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A rare and emerging pathogen: *Raoultella planticola* identification based on 16S rRNA in an infant

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ABSTRACT

Raoultella planticola is rarely associated with clinical infection, and a limited number of pediatric cases have been reported. Herein we report a case of bacteremia presumptively secondary to bilateral conjunctivitis in an infant caused by *R. planticola* which was successfully treated with piperacillin-tazobactam. It should be kept in mind that *R. planticola* can be a pathogen in pediatric age groups.

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Introduction

Raoultella, a genus comprises Gram-negative, oxidase-negative, facultative anaerobic bacteria within the *Enterobacteriaceae* family. There are three known species of *Raoultella* [1]. *Raoultella planticola* was a recently defined as a new genus in the family *Enterobacteriaceae* that was previously known as the *Klebsiella planticola. R. planticola* is a very rare pathogen and sometimes even causes fatal infections. Pediatric cases are extremely rare and have been reported recently. The other issue is an increasing concern about the emergence of carbapenem resistance in this species [2]. *R. planticola* may cause bacteremia, pneumonia, intra-abdominal infections, urinary tract infections and soft tissue infections [3]. It is also an unusual pathogen of conjunctivitis [4,5].

To our knowledge, there has not been any report of *R. planticola* conjunctivitis and bacteremia in pediatric age groups. Herein we report a case of *R. planticola* conjunctivitis and bacteremia in a preterm infant.

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Case

A 28-gestional week-old female infant weighing 880 grams was born to a preeclamptic mother. The baby was intubated in the neonatal intensive care unit (NICU), and surfactant was administered. She was extubated on the 10th postnatal day (PND) and full enteral feeding was achieved on 23rd PND. When the patient was clinically stable on 34th PND, bilateral purulent ocular discharge was detected. Conjunctival swab cultures were taken for bacteria and fungi. Empirical topical netilmicin eye drop (0.3%, four times a day) was initiated. The conjunctival swab culture was positive for *R. planticola,* which was resistant to ampicillin and piperacillin; susceptible to amoxicillin-clavulanate, gentamicin, netilmicin, cefuroxime, trimethoprim-sulfamethoxazole, piperacillin-tazobactam and carbapenems. Netilmicin was continued for seven days with clinical improvement. However, on the 45th PND fever (38,5 °C), desaturation and apnea were observed, and the patient was intubated. On the sepsis workup, she had leukopenia (2700/mm^3) and thrombocytopenia (83,000/mm^3) with elevated C-reactive protein (35 mg/L) and procalcitonin (72 μg/L) levels. Cerebrospinal fluid (CSF) analysis was normal. Blood, urine and CSF cultures were taken. Considering the unit's flora, empirical vancomycin and meropenem were started. Gram-negative bacilli appeared on gram stain and bacterial identification was reported as *R. planti-*

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cola with the same antibiogram from the blood culture. The strains were identified with VITEK 2 ID-AST (bioMíerieux, France) and Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS). The organisms were confirmed by 16S rRNA gene sequencing. The bacterial DNA was isolated by heating protocol. The partial nucleotide was amplified by PCR using universal primers 8UA (5′-AGAGTTTGATCCTGGCTCAG-3′) and 907B (5′-CCGTCAATTCMTTTAGTTT-3′), and subsequently sequenced with an ABI Prism 3100 Genetic Analyser (Applied Biosystems, Inc.). The BLAST software available at www.ncbi.nlm.nih.gov was used to search for DNA nucleotide sequences against similar nucleotide sequences in the database [6]. The 16S rRNA gene sequence of strains showed 99% nucleotide identity to that of the strain *R. planticola* (GenBank accession no: AB680059.1). Antibiotic susceptibility tests were also performed through VITEK 2 ID-AST (bioMérieux, France BioMerieux) system according to the manufacturer's instructions and the Clinical and Laboratory Standards Institute's (CLSI) criteria [7]. Antibiotherapy was de-escalated to piperacillin-tazobactam. Procalcitonin levels started to decrease on the 2nd day of the therapy. Leukopenia and thrombocytopenia also resolved after the 48th hour of antibiotherapy. CSF and urine cultures were negative. The patient was extubated on the third day of the therapy and a 14-day course of piperacillin-tazobactam was completed.

Discussion

Initially, *R. planticola* was included in the *Klebsiella* genus. It was first described as *Klebsiella planticola* in 1981 and as *Klebsiella trevisanii* in 1983 [8,9]. According to the current taxonomy, *Raoultella* was defined as a new genus in the family *Enterobacteriaceae*, based on comparative analysis of the 16S ribosomal RNA and rpoB gene sequences in 2001 [1]. The first case in humans with this organism was reported in 1984 by Freney et al. in an intensive care unit patient in France [10]. Based on partial 16S rRNA sequencing, our *Raoultella* isolates matched 99% identities with *R. planticola* strain (GenBank accession no: AB680059.1)

R. planticola is found in the soil, water, plants and insects that rarely cause clinical infection in humans. So far, there have been only a few pediatric clinical reports about *R. planticola* [11,12]. In literature, there are few cases, but we believe that the incidence of *Raoultella* spp. infections is more common all over the world than expected because of misidentification and underreported. With increasing use of VITEK 2, newly developed laboratory tests such as PCR methods for identification and MALDI-TOF MS, more cases of *Raoultella* spp. may be reported in the future [13]. To the best of our knowledge, there has been no newborn case and one pediatric report of *R. planticola* infection in Turkey [11]. A PubMed search revealed only two newborn bacteremia and a few conjunctivitis cases were reported all over the world [4,5,12].

Bacteremia, pneumonia, cellulitis, surgical site infection, cholangitis, and urinary tract infection due to *R. planticola* have been reported in the literature [3,14]. Zuberbuhler et al. reported the first case of conjunctivitis caused by *R. planticola* in a 58-year-old woman [4]. There was no known contact with the soil or water in our patient. It was a mild ocular infection and treated with the antibiotic eye drop. After this eye infection episode, the same organism was detected in the blood. Clinical descriptions of infections due to *R. planticola* are limited in children. However, the pathogenic role of *Raoultella* spp. in human infection is still difficult to elucidate. Also limited data cannot help to predict clinical courses of *Raoultella* infections. Gözmen et al. reported a case of *R. planticola* bacteremia in an 11-month-old infant hospitalized for Rotavirus gastroenteritis [11]. *R. planticola* may be an emerging pathogen capable of causing serious infections in multiple different organ systems in children. As in our case premature newborns are at high risk of *Raoultella* spp. infections, as they require longer care in neonatal intensive care units (NICUs), are exposed to more invasive procedures and have an immature immune system. Challenging infections caused by *Raoultella* spp., like those of multidrug resistant *Klebsiella* spp., will probably become a concern for pediatricians as well as other clinicians.

The antibiotic susceptibility of *R. planticola* has not been thoroughly investigated yet. Many studies have demonstrated that *R. planticola* strains are usually susceptible to third or fourth generation cephalosporin, β-lactamase inhibitor combinations (such as amoxicillin with clavulanic acid and piperacillin with tazobactam), aminoglycosides, netilmicin, ciprofloxacin, levofloxacin, tigecycline and carbapenems. However, *R. planticola* can acquire plasmid-mediated antibiotic resistance [3]. In a clinic study, 20 patients with *R. planticola* bacteremia revealed universal resistance to both ampicillin and piperacillin, while all strains were susceptible to these antibiotics when combined with b-lactamases inhibitors [14]. Although carbapenem-resistant *R. planticola* has been sporadically reported, these infections can usually be treated effectively with broad spectrum antibiotics like β-lactamase inhibitor combinations [13]. Physicians must keep in mind to the possibility of carbapenem resistance in *R. planticola.* Our case demonstrates that *R. planticola* should be considered as a potential etiologic agent of infections in NICUs. It should be kept in mind that *R. planticola* can be the etiologic agent of infections in NICUs and also in other pediatric wards. The adequate management of *R. planticola* infections in children has not been clearly established in the literature. More pediatric studies would be helpful in obtaining more understanding of the pediatric *R. planticola* infections.

Consent

Written informed consent was obtained from the patient's parent for the publication of this report.

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Competing interests

None declared.

Ethical approval

Not required.

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