Sepsis caused by Raoultella terrigena

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Reviewer
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We describe a second reported case of human infection caused by *Raoultella terrigena.*

Introduction

Raoultella terrigena (previously known as *Klebsiella terrigena*) is a rarely encountered gram-negative bacterium and mainly reported as aquatic and soil organism.[1] However, in 2007 the first human infection caused by this organism was reported in a 45-year-old patient who developed endocarditis due to *R. terrigena* post liver transplant.[2] No other case reports of infections caused by this organism have been published, and the clinical spectrum of diseases caused by this organism is unknown. The correct identification of *R. terrigena* is not easily accomplished in most clinical microbiology laboratories, and isolates can be easily misidentified as *Klebsiella pneumoniae* or other Klebsiella species.[3]

We describe a patient with sepsis with a primary infection by *R. terrigena*.

Case report

Our patient was a 69-year-old man who underwent pancreatic resection (pancreaticoduodenectomy, Whipple's procedure) for pancreatic cancer. An abdominal drain was left *in situ*, and postoperatively he made good progress until day nine when he developed fever and diarrhoea. A stool sample was positive for *Clostridium difficile* toxin and metronidazole was commenced orally. A computerized tomography (CT) scan of the abdomen showed a large 30 × 16 cm collection in the pelvis and the abdominal drain was repositioned to drain the collection. Drain fluid culture yielded *Klebsiella pneumoniae* (sensitive to co-amoxiclavulanic acid, cefotaxime, cefradine, ciprofloxacin, gentamicin and imipenem) and anaerobes, while blood culture did not show any growth.

By day 12, being more unwell with severe sepsis needing inotropic support, he was transferred to the intensive care unit. He received a stat dose of intravenous gentamicin 320 mg and vancomycin 1 gm, and was commenced empirically on imipenem 500 mg 6-hourly. The following day, a blood culture yielded gram-negative rods, later identified as *R. terrigena* sensitive to co-amoxiclavulanic acid, cefotaxime, cefradine, ciprofloxacin, gentamicin and imipenem. Drain fluid also grew *R. terrigena* with the same sensitivities as in blood culture and Candida spp. The imipenem was changed to piperacillin-tazobactam, in accordance with the local policy, and he responded to therapy. By day 15 he was able to be discharged back to the ward, where piperacillin-tazobactam was continued.

Over the subsequent three weeks, he developed a bacteremia with *Enterococcus durans*, necessitating addition of intravenous vancomycin. A repeat CT scan excluded a persistent abdominal collection but now showed a thrombus in the inferior vena cava. The abdominal drain was removed.

He was finally discharged home 50 days after admission.

Discussion

First described in 1981 as *Klebsiella terrigena*,[4] *R. terrigena* is a member of the family Enterobacteriaciae. Klebsiellae are non-motile, rod-shaped, gram-negative bacteria with a prominent polysaccharide capsule that accounts for the large appearance of the organism on gram stain, and provides resistance against many host defense mechanisms.[5]

R. terrigena was first isolated in 1981 from soil and water.[4,6] For many years following the first description of this new species no human isolates were reported. In 1991 *R. terrigena* was isolated form the stool of healthy humans, with a carriage rate of 0.9% for 5377 different stool specimens examined.[7] The significance of the isolate was uncertain, until in 1992 when 2355 clinical isolates (mostly from respiratory tract) of Klebsiella were subjected to additional tests and 10 isolates (0.4%) of *R. terrigena* were identified. However the significance of this isolation, and whether *R. terrigena* causes monomicrobial infections or participates in polymicrobial infections remained to be clarified.

Our case is the second reported case of actual clinical infection caused by *R. terrigena.* The first reported clinical infection was in 2007 when a 45-year-old old patient post liver transplant developed pneumonia, sepsis and endocarditis due to *R. terrigena*. Extended spectrum beta-lactamase (ESBL) producing *R. terrigena* and multi-resistant coagulase negative staphylococci (MRCNS) were isolated from the sputum. On postmortem examination, the aortic valve was found to be destroyed by endocarditis and samples grew MRCNS and ESBL-producing *R. terrigena*. Notably this patient was colonized with ESBL producing *R. terrigena* prior to liver transplant and prophylaxis with piperacillin-tazobactam was unable to eradicate the organism.[2]

Our case developed sepsis due to *R. terrigena* after having a laprotomy which was complicated by intra-abdominal collection. Initial drain fluid samples grew *Klebsiella pneumoniae* and mixed anerobes and later on blood cultures and drain fluid grew *R. terrigena*. Interestingly all 10 strains of *R. terrigena* isolated by Podschun *et al.* were in conjunction with other bacteria, mainly *Staphylococcus aureus* and other enterobactericiae.[8] However the simultaneous isolation of *R. terrigena* in both drain fluid and blood culture in our patient, and sputum and postmortem specimens of aortic valve in the first case report by Goegele *et al.* suggests that this organism may be able to cause mono-microbial infections.[2]

Very limited studies have been done on the sensitivity of *R. terrigena* to antimicrobial agents. Raoultella spp carry a chromosomal beta-lactamase that makes this agent naturally resistant to several antimicrobial agents.[9] *R. terrigena* in our case was sensitive to co-amoxiclavulanic acid, cefotaxime, cefradine, ciprofloxacin, gentamicin and imipenem. Our patient responded well to piperacillin-tazobactam and imipenem. Podschun *et al.* tested 10 strains for their susceptibility to antimicrobial agents; all strains were susceptible to cefotaxime, imipenem, co-amoxiclavulanic acid, doxycycline, gentamicin and ciprofloxacin, as in our case.[8]

The correct identification of *R. terrigena* can be difficult in clinical microbiology laboratories, isolates easily misidentified as other Klebsiella and Raoultella species especially *Klebsiella pneumoniae.*[10] This is because most conventional identification systems, such as the API 20E, usually fail to correctly identify these species.[10] Unfortunately, most of the additional differentiating tests required for identification are uncommon in routine practice. Differentiation between *Klebsiella pneumoniae* and *R. terrigena* is based mainly on tests for fermentation of dulcitol, melezitose and adonitol at 30˚C. Identification can be confirmed by growth at 10˚C and inability to produce gas from lactose at 44.5˚C.[8] Carbon substrate assimilation systems, such as the API 50 CH, API 50 AO and API 50 AA galleries, have identified Klebsiella isolates to the species level, but the great number of tests that have to be performed is time-consuming and the galleries are expensive.[10]

Different algorithms have been suggested to correctly identify Klebsiella and Raoultella species. A combination of two conventional tests (indole and ornithine decarboxylase tests) and four carbon substrate assimilation tests (ethanolamine, histamine, D-melezitose, and DL-3-hydroxybutyrate tests) has been suggested. This method achieved a sensitivity of 94.7% and specificity of 100% for these species. Another alternative method could be routine histamine assimilation testing to detect Raoultella species among Klebsiella isolates, followed by the use of conventional tests (i.e. indole and ornithine decarboxylase tests) on these Raoultella species to differentiate to the species level.[3]

We identified this organism by using API20E (probability 71.5%) and VITEK 2 (probability 98%). It was confirmed by the reference laboratory using specific PCR (polymerase chain reaction) and 16S sequencing.

For the initial identification of this organism, we recommend commercially available identification

systems which use a combination of biochemical tests and database. Most modern laboratories have access to these systems. The definite identification can be done using PCR and sequencing.

Conclusion

R. terrigena is a rarely encountered gram-negative rod and many microbiological laboratories still do not subtype Klebsiella and Raoultella spp beyond the species level. Although occurring occasionally in human tissues, the clinical significance of the presence of *R. terrigena* is dubious. However the isolation rate appears to be very low. We do not suggest that extending the range of standard tests for *R. terrigena* identification is warranted in the routine clinical microbiological laboratory at present. However more research is needed to understand the spectrum of diseases caused by this organism.

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