



Clinical characteristics and treatment outcomes of patients with pneumonia caused by *Raoultella planticola*

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Background: *Raoultella planticola*, considered to be an environmental organism, is a rare cause of human infections. Although in recent years the frequency of *R. planticola* infections reported in the literature has increased, few cases of pneumonia caused by *R. planticola* have been described. Here, we investigate the clinical characteristics, management, and clinical outcomes of pneumonia caused by *R. planticola*.

Methods: Consecutive patients with pneumonia caused by *R. planticola* were included. The medical records of patients with *R. planticola* pneumonia treated at Dankook University Hospital from January 2011 to December 2017 were collected.

Results: A total of 11 adult patients with *R. planticola* pneumonia were diagnosed and treated [10 males and 1 female; median age, 70 years (range: 51–79 years)]; 5 patients had underlying malignant conditions (45.5%). Antibacterial susceptibility testing showed that all isolates of *R. planticola* were susceptible to cephalosporins, carbapenems, fluoroquinolones, aminoglycosides, and beta-lactams/beta-lactamase inhibitors. Chest imaging revealed consolidation (8/11, 72.7%), ground-glass opacity (5/11, 45.5%), pleural effusion (5/11, 45.5%), and micronodules (3/11, 27.3%). Four patients (36.4%) required mechanical ventilation; three survived but one died of multiple organ dysfunction syndrome (principally pneumonia and septic shock).

Conclusions: *R. planticola* pneumonia occurred mainly in patients with underlying risk factors such as malignant disease, cerebral infarction or hemorrhage, and chronic obstructive pulmonary disease. The organism was sensitive to most antibiotics, and the clinical outcomes were favorable after empirical antibiotic therapy.

Keywords: *Raoultella planticola*; pneumonia; human infection; antibacterial agent

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Introduction

Raoultella planticola has been considered to be a relatively harmless environmental Gram-negative bacterium rarely associated with human clinical infections. However,

in recent years, the frequency of severe *R. planticola* infection reported in the literature has increased (1). This environmental organism, which infrequently causes human infections, is pathogenically similar to *Klebsiella spp.*, which is associated with severe infections (bacteremia,

pneumonia, and urinary tract infections) in hospitalized and immunocompromised patients; *Klebsiella* is responsible for 3–7% of all nosocomial infections (2). Although reports on conjunctivitis, liver abscesses, cholangitis, pancreatitis, prostate conditions, necrotizing fasciitis, and bacteremia caused by *R. planticola* have appeared (3–9), *R. planticola* pneumonia remains rare. To the best of our knowledge, only five cases have been reported in the English-language literature (10–14). The clinical characteristics and outcomes of such infections remain to be investigated. Here, we evaluated the clinical characteristics, management, and clinical outcomes of patients with pneumonia caused by *R. planticola*.

Methods

This was a retrospective chart review of patients with pneumonia caused by *R. planticola* evaluated and treated at Dankook university hospital (a 809-bed referral hospital in Cheonan, South Korea) between January 2011 and December 2017. All pulmonary secretion isolates reported as *R. planticola* were selected and the medical records of these patients were retrieved. The clinical features of the infections were reviewed, and cases with symptoms indicative of pneumonia were included in the present study. We recorded gender, age, any underlying disease, radiographic features, the number of sputum cultures yielding *R. planticola*, the antimicrobial regimen administered, any microbes other than *R. planticola* that were isolated, and outcomes. Clinical infections were defined using established criteria (15). Community-acquired pneumonia (CAP), ventilator-associated pneumonia (VAP), bloodstream infections (BSIs), sepsis, severe sepsis, and septic shock were defined by reference to the Center for Disease Control and American Thoracic Society (ATS) clinical diagnostic criteria (16–19). Pneumonia was defined as the presence of “[a] new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin, which include[s] the new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation” (16–18,20). Chest radiography and computed tomography (CT) scans were reviewed by an experienced radiologist and a single pulmonologist, and consensus diagnoses were attained. We evaluated consolidation, ground-glass opacity (GGO), micronodule status, and pleural effusion.

All kinds of specimens including blood, pulmonary secretion (sputum, tracheal aspirate), urine, pleural fluid (if patients had pleural effusion) were examined for

microbiological examination such as urinary antigen test for *Legionella pneumophila* or *Streptococcus pneumoniae*, serologic test for *Mycoplasma*, *Chlamydia*, *Coxiella*, polymerase chain reaction (PCR) for tuberculosis, respiratory viruses, culture for acid-fast bacilli (AFB), bacteria and fungus from patients with suspected pneumonia. Especially, pulmonary secretions underwent microscopic and bacteriological examinations; we engaged in both non-invasive sampling (sputum expectoration and endotracheal aspiration) and invasive sampling (bronchoscopic bronchial washing). An adequate (“good-quality”) sputum sample exhibited a polymorphonuclear cell:epithelial cell ratio of 25:10 at a magnification of 100× (21). Endotracheal aspirates samples were subjected to quantitative culture using $\geq 10^6$ colony-forming units (CFU)/mL as cutoffs (18). Microbe identification and antibiotic susceptibility tests were performed using the automated VITEK[®] 2 system (bioMérieux, Marcy l’Étoile, France) accompanied by routine bacteriologic methods. All isolates were identified with a probability score exceeding 96%. Antimicrobial susceptibility testing was performed as described by the Clinical and Laboratory Standards Institute (22). We recorded clinical characteristics, radiological features, treatments, and clinical outcomes. The need for informed consent was waived as the work was retrospective in nature. The study was approved by the institutional review board of our hospital.

Results

Clinical characteristics

Overall, 63 patients yielded positive culture results for *R. planticola* in blood, urine, bile, peritoneal fluid, pus, pleural fluid, and/or sputum samples (including those obtained via tracheal aspiration) over the 7-year period. Of these, 24 yielded sputum/tracheal aspirate-positive cultures and 11 met the diagnostic criteria for pneumonia. Most isolates were from sputum (7/11, 63.6%); four were from tracheal aspirates. In seven cases, *R. planticola* was the sole microbial isolate; microbiological examination was noted no bacteria except for *R. planticola*, no viruses, no fungus, and negative AFB smear; in four, additional microbes were also isolated only in the pulmonary secretion, reflecting either airway colonization or contamination. The number of pneumonia cases was 1–2 annually (average =1). Of the 11 patients, 10 were females and the median age was 70 years (range: 51–79 years). The major underlying disease was malignancy (five

Table 1 Characteristics of the 11 patients with *Raoultella planticola* pneumonia

Patient no.	Sex/age (years)	Underlying disease	Source of isolation	Date of first isolation	Positive/total no. of cultures ^a	Other microbes cultured	Antibiotic regimen	LOH	Outcome
1	M/70	NSCLC	Sputum	Jul. 26, 2012	2/3	None	Ceftriaxone	12	Recovered
2	M/68	Cerebral infarction or hemorrhage	Sputum	Jan. 13, 2013	2/3	None	Piperacillin/tazobactam	28	Recovered
3	M/77	COPD	Sputum	Feb. 28, 2013	1/2	None	Ceftriaxone	10	Recovered
4	F/63	ESRD on HD	Sputum	Aug. 26, 2014	2/3	None	Piperacillin/tazobactam	8	Recovered
5	M/53	Cerebral infarction or hemorrhage	Tracheal aspiration	Sep. 8, 2014	2/4	Staphylococcus aureus	Ceftriaxone, vancomycin	13	Recovered
6	M/77	COPD	Tracheal aspiration	Jan. 3, 2015	1/2	None	Piperacillin/tazobactam	14	Recovered
7	M/51	NSCLC	Sputum	Jan. 4, 2015	3/5	Acinetobacter baumannii	Ceftriaxone, meropenem	56	Recovered
8	M/61	Soft palate cancer	Sputum	Mar. 20, 2016	2/4	Acinetobacter baumannii	Meropenem, colistin	46	Recovered
9	M/77	Cerebral infarction or hemorrhage	Sputum	Apr. 23, 2016	2/3	None	Ceftriaxone, ciprofloxacin	34	Recovered
10	M/78	Pancreatic cancer with multiple metastases	Tracheal aspiration	Jun. 8, 2017	2/2	None	Meropenem	6	Expired
11	M/79	AGC with multiple metastases	Tracheal aspiration	Nov. 13, 2017	2/4	Staphylococcus aureus	Meropenem, vancomycin	89	Recovered

^aNumber of positive culture for *Raoultella planticola* and total culture from pulmonary secretion; LOH, length of hospitalization; NSCLC, non-small cell lung cancer; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; HD, hemodialysis; AGC, advanced gastric cancer.


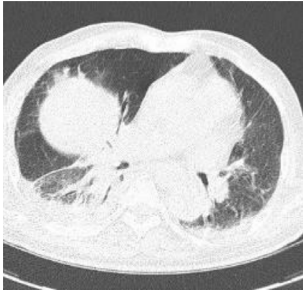

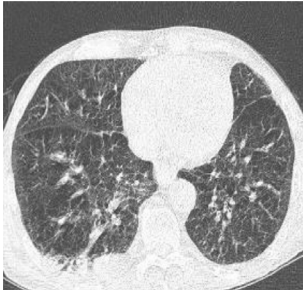

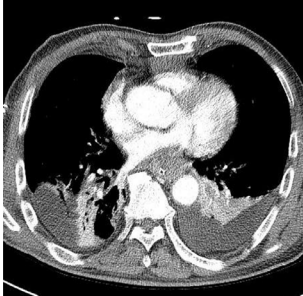
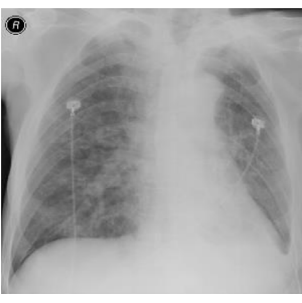

patients). Two patients had solid tumors in, or metastases to, the pancreas, gallbladder, or bile duct; two had lung cancer; and one had soft palate cancer. Three patients had been treated for cerebral infarction or hemorrhage and two had chronic obstructive pulmonary disease. The patients are described in chronological order in *Table 1*.

Radiographic features

Chest radiographs were available for all patients and chest CT scans for 10 (90.9%). Consolidation (8/11, 72.7%),

GGO (5/11, 45.5%), pleural effusion (5/11, 45.5%), and micronodules (3/11, 27.3%) were the most common findings. Diffuse GGO was predominant in three patients. Within 1 week after illness onset, focal consolidation was the predominant finding in six patients, whereas two evidenced multiple bilateral consolidations accompanied by GGO. The right and left lower lobes were most commonly involved (n=7 for both), followed by the right middle lobe (n=3), left upper lobe (n=2), and right upper lobe (n=2). The typical radiologic findings of the patients are described in the *Table 2*.

Table 2 Representative 4 types of radiologic finding in the patients with *R. planticola* pneumonia

Features	Chest radiography	Chest CT	Pt. No.
Consolidation			1, 2, 3, 5, 7, 8, 10, 11
GGO			2, 4, 6, 7, 8
Pleural effusion			1, 6, 9, 10, 11
Micronodules			1, 9, 11

CT, computed tomography; Pt, patient; GGO, ground glass opacity.

Treatments and clinical outcomes

All patients were admitted; the median hospitalization time was 14 days (range: 6–89 days). Four (36.4%) patients (patients 5, 6, 10, and 11) required mechanical ventilation of median duration 5 days (range: 4–12 days); of these patients,

three survived but one (patient 10) died of multiple organ dysfunction syndrome (principally pneumonia and septic shock). Hospital-acquired pulmonary infections (principally *Acinetobacter baumannii*) developed in three patients (patients 7, 8, and 11). No patient received systemic steroids. In

seven cases, *R. planticola* was the sole microbial isolate; in four cases, although additional microbes (*Staphylococcus aureus* or *Acinetobacter baumannii*) were isolated in their sputum or tracheal aspiration specimens, *R. planticola* were isolated at the same time when they had symptoms or signs of pneumonia, whereas *Staphylococcus aureus* or *Acinetobacter baumannii* were isolated later when antibiotics treatment for *R. planticola* was in progress. Antimicrobial susceptibility testing revealed that all isolates were resistant to ampicillin, but became susceptible when a β -lactamase inhibitor was added. All isolates were susceptible to cephalosporins, all third-generation cephalosporins, carbapenems, fluoroquinolones, tigecycline, and trimethoprim/sulfamethoxazole.

Empirical, broad-spectrum intravenous antibiotics were given to all patients. The antimicrobial agent most frequently used was ceftriaxone (45.5%, 5/11), followed by piperacillin/tazobactam (27.3%, 3/11) and carbapenems (27.3%, 3/11). When positive culture results for *R. planticola* and polymicrobial hospital-acquired pathogens were available, the antimicrobial treatment agents were modified in 36.4% (4/11) of patients. Culture study for pulmonary secretion such as sputum and/or tracheal aspirates samples performed every five to seven days and there was no change in the antimicrobial susceptibility after some days of antibiotic treatment in the all patients. The targeted antimicrobial agents most frequently used were ceftriaxone and piperacillin/tazobactam. Most patients (10/11, 91%) survived infection.

Discussion

R. planticola is an aerobic, non-capsulated, non-motile Gram-negative bacillus of the *Enterobacteriaceae* initially classified as *Klebsiella planticola* or *K. trevisanii*. Further phylogenetic analysis revealed major differences among the eight species of *Klebsiella* (23). In 2001, a new taxonomy was established based on comparative analyses of the 16S rRNA and rpoB genes, resulting in the creation of a new genus, *Raoultella*, which includes *R. planticola*, *R. ornithinolytica*, and *R. terrigena* (24,25). *R. planticola* does not typically infect humans. Several studies estimate that between 9–18% of humans are colonized with the bacterium (25,26). As infection is rare, risk factors associated with infection are largely inferred from case reports. These include an immunocompromised state, invasive medical procedures, seafood consumption, and exposure to aquatic or soil contaminants. Chun *et al.* retrospectively

studied 20 Korean patients with *R. planticola* bacteremia and found that 14 from whom *R. planticola* was the sole microbial isolate recovered after prescription of empirical antibiotics. Of six patients with polymicrobial infections, three died. Antimicrobial susceptibility testing revealed that all strains were susceptible to β -lactamase inhibitors, all tested third-generation cephalosporins, carbapenems, and fluoroquinolone agents (27). Although infections caused by *R. planticola* have increased in number, *R. planticola* pneumonia remains rare. The first case, described by Castanheira *et al.*, involved an 83-year-old female hospitalized to treat CAP. She eventually died of pneumonia and septic shock (10). Tseng *et al.* and Xu *et al.* reported pneumonia caused by a carbapenem-resistant *R. planticola* strain isolated from sputum culture (11,12). More recently, two case reports described patients with pneumonia caused by primary infection with *R. planticola* susceptible to most antibiotics, including cephalosporins, fluoroquinolones, aminoglycosides, and carbapenems (13,14). We found that all *R. planticola* isolates were susceptible to most antibiotics; most patients experienced good outcomes and only one patient, who required mechanical ventilation, died.

In general, *R. planticola* is sensitive to a wide range of antibiotics. However, like *Klebsiella* spp., *R. planticola* can acquire plasmid-borne antibiotic-resistance genes triggering severe, and even fatal, infections (10-12). Carbapenem resistance in *R. planticola* involves the production of carbapenemases, including class A β -lactamase (KPC), class B metal- β -lactamase (IMP-8, NDM-1), and class D β -lactamase (OXA-48) (10,11). Notably, *bla*_{KPC}, *bla*_{IMP-8}, and *bla*_{NDM-1} are usually located on plasmids or transposons, suggesting possible genetic exchange between *R. planticola* and other Enterobacteriaceae, such as *K. pneumoniae* (12). There were very few cases of pneumonia caused by *R. planticola* which could confirm imaging findings. In that cases, it had appeared in various radiologic finding such as consolidation (14), consolidation with pleural effusion (12), and diffuse GGO with consolidation (13). The present study showed that consolidation, GGO, pleural effusion, and micronodules were the most common findings in that order.

R. planticola may infect patients after a traumatic incident in a contaminated environment. Nosocomial infection involves bacterial introduction during an invasive hospital procedure; either dormant colonizers are activated or the instruments are contaminated. Systemic impairment of the host immune system enables dormant colonizers to become invasive. However, enteric fever and bacteremia

have been recorded in an immunocompetent patient (1). We found it difficult to distinguish between pathogenicity and colonization in some cases; however, pulmonary secretions from seven cases grew only *R. planticola*. Four patients exhibited polymicrobial infections, but it is likely that *R. planticola* caused the pneumonia because *R. planticola* emergence coincided with aggravation of the pulmonary infection. Furthermore, the specimens were only adequate; Gram-negative bacilli predominated and bacterial numbers were moderate-to-high in the gram stains and it was also consistent with the result of culture. Hence, it is likely that *R. planticola* caused the pneumonia.

Our study had the potential limitations associated with a retrospective review design. First, there may have been reviewer bias; however, most of the data were collected by the primary author using a standardized method and diagnostic criteria. Second, gram stains and culture for pulmonary secretion including sputum and tracheal aspiration are most often the first diagnostic method for pneumonia. Therefore, it is very important to achieve the adequacy of specimen. Although this study had been conducted with the adequate specimen, the possibility of colonization cannot be completely excluded. Finally, we evaluated only a small number of patients treated in a single center. However, the clinical course was consistently good even among the patients with complications; early administration of intravenous antibiotics obviates pulmonary catastrophe and ensures survival.

In conclusion, *R. planticola* may be an emerging pneumonia pathogen that could infect even immunocompetent humans. The bacterium may become multidrug-resistant, exerting an increasingly heavy toll in terms of morbidity and mortality. Pulmonologists should be familiar with the risk factors for *R. planticola* pneumonia, note the existence of carbapenemase-resistant strains, and promptly diagnose and treat these potentially deadly infections. Further studies are required on this topic.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd.2020.02.56>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The need for informed consent was waived as the work was retrospective in nature. The study was approved by the institutional review board of our hospital.

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