Nosocomial Pneumonia Likely Caused by *Stenotrophomonas maltophilia* in Two Patients with Polymyositis

Koichi AMANO, Hiroshi MARUYAMA and Tsutomu TAKEUCHI

We report two cases of polymyositis (PM) complicated with nosocomial pneumonia probably caused by *Stenotrophomonas maltophilia*, which was resistant to multiple antimicrobials. In the first case, the chest CT findings and high serum endotoxin level as well as sputum culture results were helpful for the proper diagnosis and the therapy was successful. However the second patient died of a lung abscess in spite of the intensive antibiotic therapy. When PM patients develop pneumonia unresponsive to various antibiotics, a multi-drug-resistant bacteria such as *Stenotrophomonas maltophilia* should be considered as the pathogen. (Internal Medicine 38: 910–916, 1999)

Key words: interstitial pneumonitis, multi-drug-resistant bacteria, opportunistic infection

Introduction

Nosocomial pneumonia is one of the most important complications in patients with connective tissue diseases such as systemic lupus erythematosus (SLE) and polymyositis/dermatomyositis (PM/DM) who are usually treated with high-dose steroids which can adversely affect their prognosis. Among various pathogens, bacteria which are resistant to multiple antimicrobials (multi-resistant) such as methicillin-resistant *staphylococcus aureus* (MRSA) are an emerging therapeutic problem (1). In this report, we describe two cases of PM complicated by nosocomial pneumonia, most likely caused by *Stenotrophomonas maltophilia* (formerly named *Xanthomonas maltophilia*), and discuss the clinical significance of nosocomial pneumonia caused by these multi-drug-resistant bacteria in PM/DM patients.

For editorial comment, see also p 842.

Case Reports

Case 1 (Fig. 1)

A 39-year-old housewife had been ill with fever, general malaise and myalgia in her neck and extremities from January 1996. She was admitted to our hospital on May 22 complaining of worsening proximal muscle weakness. On admission she was 152 cm tall and weighed 45 kg. Her blood pressure was 106/64 mmHg and the pulse was regular (60/min). She

was slightly anemic and many superficial lymph nodes palpable in the cervical, axillary and inguinal regions were soft and not tender. Her lungs were clear. A manual muscle test revealed symmetric proximal muscle weakness involving the neck, deltoids, triceps, biceps, iliopsoas, quadriceps and hamstrings. Laboratory tests revealed elevated serum levels of the myogenic enzymes which were creatine kinase (CK) (8,030 IU/l), lactate dehydrogenase (LDH) (2,038 IU/l) and aspartate aminotransaminase (AST) (257 IU/l). Anti-Jo-1 antibody was negative. Electromyogram (EMG) findings of short duration, low amplitude and myogenic discharges in the affected muscles suggested myopathy. Muscle biopsy from the biceps branchii showed degeneration and regeneration of the muscle fibers with slight infiltration by mononuclear cells. These findings supported the diagnosis of PM, so we started to treat her with 60 mg/day of oral prednisolone (PSL) on June 6. On June 24 the PSL was changed to an equivalent dose (8 mg/day) of betamethazone because of the poor clinical response and edema. Her muscle strength gradually recovered and the serum CK level declined. On August 28 when she was receiving 3.5 mg/day of betamethazone, she developed fever (>38.0°C), cough and sputa. Since the chest X-ray showed no abnormalities (Fig. 2 left), we thought she might have acute bronchitis and prescribed levofloxacin (300 mg/day). However her respiratory symptoms gradually worsened. On September 4, the patient's sputa was collected for the bacteriological examination and levofloxacin was substituted to parenteral piperacillin (PIPC) and tobramycin (TOB) as an empiric therapy against various kinds of bacteria including enterobacteria species. The patient

From the Second Department of Internal Medicine, Saitama Medical Center, Saitama Medical School, Kawagoe

Received for publication February 17, 1999; Accepted for publication June 5, 1999

Reprint requests should be addressed to Dr. Koichi Amano, the Second Department of Internal Medicine, Saitama Medical Center, Saitama Medical School, 1981 Kamoda, Kawagoe, 350-8550

Nosocomial Pneumonia in Two PM Patients

Figure 1. Clinical course of case 1 (H. N.).

developed dyspnea on exertion with a low PaO₂ level (60 mmHg at room air), worsening productive cough and her serum LDH level was elevated (1,696 IU/l) without myogenic enzyme abnormalities. Plain chest X-rays taken on September 5 showed slightly increased opacities in the bilateral lower lung fields (Fig. 2 right), but the finding was unremarkable for a specific diagnosis. Finally, on September 7, we received a report that *Stenotrophomonas maltophilia*, which was resistant to most antibiotics including PIPC, TOB and ofloxacin (OFLX), was isolated from her sputa. And we got another report showing that her serum endotoxin level was a high 246 pg/ml (normal range: <10) on the same day, which supported gram-negative bacterial infection. Moreover, on September 9, high resolution computerized tomography (HRCT) of the chest disclosed a diffuse ground glass appearance in both the upper and lower

lung fields bilaterally (Fig. 3 left). These findings suggested pulmonary infection rather than interstitial pneumonitis (IP), which usually involves subpleural regions in the lower lungs. PIPC and TOB were substituted with a combination of trimethoprim/ sulfamethoxazole (ST), minocycline (MINO) and cefoperazone/sulbactam (CPZ/SBT) based on the result of the antimicrobial susceptibility test (Table 1). The patient's symptoms soon disappeared and both the PaO₂ and the LDH levels improved. One month later the pulmonary opacities disappeared (Fig. 3 right).

Case 2 (Fig. 4)

A 51-year-old housewife visited her neighborhood hospital because of erythematous eruptions in her eyelids and the dorsal sides of MP (metacarpo-phalangeal) joints in November

August 28

September 5

Figure 2. Plain chest X-ray of case 1 (H. N.). The plain chest X-ray of August 28, 1996 (left) revealed no abnormalities, but on September 5 diffuse ground glass opacities became apparent in the bilateral lower lung fields (right).

September 9

October 3

Figure 3. HRCT of case 1 (H. N.). On September 9, 1996 (left) the HRCT revealed a diffuse ground glass appearance in both the upper and lower lung fields bilaterally. With clinical improvement these findings disappeared in the follow-up image obtained on October 3 (right).

Table 1. *In vitro* Antibiotic Susceptibility Test in Case 1 (H. N.)

Antimicrobial	MIC (mg/ml)	R; resistant S; sensitive
Piperacillin (PIPC)	>64	R
Clavulanic acid/ticarcillin (CVA/TIPC)	<16	S
Cefoperazone (CPZ)	>32	R
Cefoperazone/sulbactam (CPZ/SBT)	<16	S
Ceftazidime (CAZ)	>16	R
Cefsulodin (CFS)	>16	R
Flomoxef (FMOX)	>16	R
Imipenem/cilastatin (IPM/CS)	>8	R
Aztreonam (AZT)	>16	R
Gentamicin (GM)	>8	R
Tobramycin (TOB)	>8	R
Amikacin (AMK)	>32	R
Isepamicin (ISP)	>16	R
Minocycline (MINO)	<1	S
Fosfomycin (FOM)	>16	R
Ofloxacin (OFLX)	>4	R
Trimethoprim/ sulfamethoxazole (ST)	<2	S

Stenotrophomonas maltophilia isolated from the sputa was resistant to most antimicrobials, including PIPC, TOB, OFLX which were used in the early course of her illness. Only 4 antibiotics (CVA/TIPC, CPZ/SBT, MINO, ST) proved to be effective against the pathogen.

1994, and started to take 20 mg/day PSL on December 25. However her symptoms did not improve and she developed fever, cough and dyspnea. She was referred to our hospital on January 9, 1995.

On admission she had a fever (38.0°C), Gottron's sign on the dorsal sides of her MP joints and heliotrope erythema on her eyelids. A manual muscle strength test revealed symmetric proximal muscle weakness. No other physical abnormalities were found. The laboratory test results included leukocytosis (10,500/mm³) with predominant neutrophils (95%), and elevated levels of serum CK (696 IU/l), LDH (888 IU/l) and CRP (6.4 mg/dl). Anti-Jo-1 antibody was negative. Though her room air PaO₂ level was as low as 50 mmHg, a plain chest X-ray was unremarkable (Fig. 5 left). She was diagnosed as having IP associated with dermatomyositis. The dosage of PSL was increased to 60 mg/day the next hospital day. The dosage of PSL was then reduced to 55 mg/day because she looked better. She developed respiratory failure again and diffuse ground glass opacities, though not prominent, in the lower lung fields on the plain X-ray (Fig. 5 center). The chest HRCT disclosed infiltrative shadows spreading along the bronchi in both the upper and lower lungs bilaterally (Fig. 6). However she was still believed to have worsening IP associated with PM. So methyl-prednisolone pulse therapy (1g/day for 3 days) was started on January 27. On January 30 diffuse opacities with an air bronchogram became apparent in the plain chest X-ray (Fig. 5 right). Her bronchial aspirates yielded several kinds of bacteria, including MRSA, *Enterococcus* and *Stenotrophomonas maltophilia*. As shown in Fig. 4, various antibiotics were used

but the fever persisted. The patient died due to respiratory failure. A postmortem examination disclosed predominant neutrophil infiltration, suggesting she might have died due to lung abscess. The pathogen in this case seemed to be *Stenotrophomonas maltophilia* and/or MRSA, because both were isolated repeatedly during the late course of the disease. According to the antimicrobial susceptibility test (Table 2) and the therapeutic course, it is likely that *Stenotrophomonas maltophilia* may have been more responsible for the development of pneumonia rather than MRSA. Because the patient received the intensive antibiotic therapy against MRSA including MINO, vancomycin and arbekacin, while the therapy did not include OFLX, the only drug to which *Stenotrophomonas maltophilia* was sensitive *in vitro*.

Discussion

Nosocomial pneumonia due to multi-resistant bacteria such as MRSA is currently an emerging therapeutic problem (1), especially in immunocompromized hosts. In addition to MRSA, gram-negative enterobacteria including *Escherichia coli*, *Enterobacter*, *Klebsiella*, *Serratia* and other gram-negative bacilli such as *Pseudomonas* species, are the most common pathogens of these infections. The present cases were believed to have *Stenotrophomonas maltophilia* pneumonia. *Stenotrophomonas maltophilia* is reported to be one of the increasingly common causes of nosocomial infection (2). According to a previous report the annual rate of isolation was 14.1 per 10,000 patient discharges, and the mortality rate was 43% in all patients from whom the organism was cultured (3). Furthermore, most of the isolates were resistant to both aminoglycosides and beta-lactams (60% of the isolates were resistant to all aminoglycosides and 75% were resistant to all beta-lactams) (2, 3). In case 1 (H. N.), it was resistant to most antimicrobials tested, such as PIPC, CPZ, ceftazidime (CAZ), flomoxef (FMOX), cefsulodine (CFS), aztreonam (AZT), imipenem/cilastatin (IPM/CS), gentamicin (GM), TOB, amikacin (AMK) and OFLX, all of which she had never taken before. In case 2 (S. C.), the isolates were only sensitive to OFLX.

Another problem encountered in the present patients was making a differential diagnosis between nosocomial pneumonia and IP associated with PM/DM. In addition to their non-specific clinical features such as fever, cough, dyspnea with low PaO₂ levels and elevated LDH, the ineffectiveness of conventional antibiotics such as beta-lactams and aminoglycosides suggested IP rather than an infection (4) due to *candida*, *cytomegalovirus* or *pneumocystis* pneumonia. Plain chest X-ray findings for *Stenotrophomonas maltophilia* pneumonia are said to exhibit a mostly lobular or lobar pattern (5). However, they may also have a ground glass appearance, as seen in the present cases, since *candida* pneumonia is said to occur as a hematogenously seeded finely nodular diffuse infiltrate in its early stages (6). Though bronchoalveolar lavage is recommended for the differential diagnosis of nosocomial pneumonia (7), it can not always be performed because of the patient's status or other factors. In our two cases, the positive results of

Figure 4. Clinical course of case 2 (S. C.).

the sputum culture and the high serum level of endotoxin may support the diagnosis of *Stenotrophomonas maltophilia* pneumonia.

Since there are many reports indicating that the number of PM/DM patients with IP is increasing (8) and the mortality rate is high in such patients (9), many rheumatologists are making a diagnosis of IP. In one of our earlier studies, more than half of the PM/DM patients who developed respiratory failure had IP, while infections such as tuberculosis, cytomegalovirus pneumonia, fungal pneumonia and *Stenotrophomonas maltophilia* pneumonia were also significant (4). In fact the second case (S. C.) was misdiagnosed as IP when she developed respiratory failure, and the appropriate antibiotic therapy was not started until she was intubated. However, we believe

this experience led us to make a correct diagnosis of *Stenotrophomonas maltophilia* pneumonia in the first case (H. N.).

When a patient does not respond to antimicrobials such as β -lactams, aminoglycosides or fluconazole, nosocomial pneumonia due to multi-drug resistant bacteria such as MRSA and *Stenotrophomonas maltophilia* should always be kept in mind, as should *pneumocystis carinii*, cytomegalovirus and fungal pneumonia other than *candida species*. Lastly, in order to treat patients with nosocomial infections, determining the antibiotic susceptibility pattern of the isolated organisms in the hospital would be helpful.

January 9

January 21

January 30

Figure 5. Plain chest X-ray of case 2 (S. C.). The plain chest X-ray of January 9, 1995 (left) was unremarkable. However diffuse ground glass opacities (center) were observed on January 21 and diffuse opacities became apparent on January 30 (right).

January 24

Figure 6. HRCT of case 2 (S. C.). A chest HRCT disclosed infiltrative shadows along the bronchi in both the upper and lower lung fields bilaterally.

Table 2. *In vitro* Antibiotic Susceptibility Tests on Bacteria Isolated from the Sputa of Case 2 (S. C.)

Antimicrobial	<i>Stenotrophomonas maltophilia</i>	<i>Enterococcus</i>	MRSA
Ampicillin (ABPC)	n.d.	++	–
Piperacillin (PIPC)	–	++	–
Cefoperazone (CPZ)	–	n.d.	n.d.
Ceftazidime (CAZ)	–	n.d.	n.d.
Cefsulodin (CFS)	–	n.d.	n.d.
Flomoxef (FMOX)	n.d.	n.d.	–
Imipenem/cilastatin (IPM/CS)	–	++	–
Aztreonam (AZT)	–	n.d.	n.d.
Gentamicin (GM)	–	n.d.	–
Tobramycin (TOB)	–	–	–
Amikacin (AMK)	–	n.d.	n.d.
Arbekacin (ABK)	n.d.	n.d.	++
Minocycline (MINO)	–	+	+
Fosfomycin (FOM)	+	n.d.	–
Ofloxacin (OFLX)	++	–	+
Vancomycin (VCM)	n.d.	n.d.	+

–; resistant +; sensitive

Stenotrophomonas maltophilia was resistant to most antimicrobials, including MINO, and sensitive only to FOM and OFLX, which she had never taken before.

References

- 1) File TM Jr. Overview of resistance in the 1990s. *Chest* **115** (3 Suppl): 3S–8S, 1999.
- 2) Denton M, Kerr KG. Microbiological and clinical aspects of infection associated with *Stenotrophomonas maltophilia*. *Clin Microbiol Rev* **11**: 57–80, 1998.
- 3) Morrison AJ Jr, Hoffmann KK, Wenzel RP. Associated mortality and clinical characteristics of nosocomial *Pseudomonas maltophilia* in a university hospital. *J Clin Microbiol* **24**: 52–55, 1986.
- 4) Amano K, Maruyama H, Mori S, Takeuchi T. Respiratory failure in polymyositis and dermatomyositis: differential diagnosis between pulmonary infection and interstitial pneumonitis. *Kansenshogaku Zasshi* **72**: 517–525, 1998.
- 5) Fujita J, Yamadori I, Xu G, et al. Clinical features of *Stenotrophomonas maltophilia* pneumonia in immunocompromised patients. *Respir Med* **90**: 35–38, 1996.
- 6) Edwards Jr JE. *Candida* species (chapter 237). in: *Principles and Practice of Infectious Diseases*. 4th ed. Mandell GL, Bennett JE, Dolin R Ed. Churchill Livingstone, New York, 1996: 2289–2306.
- 7) Lipchik RJ, Kuzo RS. Nosocomial pneumonia. *Radiol Clin North Am* **34**: 47–58, 1996.
- 8) Songcharoen S, Raju SF, Pennebaker JB. Interstitial lung disease in polymyositis and dermatomyositis. *J Rheumatol* **7**: 353–360, 1980.
- 9) Arsura EL, Greenberg AS. Adverse impact of interstitial pulmonary fibrosis on prognosis in polymyositis and dermatomyositis. *Semin Arthritis Rheum* **18**: 29–37, 1988.