

***Raoultella ornithinolytica* urinary tract infection in a pediatric patient with T-cell precursor acute lymphoblastic leukemia**

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Abstract

Background: Currently, *Raoultella ornithinolytica* is considered an emerging pathogen of community- and hospital-acquired infection, particularly in patients with immunodeficiencies, malignancies, anatomical abnormalities, or after invasive procedures. Pediatric infections with *R. ornithinolytica* are exceedingly rare, with only six previously reported cases, of which only two were reported as a urinary tract infection. **Case report:** Here, we describe a polymicrobial urinary tract infection (*R. ornithinolytica* and *Enterococcus faecalis*) in a pediatric patient with T-cell precursor acute lymphoblastic leukemia, which was successfully treated with ampicillin-sulbactam. **Conclusions:** To the extent of our knowledge, we report the seventh case in a pediatric patient and only the third case of a urinary tract infection in this age group caused by *R. ornithinolytica*.

Keywords: Urinary tract infection. Pediatrics. Precursor T-Cell lymphoblastic leukemia-lymphoma. Colombia.

Infección de vías urinarias por *Raoultella ornithinolytica* en un paciente pediátrico con leucemia linfoblástica aguda de células T

Resumen

Introducción: Actualmente *Raoultella ornithinolytica* es considerado un patógeno emergente involucrado en infecciones adquiridas en la comunidad y en el hospital, en particular en pacientes con algún tipo de inmunodeficiencia, malignidad, alteraciones anatómicas o sometidos a procedimientos invasivos. Las infecciones pediátricas causadas por *R. ornithinolytica* son sumamente raras, con solo seis casos publicados, de los cuales nada más dos se presentaron como infección de vías urinarias. **Caso clínico:** Se describe una infección de vías urinarias polimicrobiana (*R. ornithinolytica* y *Enterococcus faecalis*) en un paciente pediátrico con leucemia linfoblástica aguda de células T, que fue tratado satisfactoriamente con ampicilina-sulbactam. **Conclusiones:** Con base en lo que se sabe hasta el momento, se reporta el séptimo caso en un paciente pediátrico y el tercer caso de infección de vías urinarias causada por *R. ornithinolytica* en este grupo de edad.

Palabras clave: Infección del tracto urinario. Pediatría. Leucemia linfoblástica de células T. Colombia.

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Introduction

The genus *Raoultella*, which belongs to the *Enterobacteriaceae* family, encompasses encapsulated Gram-negative, oxidase-negative, catalase-positive, aerobic, and non-motile bacilli^{1,2}. Initially, it was classified in the genus *Klebsiella*. However, in 2001, with phylogenetic testing including 16S rRNA and *rpoB* sequence analysis, the genus *Klebsiella* was further divided into two genera: the genus *Raoultella* and cluster II of the genus *Klebsiella* was transferred and renamed within the new genus³. Currently, *Raoultella planticola* and *Raoultella ornithinolytica* are the most important species because of their association as pathogenic agents^{1,2}.

R. ornithinolytica has been found in water environments, soil, insects, fish, ticks, and termites, but human infections are rare². The first human infection caused by *R. ornithinolytica* was reported in 2009⁴ and it is currently considered an emerging pathogen of community and hospital-acquired infection, particularly in patients with immunodeficiencies, malignancies, anatomic abnormalities, or after invasive procedures^{2,5}. Gastrointestinal and hepatobiliary infections are among the most frequently reported infections in the literature. However, urinary tract infections, wound and skin infections, bacteremia, respiratory infections, bone and joint infections, central nervous system infections, mediastinitis, pericarditis, conjunctivitis, and otitis have also been reported in adults^{2,5,6}. Pediatric infections with *R. ornithinolytica* are exceedingly rare, and only six cases have been reported previously⁷⁻¹¹, of which two cases were reported for urinary tract infection^{10,11}. Here, we describe a case of *R. ornithinolytica* urinary tract infection in a pediatric patient with T-cell precursor acute lymphoblastic leukemia.

Clinical case

A 9-year-old male patient was brought to the emergency department because of emetic syndrome, asthenia, adynamia, and weakness, without fever. A medical history of T-cell precursor acute lymphoblastic leukemia was recorded. Mild to moderate dehydration was identified with no other physical findings. Laboratory tests revealed moderate hypokalemia (2.8 mEq/L), pan-cytopenia (white blood cell count of 400 cells/mm³, red blood cell count of 2.84 million cells/mm³, platelet count of 23,000 cells/mm³), severe neutropenia (50 cells/mm³), lymphopenia (340 cells/mm³), and hemoglobin of 6.7 g/dL, requiring red blood cell and platelet

transfusions. C-reactive protein was 5.6 mg/dL, while liver enzymes and kidney function tests were normal. Fresh, spontaneous urine was collected. A urinalysis revealed negative nitrites, positive leukocytes, positive blood, 10 white blood cells/hpf, 250 red blood cells/hpf, 1+ bacteria, with the remaining parameters within normal limits. Urine and blood samples were sent for culture and sensitivity, and intravenous empiric treatment with cefepime (150 mg/kg/day) was initiated. Gram-negative bacillus and Gram-positive cocci were detected in the Gram-strain of the urine. The colony number was 100,000 cfu/mL for both bacteria on the CHROMagar Orientation Medium™ (Becton Dickinson, Germany). Through VITEK® 2xL (Biomerieux, France), the urine culture isolate was identified as *Raoultella ornithinolytica* and *Enterococcus faecalis*, and antimicrobial susceptibilities were tested. The *R. ornithinolytica* and *E. faecalis* demonstrated susceptibility to all tested antibiotics, including ampicillin-sulbactam (Table 1). The blood culture set (two aerobic and two anaerobic bottles) was negative. Treatment was changed to intravenous ampicillin-sulbactam (50 mg/kg) every 6 h to complete a total duration of 7 days of treatment. The patient's clinical condition improved, and all symptoms resolved. After appropriate antibiotic treatment and achievement of negative urine culture, the patient was discharged.

Discussion

Here, we report the seventh case in a pediatric patient and the third pediatric case of urinary tract infection caused by *R. ornithinolytica*. As in this case (male child with T-cell precursor acute lymphoblastic leukemia), all the six previously published pediatric cases were diagnosed in patients with either immunodeficiency (asplenia)⁷, malignancies (retinoblastoma and acute myeloid leukemia)^{8,9}, anatomical abnormalities (bilateral vesico-ureteral reflux and hydronephrosis)^{10,11}, or other comorbidities (IgA nephropathy)⁹. This clinical pattern is in line with the most extensive series of *R. ornithinolytica* infections in adults, which described comorbidities in more than 50% of patients^{5,12}. Therefore, more extensive studies are needed to a better understanding of the clinical features of *R. ornithinolytica* in childhood to confirm which comorbidities are risk factors.

Only one of the previously reported pediatric cases showed polymicrobial infection: a case of a febrile 8-year-old female patient with a history of retinoblastoma, neurogenic bladder, and frequent urinary tract infections⁸. Blood and urine cultures yielded

Table 1. Antimicrobial susceptibility of *Raoultella ornithinolytica* and *Enterococcus faecalis* using VITEK® 2 XL (Biomerieux, France)

<i>Raoultella ornithinolytica</i>		
Antimicrobial	MIC (µg/mL)	Susceptibility interpretation
Amikacin	≤ 2	Susceptible
Ampicillin-sulbactam	4	Susceptible
Cefepime	≤ 1	Susceptible
Cefoxitin	≤ 4	Susceptible
Ceftazidime	≤ 1	Susceptible
Ceftriaxone	≤ 1	Susceptible
Ciprofloxacin	≤ 0.25	Susceptible
Doripenem	≤ 0.12	Susceptible
Ertapenem	≤ 0.5	Susceptible
Gentamicin	≤ 1	Susceptible
Imipenem	≤ 0.25	Susceptible
Meropenem	≤ 0.25	Susceptible
Piperacillin-tazobactam	≤ 4	Susceptible
<i>Enterococcus faecalis</i>		
Antimicrobial	MIC (µg/mL)	Susceptibility interpretation
Ampicillin	≤ 2	Susceptible
Penicillin G	2	Susceptible
Ciprofloxacin	1	Susceptible
Daptomycin	1	Susceptible
Teicoplanin	≤ 0.5	Susceptible
Tetracycline	≤ 1	Susceptible
Vancomycin	≤ 0.5	Susceptible

MIC, minimum inhibitory concentration.

R. ornithinolytica and *Proteus mirabilis*⁸. The present report describes a polymicrobial urinary tract infection (*R. ornithinolytica* and *E. faecalis*). Regarding the most extensive series of *R. ornithinolytica* infections, Chun et al. (2015) and Seng et al. (2016) described 31% and 17% polymicrobial infection in adults associated with *E. faecalis* in 19% and 16%, respectively^{5,12}. Whether polymicrobial infections are related to more or less severe disease in *R. ornithinolytica* infection is an interesting hypothesis that requires further investigation.

Interestingly, although *Raoultella* spp. exhibited intrinsic resistance to ampicillin (similarly to some *Klebsiella* species) because of chromosomally encoded beta-lactamases², we achieved a satisfactory treatment using ampicillin-sulbactam. This outcome could be explained by Walckenaer et al. findings, who observed that a combination of amino- and carboxypenicillin with clavulanic acid makes *R. ornithinolytica* environmental isolates susceptible to these molecules¹³. As ampicillin-sulbactam is an aminopenicillin combination with an inhibitor of bacterial beta-lactamase (as well as clavulanic acid), these characteristics support our results. In any case, this hypothesis must be confirmed in further studies.

Finally, in Colombia, only a few previous studies have reported *Raoultella* spp. infections. In 2012, Molano et al. described bacterial isolations of urinary tract infection in women with urethral catheters from Bogotá city and Soacha municipality and found *R. ornithinolytica* < 3% of the urine cultures¹⁴. Later, in 2016, Márquez-Herrera et al. described the clinical characteristics of patients with carbapenemase-producing *Klebsiella* isolates in a tertiary pediatric hospital between 2012 and 2015 in Bogotá, reporting only one case of “*Klebsiella ornithinolytica*” bacteremia in a patient with nephrotic syndrome¹⁵. The last report was published in 2017, where Ramírez-Quintero et al. described a 41-year-old female patient from Medellín city with community-acquired *R. planticola* bacteremia of gastrointestinal origin¹⁶. While the first two studies used API 20E and VITEK (probably VITEK Legacy), respectively, as phenotypic identification systems^{14,15}, Ramírez-Quintero et al. used the VITEK 2 system¹⁶. Moreover, Park et al. evaluated the ability of three phenotypic systems (VITEK 2, MicroScan, and API 20E) to identify *R. ornithinolytica* and found that only VITEK 2 was able to identify all the isolates correctly¹⁷. Thus, since we used the VITEK2 system, our microbiological identification was accurate and reliable.

In conclusion, this case report describes a polymicrobial urinary tract infection (*R. ornithinolytica* and *E. faecalis*) in a pediatric patient with T-cell precursor acute lymphoblastic leukemia, which was successfully treated with ampicillin-sulbactam. We highlight the importance of considering *R. ornithinolytica* as an emerging pathogen in pediatric patients and the use of reliable diagnostic methods for accurate microbiological identification.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on patient data publication.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Conflicts of interest

The authors declare no conflict of interest.

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