Emergence of *Raoultella ornithinolytica* on O'ahu: A Case of Community-acquired *R. ornithinolytica* Urinary Tract Infection

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Abstract

Human infection with Raoultella ornithinolytica *is rare, with only ten cases having been reported previously. This case report describes a local patient diagnosed with community-acquired* R. ornithinolytica *urinary tract infection in 2014.*

Keywords

Klebsiella, *Raoultella, ornithinolytica*, Hawai'i, urinary tract infection

Introduction

Raoultella ornithinolyitca is a gram negative, non-motile, encapsulated, aerobic bacillus formerly named *Klebsiella ornithinolytica*.[1] It belongs to the family *Enterobacteriaceae*, and has been isolated from insects, fish, and brackish water. This bacterium, along with the closely related species *R. planticola*, has been shown to be the causative agent of histamine toxicity from fish (also known as scombroid syndrome), but is frequently misidentified as *Klebsiella pneumoniae*.[2] Histamine toxicity results from the expression of histidine decarboxylase, which enables the bacterium to convert histidine,[2] and produces symptoms that include flushing, pruritus, headache, and abdominal cramping.[3]

Over the past decade, *R. ornithinolytica* has emerged as an infrequent, but important causal agent of human infections. To our knowledge, ten cases of *R. ornithinolytica* infection have been reported, linking this pathogen to bacteremia and sepsis, and soft tissue and other infections.[4-11] *R. ornithinolytica* expresses ß-lactamase, which provides resistance to commonly used antibiotics.[12] In this report, we describe and discuss a case of community-acquired *R. ornithinolytica* cystitis occurring in Honolulu in 2014.

Case Report

This is a 73-year-old Japanese woman, with a history significant for rheumatoid arthritis, treated with methotrexate, and urosepsis due to community-acquired extended-spectrum ß-lactamase (CA-ESBL) *Escherichia coli* in 2010.[13] She presented to her primary care physician with symptoms of urinary urgency of two days duration, with associated urinary incontinence and cloudy-appearing urine. Pertinent negative symptoms included dysuria, hematuria, flank pain, nausea, vomiting, and abdominal pain. No costovertebral angle tenderness or abdominal tenderness, including suprapubic tenderness, was noted on physical exam. Urinalysis performed during the office visit revealed 1+ nitrites (normal: negative), 3+ leukocyte esterase (normal: negative), 1+ blood (normal: negative), and 15-20 white blood cells per hpf (normal range: 0-5), with the remaining parameters within normal limits. Her urine was sent for culture and sensitivity, during which time she was started on a 3-day course of oral double strength trimethoprim-sulfamethoxazole (TMP-SMX) 160-800 mg BID empirically. Urine culture and sensitivity returned positive for *Raoultella ornithinolytica*, >100,000 CFU/mL, resistant to ampicillin and susceptible to all other tested antibiotics (Table 1). On follow-up two days after completion of the course of TMP-SMX, the patient reported resolution of her urinary symptoms. However, repeat urinalysis continued to show 3+ leukocyte esterase and 15-20 white blood cells per hpf on microscopy. At that time, the patient was started on oral ciprofloxacin 500 mg for 5 days. The patient returned for repeat follow-up 1 day after completion of the course of ciprofloxacin, and urinalysis performed at that time showed negative bacteria and trace white blood cells (< 3/hpf), indicating eradication of *R. ornithinolytica* infection.

Discussion

R. ornithinolytica is a *Klebsiella*-like bacterium that expresses histidine decarboxylase, allowing it to produce histamine toxicity following ingestion of improperly preserved fish.[2] It has also been associated with acute suppuration of the pancreatic duct,[4] enteric fever,[5] renal cysts,[6] bacteremia, and sepsis,[7,9,11] soft tissue infection,[8] and urinary tract infection (UTI).[10] This is the first published case report of community-acquired *R. ornithinolytica* infection in the State of Hawai'i.

Table 1. Urine antibiotic sensitivity report for the patient.

ANTIBIOTIC	SENSITIVITY	MIC*
Ampicillin	Resistant	≥32 µg/mL
Ampicillin-sulbactam	Susceptible	4 µg/mL
Amikacin	Susceptible	≤2 µg/mL
Ceftriaxone	Susceptible	≤1 µg/mL
Gentamicin	Susceptible	≤1 µg/mL
Tobramycin	Susceptible	≤1 µg/mL
Cefepime	Susceptible	≤1 µg/mL
Ciprofloxacin	Susceptible	≤0.25 µg/mL
Nitrofurantoin	Susceptible	≤16 µg/mL
Ertapenem	Susceptible	≤0.5 µg/mL
Piperacillin-tazobactam	Susceptible	≤4 µg/mL
Trimethoprim-sulfamethoxazole	Susceptible	≤20 µg/mL

*Minimum Inhibitory Concentration

The patient's female sex, advanced age and post-menopausal status, long-term low-dose methotrexate use for rheumatoid arthritis, and past history of CA-ESBL *Escherichia coli* infection put her at risk for UTIs. She presented with typical symptoms and laboratory of an uncomplicated cystitis, including urinary frequency with associated incontinence, cloudy urine, and urinalysis positive for nitrites, leukocyte esterase, bacteriuria, and pyuria. In post-menopausal women, the loss of estrogen creates an environment less hospitable for vaginal lactobacillus growth, thereby increasing vaginal pH and promoting the growth of fecal organisms such as *Escherichia coli*. Furthermore, in the elderly population, *E. coli* is isolated from urine samples in up to 75% of patients who have an uncomplicated cystitis.[14] Other pathogens that are more frequently identified in patients ≥65 years of age as compared to younger adults include *Proteus*, *Klebsiella*, *Pseudomonas*, *Enterococcus*, and *Staphylococcus*.[14] Identification of *Raoultella ornithinolytica* in the patient's urine sample was therefore unexpected.

While *R. ornithinolytica* is an uncommon human pathogen, there are two clinical challenges associated with infection due to this bacterium. Firstly, *R. ornithinolytica* shares many characteristics with the related bacterium *Klebsiella pneumoniae*, which often results in misidentification of the organism. This has been shown to be the case for incidents of histamine fish toxicity, in which the histamine-producing *R. ornithinolytica* and the closely related *R. planticola* have been misidentified as the non-histamine producing bacterial species *K. pneumoniae* and *K. oxytoca*.[2]

The second challenge associated with *R. ornithinolytica* infections is the bacterium's expression of chromosomal class A ß-lactamases, which confer resistance to ampicillin, and other aminopenicillins. A penicillin in combination with a ß-lactamase inhibitor may provide good coverage, but *R. ornithinolytica* can be resistant to other commonly used antibiotics.[1] Sensitivity screening showed that this community acquired *R. ornithinolytica* species was susceptible to TMP-SMX and nitrofurantoin, the most common first-line antibiotic agents used for uncomplicated UTIs.[15] Empiric therapy with TMP-SMX resolved urinary symptoms but was unsuccessful in resolving bacteriuria and pyuria. Follow-up treatment with ciprofloxacin was required to resolve bacteriuria and pyuria, highlighting the challenge of eradicating *R. ornithinolytica* infection.

Conclusions

Raoultella ornithinolytica is an uncommon human pathogen, with only ten cases having been previously reported. This organism can be misdiagnosed as *Klebsiella pneumoniae* or *Klebsiella oxytoca*, and its expression of ß-lactamase confers resistance to ampicillin and other commonly used antibiotics. *R. ornithinolytica* is emerging as a causative agent of community-acquired UTIs which pose a potential challenge to the identification and treatment of these infections.

Conflict of Interest

None of the authors identify a conflict of interest.

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References

1. Walckenaer E, Poirel L, Leflon-Guibout V et al. Genetic and Biochemical Characterization of the chromosomal class A ß-lactamases of *Raoultella* (formerly *Klebsiella*) *planticola* and *Raoutella ornithinolytica*. *Antimicrob Agents Chemother.* 2004;48(1):305-312.
2. Kanki M, Yoda T, Tsukamoto T, Shibata T. *Klebseilla pneumoniae* produces no histamine: *Raoutella plantico* and *Raoutella ornithinolytica* strains are histamine producers. *Appl Environ Microbiol.* 2002;68(7):3462-3466.
3. Ferran M, Yébenes M. Flushing associated with scombroid fish poisoning. *Dermatol Online J.* 2006;12:15.
4. Deeb LS, Bajaj J, Bhargava S, Alcid D, Pitchumoni CS. Acute suppuration of the pancreatic duct in a patient with tropical pancreatitis. *Case Rep Gastroenterol.* 2008;2(1):27-32.
5. Morais VP, Daporta MT, Bao AF, Campello MG, Andrés GQ. Enteric fever-like syndrome caused by *Raoultella ornithinolytica* (*Klebsiella ornithinolytica*). *J Clin Microbiol.* 2009;47(3):868-869.
6. Vos B, Laureys M. Giant renal cyst as cause of colic obstruction. *Rev Med Brux.* 2009;30(2):107-109.
7. Mau N, Ross LA. *Raoultella ornithinolytica* bacteremia in an infant with visceral heterotaxy. *Pediatr Infect Dis J.* 2010;29:477-478.
8. Solak Y, Gul EE, Atalay H, Genc N, Tonbul HZ. A rare human infection of *Raoultella ornithinolytica* in a diabetic foot lesion. *Ann. Saudi Med.* 2011;31(1):93-94.
9. Hadano Y, Tsukahara M, Ito K, Suzuki J, Kawamura I, Kurai H. *Roultella ornithinolytica* bacteremia in cancer patients: report of three cases. *Intern Med.* 2012;51(22):3193-3195.
10. Lehloenya R, Christians S. A case of chronic urticaria complicated by *Raoultella ornithinolytica* urinary tract infection, bronchospasm, and angioedema. *World Allergy Organ J.* 2012;5(Suppl2):S204.
11. Sandal G, Ozen M. Fatal *Raoultella ornithinolytica* sepsis and purpura fulminans in a preterm newborn. *Indian J Paediatr Dermatol.* 2014;15(1):24-26.
12. Hostacká A, Klokocníková. Antibiotic susceptibility, serum response and surface properties of Klebsiella species. *Microbios.* 2001;104:115-24.
13. Hoshide RR, Chung H, Tokeshi J. Emergence of community-acquired extended-spectrum beta-lactamase *Escherichia coli* (ESBLEC) in Honolulu: A case series of three individuals with community-acquired ESBLEC bacteriuria. *Hawaii Med J.* 2011;70(9):193-195.
14. Matthews SJ, Lancaster JW. Urinary tract infections in the elderly population. *Am J Geriatr Pharmacother.* 2011;9(5):286-309.
15. Hooton, TM. Uncomplicated urinary tract infection. *N Engl J Med* 2012;366(11):1028-1037.
16. Becker, K., K. Southwick, J. Reardon, R. Berg, and J. N. MacCormack. Histamine poisoning associated with eating tuna burgers. *JAMA.* 2001;285:1327-1330.