CASE REPORT

A Chronic Respiratory Pasteurella multocida Infection Is Well-Controlled by Long-Term Macrolide Therapy

Masafumi Seki¹, Tomomi Sakata², Masahiro Toyokawa³, Isao Nishi² and Kazunori Tomono¹

Abstract

A 57-year-old woman with severe bronchiectasis frequently received antibiotics, including penicillin, for acute exacerbations due to Pasteurella multocida. Although the bacteria showed a decrease in antibiotic susceptibility, her symptoms and X-ray findings became stable, and severe exacerbations were not observed for the last few years after a low-dose erythromycin treatment was started. The development of a respiratory infection with Pasteurella multocida is relatively uncommon, but it can be controlled by immunomodulation which is associated with long-term macrolide therapy.

Key words: chronic respiratory infection, macrolides, Pasteurella multocida, opportunistic pathogen

(Intern Med 55: 307-310, 2016)  (DOI: 10.2169/internalmedicine.55.4929)

Introduction

Pasteurella species are highly prevalent among animals and have become one of the most important opportunistic pathogens that are associated with epizootic outbreaks in humans (1). Among these species, P. multocida is the most prevalent in human infections, and it is usually acquired through contact with animals; including bites, scratches, or contact with mucous secretions derived from dogs, cats, and birds (2, 3).

Common symptoms of pasteurellosis on human skin are swelling, diffuse or localized inflammation with redness and pain, and bloody or purulent exudate at the animal bite sites (1, 4). However, it is possible that a respiratory infection can develop in patients with chronic pulmonary disease (1, 4, 5). In these cases, pasteurellosis can also present as a severe bilateral pneumonia and cause lymphadenopathy, epiglottitis, and abscess formation with increased sputum and chest pain (5).

In this report, a case of chronic respiratory infection due to P. multocida with bronchiectasis is described. Bacteria isolated from the patient’s sputum showed a decrease in antibiotic susceptibility after the patient had received treatment for frequent exacerbations, but the patient’s condition could be successfully controlled by long-term macrolide therapy.

Case Report

A 57-year-old woman visited our university hospital in December 2011 with a cough, chronic sputum, and mild recurrent exertional dyspnea. She had a previous history of severe pneumonia when she was 10 years old and bronchiectasis that affected both lungs (Fig. 1A, D).

Physical examination showed a thin, slightly febrile woman, with slight clubbing of the fingers and no cyanosis. Coarse breath sounds and scattered inspiratory rhonchi were heard throughout both lung fields. Laboratory data included a WBC count of 6,320/μL (neutrophils 70.3%) and a C-reactive protein (CRP) level of 0.37 mg/dL.

P. multocida, which is known to colonize dogs, was isolated from her sputum (Fig. 2), and it demonstrated susceptibility to antibiotics at that time (Table). Phagocytosis of the bacilli was observed, and P. multocida was semi-quantitatively cultured as (3°), which suggested >10⁷ cfu/mL. No mycobacterial species or Pseudomonas species were collected from her sputum during the follow-up period. Her condition was generally good, but she developed frequent exacerbations every one or two months after the first visit. She received antibiotics, including oral amoxicillin/clavula-

¹Division of Infection Control and Prevention, Osaka University Hospital, Japan and ²Laboratory for Clinical Investigation, Osaka University Hospital, Japan

Received for publication January 9, 2015; Accepted for publication March 15, 2015

Correspondence to Dr. Masafumi Seki, sekimm-ngs@umin.ac.jp
nate and minocycline, from December 2011 to 2012 in the outpatient department and became afebrile each time, but she required home oxygen therapy that started in July 2012.

In December 2012, *P. multocida* was continuously isolated from her sputum and semi-quantitative culture results still indicated an abundant amount of *P. multocida* (3+), even though she ceased being a pet owner. *P. multocida* drug susceptibility decreased, especially to penicillin (Table). Her chest radiography also showed increased consolidations, centrilobular granular shadows with mucoid impaction, and cystic bronchiectasis (Fig. 1B, E).

Due to concerns about the increase in antibiotic resistance, the patient was given oral erythromycin (400 mg/day) in January 2013, which was half of the usual dose, but appropriate for use as an immunomodulatory drug, although the isolated *P. multocida* showed no susceptibility to erythromycin from the start of follow-up for this patient (Table).

After she started to receive the erythromycin, the amount of sputum did not change and it became serous, although the number of *P. multocida* remained high (3+). Furthermore, no exacerbations with respiratory symptoms had been observed, and the chest imaging results did not reveal a progression of symptoms in December 2014 (Fig. 1C, F).

**Discussion**

Pulmonary infections with *P. multocida* are uncommon, but there has been a recent increase in the number of such cases being reported (1). The patients are usually middle-aged men with a clinical diagnosis of chronic respiratory diseases, including bronchiectasis. In addition, about 80% of the reported patients have a history with antecedent exposure to infected animals and pets. Although the present patient was a woman, her age, underlying pulmonary disease, and pet history were consistent with previously reported cases (2, 4).
**Table.** Drug Susceptibility of *Pasteurella multocida* Isolated from the Patient (sputum).

| Date      | 2011 Dec | 2012 Jul | 2012 Dec | 2013 Jan | 2013 May | 2013 Dec | 2014 Apr |
|-----------|----------|----------|----------|----------|----------|----------|----------|
| Ampicillin| 0.25, S  | 0.5, S   | 2, R     | 1, R     | 2, R     | >4, R    | 2, R     |
| Penicillin G| 0.12, S | 0.5, S   | 1, R     | 1, R     | >4, R    | 1, R     | 2, R     |
| Ceftriaxone| ≤0.12, S | ≤0.12, S | ≤0.12, S | ≤0.12, S | ≤0.12, S | ≤0.12, S | ≤0.12, S |
| AMPC/CVA  | ≤1, S    | ≤1, S    | 2, R     | 1, R     | ≤1, S    | 1, R     | 2, R     |
| Erythromycin| >1, R  | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    |
| Clarithromycin| >1, R  | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    |
| Azithromycin| >1, R  | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    | >1, R    |
| Tetracycline| ≤0.5, S | 1, S     | ≤0.5, S  | ≤0.5, S  | 2, R     | 2, R     | 2, R     |
| Levofloxacin| ≤0.25, S| ≤0.25, S | ≤0.25, S | ≤0.25, S | ≤0.25, S | ≤0.25, S | ≤0.25, S |
| Sulfamethoxazole/Trimethoprim| ≤0.5, S| ≤0.5, S  | ≤0.5, S  | ≤0.5, S  | ≤0.5, S  | ≤0.5, S  | ≤0.5, S  |

Each number indicates minimum inhibitory concentration (MIC) of each antibiotic for *P. multocida*.

AMPC/CVA: amoxicillin/clavulanate, S: sensitive, R: resistant

*P. multocida* sometimes causes sepsis and bacteremia in many animals, but the most common human infection with *P. multocida* is a local cellulitis following animal-inflicted wounds that are related to dogs or cat bites and scratches (1, 3). Recognition of clinical disease with *P. multocida* requires a knowledge of its pathogenicity because a delay in diagnosis may result in the progression of severe pneumonia and abscess formation (1).

The present patient ceased being a pet owner and received antibiotics after it was discovered that she had a *P. multocida* infection, but *P. multocida* continued to be isolated from her sputum in high numbers (3’). Recognition of clinical disease with *P. multocida* requires a knowledge of its pathogenicity because a delay in diagnosis may result in the progression of severe pneumonia and abscess formation (1).

The present patient ceased being a pet owner and received antibiotics after it was discovered that she had a *P. multocida* infection, but *P. multocida* continued to be isolated from her sputum in high numbers (3’). Recognition of clinical disease with *P. multocida* requires a knowledge of its pathogenicity because a delay in diagnosis may result in the progression of severe pneumonia and abscess formation (1).

The authors state that they have no Conflict of Interest (COI).

Masafumi Seki and Tomomi Sakata contributed equally to this work.

**References**

1. Wilson BA, Ho M. *Pasteurella multocida*: from zoonosis to cellular microbiology. Clin Microbiol Rev 26: 631-655, 2013.
2. Beyt BE Jr, Sondag J, Roosevelt TS, Bruce R. Human pulmonary pasteurellosis. JAMA 242: 1647-1648, 1997.
3. Holst E, Rollof J, Larsson L, Nielsen JP. Characterization and distribution of Pasteurella species recovered from infected humans. J Clin Microbiol 30: 2984-2987, 1992.
4. Rollof J, Johansson PJ, Holst E. Severe *Pasteurella multocida* infections in pregnant women. Scand J Infect Dis 24: 453-456, 1992.
5. Myers EM, Ward S, Myers JP. Life-threatening respiratory pasteurellosis associated with palliative pet care. Clin Infect Dis 54: e55-e57, 2012.

6. Kakeya H, Seki M, Izumikawa K, et al. Efficacy of combination therapy with oseltamivir phosphate and azithromycin for influenza: a multicenter, open-label, randomized study. PLoS One 9: e91293, 2014.

7. Zarogoulidis P, Papanas N, Kioumis I, Chatzaki E, Maltezos E, Zarogoulidis K. Macrolides: from in vitro anti-inflammatory and immunomodulatory properties to clinical practice in respiratory diseases. Eur J Clin Pharmacol 68: 479-503, 2012.

8. Kaneko Y, Yanagihara K, Seki M, et al. Clarithromycin inhibits overproduction of muc5ac core protein in murine model of diffuse panbronchiolitis. Am J Physiol Lung Cell Mol Physiol 285: L847-L853, 2003.

9. Yanagihara K, Seki M, Cheng PW. Lipopolysaccharide induces mucus cell metaplasia in mouse lung. Am J Respir Cell Mol Biol 24: 66-73, 2001.

10. Imamura Y, Yanagihara K, Mizuta Y, et al. Azithromycin inhibits MUC5AC production induced by the Pseudomonas aeruginosa autoinducer N-(3-Oxododecanoyl) homoserine lactone in NCI-H292 Cells. Antimicrob Agents Chemother 48: 3457-3461, 2004.

11. Kudoh S, Azuma A, Yamamoto M, Izumi T, Ando M. Improvement of survival in patients with diffuse panbronchiolitis treated with low-dose erythromycin. Am J Respir Crit Care Med 157: 1829-1831, 1998.

12. Jaffé A, Francis J, Rosenthal M, Bush A. Long-term azithromycin may improve lung function in children with cystic fibrosis. Lancet 351: 420, 1998.

13. Tamaoki J, Isono K, Sakai N, Kanemura T, Konno K. Erythromycin inhibits Cl secretion across canine tracheal epithelial cells. Eur Respir J 5: 234-238, 1992.

14. Malott RJ, Lo YR. Studies on the production of quorum-sensing signal molecules in Mannheimia haemolytica A1 and other Pasteurellaceae species. FEMS Microbiol Lett 206: 25-30, 2002.

© 2016 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html