC, Tombridge TL, Baker WJ, Kinney RJ. beta-hemolytic streptococcal pneumonia: report of an outbreak in a military population. Am J Med Sci. 1961;242:157-165.
6. Crum NF, Russell KL, Kaplan EL, Wallace MR, Wu J, Ashtari P, Morris DJ, et al. Pneumonia outbreak associated with group a Streptococcus species at a military training facility. Clin Infect Dis. 2005;40(4):511-518.
7. Barnham M, Weightman N, Anderson A, Pagan F, Chapman S. Review of 17 cases of pneumonia caused by

Streptococcus pyogenes. Eur J Clin Microbiol Infect Dis. 1999;18(7):506-509.
8. Tamayo E, Montes M, Vicente D, Perez-Trallero E. Streptococcus pyogenes Pneumonia in Adults: Clinical Presentation and Molecular Characterization of Isolates 2006-2015. PLoS One. 2016;11(3):e0152640.
9. McMurray JJ, Fraser DM, Brogan O. Fatal Streptococcus pyogenes pneumonia. J R Soc Med. 1987;80(8):525-526.
10. McIntyre HD, Armstrong JG, Mitchell CA. Streptococcus pyogenes pneumonia with abscess formation. Aust N Z J Med. 1989;19(3):248-249.
11. McWhinney PH, Nathwani D. Streptococcus group A pneumonia in an intravenous drug misuser (IVDM). Eur Respir J. 1991;4(6):761-763.
12. Hamour A, Bonnington A, Wilkins EG. Severe community acquired pneumonia associated with a desquamating rash due to group A beta-haemolytic streptococcus. J Infect. 1994;29(1):77-81.
13. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 13-1996. A 51-year-old man with the adult respiratory distress syndrome. N Engl J Med. 1996;334(17):1116-1123.
14. Kalima P, Riordan T, Berrisford RG, Sarsfield PT. Necrotizing pneumonia associated with group A streptococcal bacteraemia. Eur J Clin Microbiol Infect Dis. 1998;17(4):296-298.
15. Birch C, Gowardman J. Streptoccocus pyogenes: a forgotten cause of severe community-acquired pneumonia. Anaesth Intensive Care. 2000;28(1):87-90.
16. Taylor MB, Barkham T. Fatal case of pneumonia caused by a nonhemolytic strain of Streptococcus pyogenes. J Clin Microbiol. 2002;40(6):2311-2312.
17. Papadas TA, Karkoulias KP, Mastronikolis NS, Sampsonas FL, Spiropoulos KB. Concurrent tonsillitis and pneumonia due to S. pyogenes. Clin Ter. 2008;159(1):33-34.
18. Saldias F, Yanez J, Saldias V, Diaz O. [Community-acquired pneumonia caused by Streptococcus pyogenes: report of one case]. Rev Med Chil. 2008;136(12):1564-1569.
19. Izumiyama N, Miki H, Shishikura Y, Kawaguchi C, Saitou W, Kikuchi T, Kumagai K, et al. [Case of severe streptococcus pyogenes pneumonia with streptococcus toxic shock syndrome]. Nihon Kokyuki Gakkai Zasshi. 2008;46(6):488-492.
20. Weinblatt ME, Abbott GF, Koreishi AF. Case records of the Massachusetts General Hospital. Case 13-2009. A 54-year-old woman with respiratory failure and a cavitary lesion in the lung. N Engl J Med. 2009;360(17):1770-1779.
21. Aebi T, Weisser M, Bucher E, Hirsch HH, Marsch S, Siegemund M. Co-infection of Influenza B and Streptococci causing severe pneumonia and septic shock in healthy women. BMC Infect Dis. 2010;10:308.
22. Lam KW, Sin KC, Au SY, Yung SK. Uncommon cause of severe pneumonia: co-infection of influenza B and Streptococcus. Hong Kong Med J. 2013;19(6):545-548.
23. Rohde M, Cleary PP. Adhesion and invasion of streotococcus pyogenes into host cells and clinical relevance of intracellular streptococci. In: Streptococcus pyogenes: basic biology to clinical manifestations [internet]. Ferretti JJ, Stevens DL, Fischetti VA, Eds. Oklahoma City (OK): University of Oklahoma Health Science Center, 2016. Available at http://www.ncbi.nlm.nih.gov/books/NBK333424/.