DOI: 10.7860/JCDR/2024/67516.19192

Case Series

Microbiology Section

Raoultella ornithinolytica: A Case Series of Clinical Presentations and its Role in Various Infections from a Tertiary Care Centre in Tumkur, Karnataka, India

RASHMI BELODU[1], BV RENUSHRI[2], TS KIRAN[3], G VIJAYAKUMAR[4]

ABSTRACT

Raoultella ornithinolytica (R. ornithinolytica), a Gram-negative bacillus, has characteristics resembling those of *Klebsiella* spp. This bacterium is present in soil and aquatic environments and seldom causes Healthcare-Associated Infections (HAIs). However, clinical features and outcomes of human infections caused by *R. ornithinolytica* have been reported for only a limited number of cases. Here, multiple cases of adult patients with clinical features of community-acquired infections at different body sites are presented. *R. ornithinolytica* was identified in the laboratory from respective samples sent for culture and sensitivity. These patients were treated with good outcomes. *R. ornithinolytica* is a saprophyte known to cause secondary infections in patients with risk factors and sometimes exhibits antibiotic resistance. However, all the patients presented to the institution recovered fully from the infections and were discharged.

Keywords: Community-acquired, Multidrug resistance, Wound infection

INTRODUCTION

Raoultella ornithinolytica is a capsulated, non motile Gram-negative bacterium, which was previously named as *Klebsiella ornithinolytica*. However, in 2001, it was renamed *Raoultella*, along with other *Klebsiella* species, based on 16S rRNA and *rpoB* gene analysis [1,2]. *R. ornithinolytica* is found in water, soil, plants, and occasionally in animals [1,2]. In humans, the bacterium causes a variety of infections. While Hospital-Acquired Infections (HAI) is widely reported [2-5], it also causes infections in children, newborns, and fatal infections in premature babies [6]. In the elderly and those with underlying chronic diseases and malignant tumours, secondary infections with *R. ornithinolytica* are common during hospitalisation or following invasive procedures [4-6]. However, soft-tissue infections and wound infections have shown good recovery in healthy, young individuals with appropriate timely treatment [7]. Rarely, *R. ornithinolytica* infections have been reported as community-acquired infections and in healthy individuals, in enteric fever-like infections, and urinary tract infections [8,9]. *R. ornithinolytica* shows sensitivity to most antibiotic classes as reported in the literature [9]. Susceptibility has been observed to different classes of antibiotics like cephalosporins, sulphonamides, aminoglycosides, quinolones, combination of β-lactam/β-lactamase inhibitors, carbapenems, and carbapenem/β-lactamase inhibitor combinations [10]. However, they exhibit intrinsic resistance to ampicillin and ticarcillin due to chromosomally encoded beta-lactamases [10]. Strains exhibiting extended-spectrum beta-lactamases belonging to the SHV, TEM, and CTX-M have been reported in the literature, as well as AmpC production. Carbapenem resistance has also been described in other studies [11,12].

CASE SERIES

Case 1

A 29-year-old healthy female adult without any co-morbidities was admitted to the surgical department with complaints of a large non healing ulcer on the dorsum of the left foot and ankle [Table/Fig-1], with a history of a snake bite to the left ankle while working in an agricultural field one month prior. On examination, her vitals were stable, with no other complaints. Routine blood examination on admission was normal. A pus sample from the wound was sent for culture and sensitivity, which showed the growth of grey, non haemolytic mucoid colonies on blood agar and lactose-fermenting mucoid colonies on MacConkey agar [Table/Fig-2], subsequently identified as *R. ornithinolytica* by the automated VITEK 2 compact system™ by Biomerieux. The isolate was sensitive to aminoglycosides, quinolones, sulphonamides, cephalosporins, carbapenems, combinations of β-lactam/β-lactamase inhibitors, and carbapenem/β-lactamase inhibitor combinations.

[Table/Fig-1]: Foot ulcer. **[Table/Fig-2]:** MacConkey agar showing mucoid lactose fermenting colonies of *Raoultella ornithinolytica*. (Images from left to right)

The patient was diagnosed with an ulcer on the dorsum of the left foot and ankle with a wound infection secondary to a snake bite. She was started on Inj. Diclofenac 75 mg i.v. and Injection Cefixime 500 mg i.v. BD, which was continued for 10 days. Nutritional and protein supplements were added to her diet. She was transfused with one unit of packed Red Blood Cells (RBC) to correct her anaemia. In addition to vacuum suction for the removal of pus, daily dressing was started. Skin grafting was postponed in view of the culture report and the pus discharge from the wound. The patient responded gradually to the treatment, wound care, and daily dressings. The patient was advised to continue admission

until most of the wound had developed granulation and pus was very minimal, which lasted for about three weeks. A repeat pus sample from the wound site was sent for culture and sensitivity, which resulted in no growth. Split skin grafting was postponed in view of the healing wound and to be decided in follow-up. She was advised regular wound care and dressing at a healthcare facility and for follow-up in the surgical outpatient department as per her request. She was advised skin grafting following the resolution of the infection and ulcer.

Case 2

A 59-year-old gentleman, known case of diabetes mellitus type 2 for the last 15 years, and previously operated for craniopharyngioma, presented to the emergency department with complaints of altered sensorium and loose stools, along with dyselectrolytemia. The patient also exhibited clinical features of acute renal injury, presenting as oliguria and fatigue, which was confirmed with serum creatinine levels of 1.4 mg/dL, leading to his admission to the ward. On admission, he was found to be febrile, with a temperature of 39°C. However, he was normotensive, and there were no abnormal findings in the cardiovascular system, respiratory system, or per abdominal examination. Blood samples sent for analysis showed high potassium levels and increased procalcitonin (1.45 ng/mL). Haemoglobin was within normal limits, and total counts were elevated. A 2D Echo showed no abnormalities. Cerebrospinal Fluid (CSF) was sent for complete analysis and culture sensitivity. However, CSF, blood, and urine samples showed no growth in culture. A stool sample was sent to the microbiology laboratory for culture and sensitivity due to loose stools and continued increased temperature. The processed stool sample showed growth of mucoid lactose-fermenting colonies [Table/Fig-2] in MacConkey agar and was processed using the automated VITEK 2 compact system™ by Biomerieux for identification and susceptibility pattern. The isolate was identified as *R. ornithinolytica* susceptible to aminoglycosides, quinolones, sulphonamides, cephalosporins, carbapenems, combinations of β-lactam/β-lactamase inhibitor, and carbapenem/β-lactamase inhibitor combinations. The patient was diagnosed with acute gastroenteritis with dyselectrolytemia. Treatment was started with Piperacillin/Tazobactam and Metronidazole for three days in the intensive care unit initially, followed by Injection meropenem 500 mg for three days, Injection doxycycline 100 mg, and with probiotics, zinc, and vitamins for the correction of electrolytes. The patient improved significantly in the next three days with no other complications or complaints and was discharged.

Case 3

A 47-year-old lady, known to have type 2 diabetes mellitus for 10 years, presented to the outpatient department with swelling of the left foot and left ankle joint pain for three days. On examination, she was febrile, with a temperature of 38°C, and had features of left sole necrotising fasciitis and left big toe swelling and gangrene. She was admitted to the surgery department and advised surgical treatment of the left foot. Blood samples were collected appropriately for tests, which showed impaired blood glucose levels of 220 mg/dL, elevated Alkaline phosphatase levels of 150 IU/L, and elevated serum creatinine of 1.3 mg/dL. Ultrasonography of the abdomen showed no other abnormalities. She underwent surgical treatment with amputation of the left big toe of the left foot and debridement and drainage of pus. The pus sample was sent for culture and sensitivity, and *R. ornithinolytica* [Table/Fig-2] was identified and isolated in culture using Vitek 2 and tested by the Gram-negative panel simultaneously. The isolate was found to be sensitive to aminoglycosides, quinolones, sulphonamides, cephalosporins, carbapenems, combinations of β-lactam/β-lactamase inhibitor, and carbapenem/β-lactamase inhibitor combinations.

She was diagnosed with left foot necrotising fasciitis with gangrene. Subsequently, she was treated with Injection clindamycin 600 mg i.v. and piperacillin-tazobactam 2.25 g i.v., and appropriate anti-inflammatory medication, as well as treatment for glycaemic control. She was medically treated with wound care and showed significant improvement in the left foot and her general condition, and was discharged. She followed-up in the outpatient department under surgical care, and a repeat sample of the pus collected in the outpatient department yielded no growth.

Case 4

A 74-year-old male patient who was not diabetic or hypertensive, and had no other significant complaints presented to the outpatient department with complaints of burning micturition and fever for two days. Upon presenting at the outpatient department, blood samples were collected and sent for biochemical evaluation and fever assessment. The blood biochemistry results were within normal limits. Blood tests showed negative results for malaria, typhoid, or dengue. A urine sample collected on an outpatient basis was sent for culture and sensitivity testing. The patient was started on empirical treatment with fluoroquinolones and appropriate hydration, with advice to follow-up in the outpatient department. The urine culture showed significant growth of mucoid lactose-fermenting colonies [Table/Fig-2] on MacConkey agar, identified as *R. ornithinolytica* by the Vitek 2 automated system and tested for the antimicrobial resistance pattern by the Gram-negative panel. The isolate was found to be sensitive to aminoglycosides, quinolones, sulphonamides, cephalosporins, carbapenems, combinations of β-lactam/β-lactamase inhibitor, and carbapenem/β-lactamase inhibitor combinations. He was diagnosed as a case of community-acquired urinary tract infection. The patient followed-up in the outpatient department and was advised to continue with the same treatment for a total of 10 days, with appropriate supportive treatment. During follow-up, the patient had no other complaints, and the symptoms had subsided. He was compliant with the treatment.

DISCUSSION

Between the 1980s and 2006, only four cases of human *Raoultella* infection were reported. However, this has steadily increased, and up to 2022, around 130 cases have been reported in the literature [13]. *R. ornithinolytica* causing infections has emerged globally, with an overall increasing incidence trend. *Raoultella* infections have been reported in immunocompromised individuals, the elderly, and those with risk factors such as preexisting diseases [5]. In India, cases of neonatal sepsis and subhepatic abscess have been reported [14,15]. However, a preliminary search for case reports or studies on *R. ornithinolytica* in Medline, PubMed, and Google Scholar databases revealed no results from the region of South India. Among community acquired infections of *R. ornithinolytica*, diabetic foot infections, paronychia, and other soft-tissue infections have been reported as co-morbid conditions [16]. A review by Seng P et al., of *R. ornithinolytica* infections showed that 51% of 112 cases were community-acquired. Among these, 25% involved were immunocompromised individuals, and 25% were associated with concurrent malignancy, with diabetes mellitus present in 22% of cases [5]. Risk factors such as these and extremes of age are important determinants of an individual's susceptibility.

In the cases included here, patients residing in different locations surrounding the city presented to the hospital with various complaints. They were treated by doctors in different specialties and admitted in different wards, with no overlap in their time of stay or common environment in the hospital. Standard infection control practices, including hand hygiene and environmental disinfection, were followed in the wards. Segregation of the patients was implemented in the case of snake bites due to extensive wounds. However, clonal relatedness was not tested, and this was a limitation of this case series.

S. No.	Authors	Publication year	Risk factors	Clinical presentations	Treatment given	Outcome	Resistance pattern
1	Hadano Y et al., [4]	2012	Cancer, Elderly	Fever, altered sensorium	Case 1- piperacillin/tazobactam for two weeks Case 2 - Imipenem- cilastatinn at a dose of 0.5 g six hourly plus cefmetazole administered at 1 g every six hours for an 9 days Case 3 - piperacillin/tazobactam at a dose of 4.5g six hourly for 7 days, plus oral amoxicillin/ clavulanate f 500 mg/125 mg 8 hourly 7 days	Satisfctory improvement	Ampicillin
2	Ozkan EA et al., [6]	2014	Neonate, Atrial septal defect	Vomiting restlessness	Amikacin sulphate was administered 15 mg/kg/ day/qd	Symptoms subsided, resolved	Amplicillin+third generation cephalosporins
3	Sibanda M et al., [18]	2014	Elderly	Suprapubic pain and dysuria emesis and fever	Intravenous amoxicillin/clavulanic acid for six days	Resolved	Amplcilin
4	Sękowska A, et al., [2]	2015	Brain tumour, Paediatric age group, Neurogenic bladder, Frequent Urinary Tract Infection (UTI)	Fever Suspected UTI	Piperacillin and Tazobactam 4×3.5 g, i.v.) and amikacin (1×500 mg, i.v.) for six days	Recovered	Ampicillin and amoxicillin with clavulanic acid
5	Kabbara WK and Zgheib YR [3]	2015	Elderly, Diabetic, hypertension, chronic kidney disease, dyslipidaemia	Fever, diabetic foot ulcer	Empirical antimicrobial treatment consisting of amoxicillin-clavulanate 1.2 g (of amoxicillin) i.v. every 12 hours and ciprofloxacin 200 mg i.v. every 12 hours, Switched to Oral×14 days	Resolved	Cefazolin and ampicillin
6	Bhatt P et al., [15]	2015	Elderly Diabetic Hypertensive, hepatobiliary surgery	Abdominal pain and postsurgical drain fluid	Not mentioned	Resolved	Multidrug resistant sensitive only to colistin and tigecycline
7	Abbas A and Ahmad I [14]	2018	Neonate, Premature rupture of membranes	Tachypnea, Nasal flaring , leukocytosis	Started with cefotaxime (50 mg/kg every 12 h), amikacin (15 mg/kg every 24 h) and changed to colistin (75,000 IU/kg/day in three divided doses)	Resolved	Multi drug resistant - Sensitive only to colistin and trimethoprim/ sulfamethoxazole
8	Chen X et al., [20]	2021	Nil	Fever, chills paroxysmal cough	Meropenem 1 g; q8h; i.v. for 6 days+oral Faropenem×200 mg TID×7 days	Resolved	Not mentioned
9	Present study	2024	Diabetes, elderly, wound infection	Fever, chills, diarrhoea, dysuria, would infection	Injection cefixime 500 mg i.v. BD, piperacillin/ tazobactam	Resolved	Sensitive to tested antibiotics by Vitek

[Table/Fig-3]: Table comparing case reports of *Raoultella* infections with risk factors and outcome over past 10 years [2-4,6,14,15,18,20].

Community-acquired infections by *Raoultella* are rare, considering that most reported cases in the literature are hospital-acquired. The Genus *Raoultella* closely resembles *Klebsiella* spp, and accurate identification by automation or conventional methods is important for diagnosis. By conventional methods of identification, *Raoultella* are Gram-negative capsulated bacilli, non fastidious, lactose fermenters, with mucoid colonies on MacConkey's agar, catalase positive, oxidase negative with indole and Methyl Red (MR) positive, and can be differentiated into species with ornithine decarboxylase positive reaction [10]. *Raoultella* spp. are intrinsically resistant to ampicillin, and identification of the genus helps in guiding treatment. Currently, in the reported cases, the strains were sensitive and resolved with treatment. However, multidrug-resistant *Raoultella* are emerging, requiring alertness in diagnosis, proactive treatment, and vigilance of resistance patterns. The pathogenicity of the bacterium is attributed to its ability to form biofilms, polysaccharide capsules, siderophores, and fimbriae, as well as the presence of the chromosomal *bla* gene, which has been postulated to give it resistance to beta-lactam antibiotics, including penicillins [17].

Raoultella species have been reported to cause an enteric fever-like syndrome, gastroenteritis, pancreatitis, cholangitis, hepatic abscess, acute cholecystitis, and peritoneal dialysis-associated peritonitis [15,18,19]. In case 2 the continued fever with diarrhoea with culture negative samples prompted the investigation into the stool sample and further identification of the isolate. Furthermore, all isolates here were sensitive to aminoglycosides, quinolones, sulphonamides, cephalosporins, carbapenems, combinations of β-lactam/β-lactamase inhibitor, and carbapenem/β-lactamase inhibitor. In patients, co-morbidities and risk factors reported in the literature include cancer, post-urethral trauma, and post-invasive procedures [5].

The various risk factors and outcomes in different cases have been consolidated in [Table/Fig-3] [2-4,6,14,15,18,20].

CONCLUSION(S)

R. ornithinolytica poses difficulties in identification when using conventional methods and infections in humans may be underestimated. Automated systems have improved identification and implication in infections. Various risk factors in patients contribute to the susceptibility of the individual to infection, and community-acquired infections are common. However, there is a difficulty in assigning a pathogenic role especially in stool sample and with cases of diarrhoea. All the strains were sensitive to different classes of antibiotics tested. In the cases presented here, it is noteworthy that *R. ornithinolytica* showed susceptibility to most antibiotics tested and had a good response to treatment in the patients, as well as good outcomes.

REFERENCES

[1] Drancourt M, Bollet C, Carta A, Rousselier P. Phylogenetic analyses of *Klebsiella* species delineate *Klebsiella* and *Raoultella* gen. nov., with description of *Raoultella ornithinolytica* comb. nov., *Raoultella terrigena* comb. nov. and *Raoultella planticola* comb. nov. Int J Syst Evol Microbiol. 2001;51(3):925-32.
[2] Sękowska A, Dylewska K, Gospodarek E, Bogiel T. Catheter-related blood stream infection caused by *Raoultella ornithinolytica*. Folia Microbiologica. 2015;60(6):493-95.
[3] Kabbara WK, Zgheib YR. Diabetic foot infection caused by *Raoultella ornithinolytica*. Am J Health Syst Pharm. 2015;72(24):2147-49.
[4] Hadano Y, Tsukahara M, Ito K, Suzuki J, Kawamura I, Kurai H. *Raoultella ornithinolytica* bacteremia in cancer patients: Report of three cases. Intern Med. 2012;51(22):3193-95.
[5] Seng P, Boushab BM, Romain F, Gouriet F, Bruder N, Martin C, et al. Emerging role of *Raoultella ornithinolytica* in human infections: A series of cases and review of the literature. Int J Infect Dis. 2016;45:65-71.
[6] Ozkan EA, Khosroshahi HE, Yilmaz N, Gecit UA, Domur E. A rare case of a newborn with urinary tract infection by *Raoultella ornithinolytica*. Am J Health Res. 2014;2(6):375-77.

[7] Ayoade F, Mada PK, Alam M. Fat necrosis and polymicrobial wound infection caused partly by *Raoultella ornithinolytica* after reduction mammoplasty. Case Reports. 2018;2018:bcr-2018.
[8] BŘyŘkcam A, Bışakşıgil A, Kara A, Sancak B. A case of *Raoultella ornithinolytica* urinary tract infection in a pediatric patient. J Infect Chemother. 2019;25(6):467-69.
[9] 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):868-69. Doi: 10.1128/JCM.01709-08. Epub 2009 Jan 14. PMID: 19144809; PMCID: PMC2650892.
[10] Hajjar R, Ambaraghassi G, Sebajang H, Schwenter F, Su SH. *Raoultella ornithinolytica*: Emergence and resistance. Infection and Drug Resistance. 2020;15:1091-104.
[11] Zurfluh K, Hächler H, Nüesch-Inderbinen M, Stephan R. Characteristics of extended-spectrum β-lactamase-and carbapenemase-producing Enterobacteriaceae isolates from rivers and lakes in Switzerland. Appl Environ Microbiol. 2013;79(9):3021-26.
[12] Abid IN. Emergence of *Raoultella ornithinolytica* producing AmpC-beta-lactamases in the different clinical specimens. J Nat Res Sci. 2016;6:124-29.
[13] Appel TM, Quijano-Martínez N, De La Cadena E, Mojica MF, Villegas MV. Microbiological and Clinical Aspects of *Raoultella* spp. Front Public Health. 2021,2;9:686789.
[14] Abbas A, Ahmad I. First report of neonatal early-onset sepsis caused by multi-drug-resistant *Raoultella ornithinolytica*. Infection. 2018;46(2):275-77.
[15] Bhatt P, Tandel K, Das NK, Rathi KR. New Delhi metallo-β-lactamase producing extensively drug-resistant *Raoultella ornithinolytica* isolated from drain fluid following Whipple's pancreaticoduodenectomy. Med J Armed Forces India. 2015;71(Suppl2):S609-11. Doi: 10.1016/j.mjafi.2015.01.005. Epub 2015 Mar 12. PMID: 26858504; PMCID: PMC4705201.
[16] 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.
[17] Riwu KH, Effendi MH, Rantam FA, Khairullah AR, Widodo A. A review: Virulence factors of *Klebsiella pneumonia* as emerging infection on the food chain. Veterinary World. 2022;15(9):2172.
[18] Sibanda M. Primary peritonitis caused by *Raoultella ornithinolytica* in a 53-year-old man. JMM Case Reports. 2014;1(3):e002634.
[19] Goggins A, Lykins J, Aston A, Shaw J. Acute cholecystitis secondary to *Raoultella ornithinolytica* infection, complicated by sepsis, gallbladder perforation, hepatic abscess and bacteraemia. BMJ Case Reports CP. 2022;15(12):e250766.
[20] Chen X, Zhou X, Cao J, Ma K, Xia Z. A case report of community-acquired *Raoultella ornithinolytica* infection in a healthy, young individual. BMC Infect Dis. 2021;21(1):1095.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Microbiology, Siddaganga Medical College and Research Institute, Tumakuru, Karnataka, India.
2. Professor and Head, Department of Microbiology, Siddaganga Medical College and Research Institute, Tumakuru, Karnataka, India.
3. Professor, Department of Microbiology, Siddaganga Medical College and Research Institute, Tumakuru, Karnataka, India.
4. Assistant Professor, Department of Microbiology, Siddaganga Medical College and Research Institute, Tumakuru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rashmi Belodu,
c/o Department of Microbiology, Siddaganga Medical College and Research Institute, Tumakuru-572102, Karnataka, India.
E-mail: drbrashmi@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 15, 2023
- Manual Googling: Nov 18, 2023
- iThenticate Software: Jan 08, 2024 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Sep 14, 2023**
Date of Peer Review: **Nov 09, 2023**
Date of Acceptance: **Jan 10, 2024**
Date of Publishing: **Mar 01, 2024**