**Rahnella aquatilis** Bacteremia in an Oncologic Patient with Intestinal Obstruction. Identification of Unusual Bacteria is not Always Easy. Literature Review

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**Abstract**

*Rahnella aquatilis* is a gram-negative rod that belongs to the Enterobacteriaceae family. Few cases of infections by this bacteria have been reported in humans. Most of them are opportunistic infections in immunocompromised patients, but some cases have also been described among immunocompetent subjects.

In this article, we present a case of bacteremia originated by this microorganism in a patient with advanced stage breast cancer. The patient was receiving palliative treatment, and presented a long-term intestinal obstruction.

Initial identification of this bacterium was uncertain with biochemical methods, and the strain was identified as *Rahnella aquatilis* by MALDI-TOF mass spectrometry (MS). The identification of *Rahnella* was definitely confirmed by 16S sequencing.

In addition, a review of cases of infection by *R. aquatilis* has been made in the literature. We tried to show the patients and what types of infections are caused by *Rahnella*.

**Keywords:** *Rahnella aquatilis*, Bacteremia; Breast cancer; Maldi MS; Intestinal obstruction; Opportunistic infections

**Introduction**

*Rahnella aquatilis* is a gram-negative rod that belongs to the Enterobacteriaceae family. Izard et al. named the genus *Rahnella* in honor of the German bacteriologist Otto Rahn, and the aquatilis species, because the first strains that were isolated were mostly in water samples [1].

*Rahnella* is an environmental bacteria that grows, as other nitrogen-fixing bacteria, symbiotically in rhizospheres nodules and plant roots [2]. It has also been isolated in food and drinks such as beer, minced meat, milk and pasteurized cream [3,4]. Contamination of parenteral nutrition solutions has also occurred [5]. In addition, it can colonize the intestinal mucosa in a low percentage of people [6].

The first report of clinical isolation of *Rahnella aquatilis* was in 1985 [2]. The specimen came from a burn wound infection [1]. Very few cases of infections by this bacteria have been reported ever since which are mostly opportunistic infections in immunocompromised patients [7-9] and exceptionally among immunocompetent patients [2,10].

In this article we present a case of bacteremia by *Rahnella* in a patient with an advanced-stage breast cancer. The patient was receiving symptomatic treatment for palliative purposes when she presented a persistent intestinal obstruction.

In addition, a review of cases by *Rahnella aquatilis* in the literature was made. The present manuscript tries to highlight interesting clinical and microbiological aspects of the infection by this unusual microorganism.

**Case Report**

A 50-year-old female came to our hospital complaining that she had been suffering from abdominal pain for 7 weeks. She presented general discomfort and the physical examination showed a distended abdomen and tenderness to abdominal palpation but ruled out signs of intestinal perforation. The patient had a history of an infiltrating ductal breast cancer that was diagnosed 2 years before, which was triple negative for estrogen (ER-), progesterone (PR-), and HER2 receptors (HER2-) and had a Ki67 index of 35%. She received neoadyuvant chemotherapy and had a performance status of 3 in the ECOG (Eastern Cooperative Oncology Group) scale.

On admission, a CT scan was performed showing multiple thoracic and abdominal metastases, bilateral pleural effusion, peritoneal ascites, and sigmoid stenosis with mural thickening. The patient had a performance status of 3 in the ECOG (Eastern Cooperative Oncology Group) scale.

Blood analysis showed the following values: leukocyte $2.9 \times 10^9/L$, neutrophils $2.2 \times 10^9/L$, lymphocytes $0.48 \times 10^9/L$, hemoglobin 126 g/L, platelets $256 \times 10^9/L$, creatinine 45.08 µmol/L and total proteins 56.1 g/L. Serology was negative for HIV but positive for hepatitis C virus. As far as we knew, the patient had not been treated for hepatitis...
C. and there was no study on viral load. The gamma-glutamyltranspeptidase (GGT) value was 173 IU.

An intestinal occlusion was suspected when, in addition to the abdominal pain, the patient presented new symptoms such as persisting vomiting, meteorism and constipation, which led to the placement of a nasogastric tube, obtaining very large debits of more than 5000 cc of bilious and fecoidal material.

Posteriorly, she presented fever of 38.5°C, a leukocyte count of 11 × 10^9/L, 93.8% neutrophils, motivating the obtention of urine and blood cultures. Blood cultures were incubated in a Bactec FX (Becton Dickinson, USA). Urine culture result was negative. Aerobic and anaerobic blood cultures were positive in 16 and 18 h respectively. Gram-negative rods were detected with a microscope after Gram stain. Positive lactose colonies grew after 24 h of incubation in MacConkey medium. The colonies were identified as Leclercia adecarboxylata through Phoenix 100 (Becton Dickinson, USA) automated commercial identification system. To confirm these preliminary results we used an API 20E (BioMérieux, France) biochemical test panel which showed discrepancy with the former and resulted positive for Rahnella aquatilis. To obtain etiological confirmation the strain was sent to a tertiary hospital where they used a MALDI-TOF (MS) identification system and the result was positive for R. aquatilis. The identification of Rahnella was definitively confirmed by 16S sequencing.

Antibiotic sensitivity study was made, and the bacteria resulted sensitive to ceftazidime, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefepime, aztreonam, aminoglycosides, quinolones, fosfomycin and cotrimoxazole and was resistant to cefuroxime and carbapenems, quinolones or aminoglycosides has been found (Table 1).

At the same time, she had symptoms of pneumonia and chest-x ray was compatible with respiratory infection. A carbapenemase producing multiresistant Pseudomonas aeruginosa grew in a sputum culture, which led to the application of isolation measures.

The patient received antibiotic treatment based on levofloxacin and fosfomycin for 12 days. At the end she had no respiratory symptoms, no fever and leukocyte count of 6.9 × 10^9/L.

A new CT scan showed progression of her disease, ascites with very extensive and diffuse carcinomatosis, retroperitoneal and bony infiltration, and increase of the pleural effusion. Due to the absence of any curative options on both surgical and medical approaches, a symptomatic-palliative treatment was decided and agreed by the patient. The patient finally submitted a voluntary discharge to return to Morocco, her country of origin.

Discussion

Although episodes of bacteremia by R. aquatilis have been generally associated to immunocompromised patients [11], bacteremia cases of catheter infection [12], and related to contaminated parenteral medication have been reported [10]. A small number of cases of urinary infection [2,13], pneumonia [9], endocarditis [14], burns and surgical wound infection are also described in the literature [15]. The present case shows a bacteremia by R. aquatilis in a patient with advanced breast cancer and positive serology for hepatitis C. Therefore, it should be considered that the patient was immunocompromised.

A bibliographic review of the cases of Rahnella infection in the literature was made. As shown in Table 1, eighteen published cases of infection by this microorganism were found. Six cases were in patients with cancer, most of them onc hematological. No case in breast cancer was found. Eleven cases were in patients with diseases in which immunosuppression is associated. The other seven cases were in patients apparently immunocompetent. Regarding the type of infection, in eleven of the eighteen cases R. aquatilis was isolated in blood. In another three cases in respiratory samples, one case in urine sample, two cases in stools and one case in a surgical wound [16].

R. aquatilis infection has generally been associated to immunocompromised patients. However, after reviewing the literature, several significant cases have been found in immunocompetent patients, 7 of 18, representing 40% of the cases. Therefore, infection by this microorganism is not exclusive of immunocompromised patients.

The infection appears in most cases, in people who already have another underlying disease. For this reason, it can be said that Rahnella is a clearly opportunistic bacterium. Six out of eighteen cases (33%) were among cancer patients; three onc hematological and three solid tumors.

Our patient had an advanced breast cancer and presented a long-term intestinal obstruction, which required the placement of a nasogastric tube. Intestinal obstruction allows overgrowth of intestinal bacteria and the increase of the permeability and the damage of the intestinal mucosa [17]. Our hypothesis is that the patient had intestinal colonization of Rahnella, added to the host immune system deficiency due to cancer, led to bacteremia by translocation of the intestinal flora [18].

Regarding sensitivity literature review, as it is shown in table 2, all isolates of R. aquatilis were resistant to aminopenicillins, and in most cases, to first-generation cephalosporins [19]. No strain resistancy to carbapenems, quinolones or aminoglycosides has been found (Table 1).

<table>
<thead>
<tr>
<th>Main (reference)</th>
<th>Author (year)</th>
<th>Immunocompromised patient</th>
<th>Underlying main disease</th>
<th>Type of infection</th>
<th>Isolation sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christiaens [7]</td>
<td>Yes</td>
<td>Chronic lymphocytic leukemia, emphysema</td>
<td>Bronchopulmonary infection</td>
<td>Sputum</td>
<td></td>
</tr>
<tr>
<td>Goubau [8]</td>
<td>Yes</td>
<td>Chronic leukemia</td>
<td>Bacteremia</td>
<td>Blood</td>
<td></td>
</tr>
<tr>
<td>Harrell [9]</td>
<td>Yes</td>
<td>HIV</td>
<td>Pneumonia</td>
<td>Bronchoalveolar lavage</td>
<td></td>
</tr>
</tbody>
</table>
Table 1: Cases of Infection by *Rahnella*, patient immune condition, underlying main disease, type of infection and sample where the bacteria has been isolated.

It has been shown that some strains of *Rahnella* can produce an Ambler class A extended spectrum Beta-lactamase [20]. For this reason treatment of bacteraemia using penicillins or cephalosporins should be avoided. In our case the strain was resistant to cefuroxime and cefotaxime probably due to this beta-lactamase production. The suitable antibiotics in the treatment of *Rahnella* infection would be the carbapenems, piperacillin-tazobactam, aminoglycosides, or quinolones since to date, no resistant strains have been found to any of them. In our case the patient received antibiotic treatment with quinolones and fosfomycin, after this fever and signs of infection disappeared (Table 2).

<table>
<thead>
<tr>
<th>Main Author (Reference) (Year)</th>
<th>Antibiotics tested as sensitive</th>
<th>Antibiotics tested as resistant</th>
</tr>
</thead>
</table>
Table 2: Sensitivity to antibiotics per case.

To identify the bacteria a biochemical automated commercial system was used at first. The initial identification was a false positive for Leclercia adecarboxylata. R. aquatilis was posteriorly confirmed using two independent methods: MALDI-TOF MS and 16S sequencing. Identifying *Rahnella* by biochemical methods can sometimes be difficult and has previously been misidentified as another member of the Enterobacteriaceae family, usually as an Enterobacter [21]. In our case, we think that the identification failure could be due an error in the expected value for the citrate test in the analyzer database [22]. New identification methods, such as the MALDI-TOF MS system provide advantages compared to biochemical analyzers allowing the correct identification of rare enterobacteria [23].

We believe that infection by *Rahnella* is underdiagnosed mainly because biochemical methods that are commonly used sometimes are ineffective for its detection. The correct diagnosis of these rare species could improve by using more sensitive tools such as MALDI-TOF MS systems. We think that our findings in the laboratory are clinically relevant. There could be an impact on morbidity and mortality of patients when detecting uncommon species on time, which would allow an early and directed antibiotic treatment. This effect could be especially interesting among immunocompromised and cancer patients, in which the decision of administrating the right antibiotic may be vital.

Acknowledgment

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References


