Citrobacter braakii, um Organismo Incomum: Caso Clínico e Revisão de Literatura

Citrobacter braakii, an Unusual Organism: Case Report and Literature Review

Alexandra S. Machado, Luís Fernandes, Diana Dias, Heloísa Ribeiro

Resumo:

Citrobacter braakii, bactéria Gram-negativa pertencente à família Enterobacteriaceae, é reconhecida como patógeno oportunista.

Apresentamos o caso de um homem de 81 anos, imunodeprimido, com múltiplas comorbilidades, incluindo síndrome mielodisplásica e adenocarcinoma retal. O doente apresentou inicialmente febre, declínio do estado geral e recusa alimentar. Do estudo complementar inicial, foi diagnosticada COVID-19 e iniciados cuidados de suporte. Durante o internamento, dada persistência de febre e marcadores inflamatórios elevados repetimos o estudo microbiológico, revelando bacteremia por *Citrobacter braakii*. Imagens subsequentes identificaram um abcesso relacionado à deiscência anastomótica, fonte mais provável da infeção.

Com a descrição deste caso, pretendemos alertar para a importância de reconhecer *C. braakii* como um agente potencial, principalmente em doentes imunocomprometidos.

Palavras-chave: Abcesso/complicações; Bacteremia; Citrobacter; Infecções por Enterobacteriaceae; Resistência Microbiana a Medicamentos.

Abstract:

Citrobacter braakii, a Gram-negative bacterium belonging to the Enterobacteriaceae family, is recognized as an opportunistic pathogen.

We present the case of an 81-year-old man, immunocompromised, with multiple comorbidities, including myelodysplastic syndrome and rectal adenocarcinoma. The patient initially presented with a fever, decline in general condition and refusal to eat. From the initial complementary study, COVID-19 was diagnosed, and supportive care was initiated. During hospitalization, given the persistence of fever and elevated inflammatory markers, we repeated the microbiological study, revealing bacteremia caused by *Citrobacter braakii*. Subsequent images identified an abscess related to anastomotic dehiscence, the most likely source of infection.

With the description of this case, we intend to raise awareness of the importance of recognizing *C. braakii* as a potential agent, especially in immunocompromised patients.

Keywords: Abscess/complicações; Bacteremia; Citrobacter; Drug Resistance, Microbial; Enterobacteriaceae Infections.

Learning points

1. *Citrobacter braakii* is a Gram-negative bacterium classified under the Enterobacteriaceae family that is considered an opportunistic pathogen, especially in immunocompromised patients.
2. *C. braakii* is rarely associated with infections compared to other Citrobacter species such as *C. freundii* and *C. koseri*. There are few documented reports of *C. braakii* infections in the medical literature.
3. Proper identification and antibiotic susceptibility testing are crucial for the effective management of infections caused by *C. braakii*, since Beta-lactam resistance is common and resistance to carbapenems as also been reported.
4. Understanding the microbial diversity and antibiotic resistance patterns of *C. braakii* is important for public health. Future research could focus on the genetic and molecular characteristics of the bacteria, as well as mechanisms of antibiotic resistance.

Introduction

Citrobacter braakii is a Gram-negative bacterium classified under the Enterobacteriaceae family. It is closely related to other Citrobacter species, such as *Citrobacter freundii* and *Citrobacter koseri*, however, it is not as frequently associated with disease as these, since it's considered an opportunistic pathogen.[1-3] This bacterium is commonly found in various environmental sources, including soil, water, and sewage, but

Serviço de Medicina Interna, Unidade Local de Saúde de Entre o Douro e Vouga, Santa Maria da Feira, Portugal

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it can also be present in the human gastrointestinal tract.[3,4] Infections caused by *C. braakii* can range from urinary tract infections to sepsis.[1,3,4]

Herein, we report a case of bacteremia caused by *C. braakii* in an immunocompromised patient.

Case Report

An 81-year-old man presented to the emergency department (ED) with a one-month history of fever associated with a decline in general health and refusal to eat over the last 3 days. The patients' medical history included myelodysplastic syndrome followed by Hematology and treated with epoetin 30 000 UI/week; moderately differentiated adenocarcinoma of the middle rectum, which had been treated with surgery in 2019 following neoadjuvant chemotherapy and radiotherapy, resulting in nearly complete response to the treatment but with disease persistence. The patient continued follow-up with Oncology and General Surgery, with no evidence of progression in the last evaluation (six months prior).

Upon admission to the ED, the patient appeared pale and dehydrated. Vital signs were as follows: blood pressure 108/57 mmHg, heart rate 110/min, respiratory rate 20 cycles/minute, temperature 35.8°C. Arterial blood gas showed respiratory alkalosis, hypokalemia (3.1 mmol/L) and mild hyperlactacidemia (1.7 mmol/L). Blood analysis revealed anemia (hemoglobin 4.3 g/dL, mean corpuscular volume 95.3 fL, mean corpuscular hemoglobin concentration 30.3 g/dL), white blood cell counts of 4300/µL, platelets 33 000/µL, and a C-reactive protein (CRP) level of 409.6 mg/L. Peripheral blood smear showed 13% blasts, compared to the previous 3%, and dysplasia of monocytic and granulocytic lines. A rapid antigen test for SARS-CoV-2 was positive. Supportive treatment was initiated with the transfusion of 2 units of red blood cells and a therapeutic regimen of nirmatrelvir/ritonavir. The patient was admitted to the Internal Medicine department for further care. We also established contact with Hematology, who agreed that it was a likely transformation into acute myeloid leukemia, since there was no blood loss. Still, given the patient's current condition, the plan was to continue supportive care only.

On the fourth day of hospitalization, due to persistent fever and elevated inflammatory markers, a new septic screening was performed, indicating a urinary tract infection. Empirically, ceftriaxone was initiated, although fever persisted (interpreted in the context of myelodysplastic syndrome transformation into acute myeloid leukemia), there was some improvement in inflammatory markers, with a decrease in CRP to 347 mg/L. On the seventh day, following the isolation of *Escherichia coli* in a urine culture, the antibiotic treatment was changed to amoxicillin/clavulanic acid, according to the antibiogram, with analytical improvement and CRP decreasing to 308 mg/L.

However, on the tenth day, due to a recurrence of inflammatory markers (CRP 421 mg/L), a new septic workup was performed with urine and blood culture, and antibiotic therapy was escalated to piperacillin/tazobactam. On the twelfth day of hospitalization, after the isolation of *Citrobacter braakii* in a blood culture, an abdominopelvic computed tomography was performed, showing thickening of the distal rectum and distal sigmoid, with no clear definition of the previous surgical anastomosis. On the posterior aspect of the rectosigmoid transition, there was a discontinuity with a maximum transverse extension of 10 mm and a longitudinal extension of 8 mm, communicating with a large presacral collection measuring about 90 x 66 x 28 mm, suggesting a probable abscess due to anastomotic dehiscence (Fig. 1).

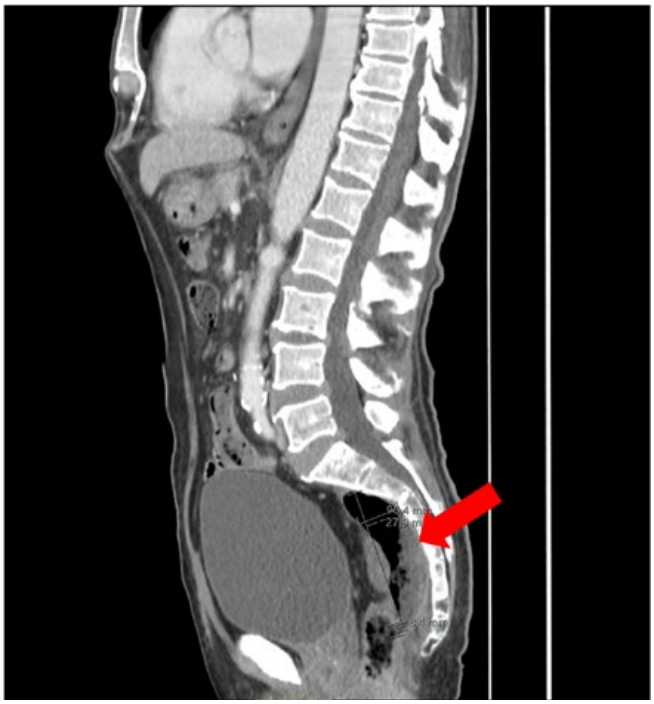

Figure 1: Sagittal section of abdominal computed tomography (CT) with presacral collection measuring about 90 x 66 x 28.

The antibiotic therapy was changed to ertapenem for the newly isolated microorganism, and collaboration with interventional radiology was requested for abscess drainage. However, the patient's overall condition significantly deteriorated the following day, ultimately leading to his demise.

Discussion

The course of this patient highlights the important relationship between an unusual pathogen, *C. braakii*, in an immunocompromised patient with multiple comorbidities. To date, there are only a limited number of documented *C. braakii* infections reported in the literature. In a PubMed search by *Citrobacter braakii* published in english from 2000 up to 2023, only seven case reports were found. We could only obtain information about 6 of those cases, which are summarized in Table 1.[5-11]

Along with our case, the patients' median age was 57 years (range: 38-81 years) with 62.5% of male sex, a

Table 1: Cases infected with *Citrobacter braakii* reported in PubMed from 2000 to 2023.

Case	Study	Age (years)	Sex	Diagnosis	Underlying disorders	Portal of entry	Treatment	Outcome
1	Gupta *et al* 2003[5]	48	F	Cellulitis	Renal transplant, diabetes mellitus	Probable BTFIT	LVFX + CLM -> LVFX + AZT	Recovered
2	Carlini *et al* 2005[6]	62	M	Peritonitis	Peritoneal dialysis	Peritoneum	CFT + TBC + CPFX	Recovered
3	Hirai *et al* 2015[7]	38	F	Bacteremia	Uterus cancer	Possible BTFIT	CMZ -> CPFX	Recovered
4	Yumoto *et al* 2017[8]	75	M	Bacteremia	Pancreatectomy and right lobectomy for pancreatic and lung cancer	Probable BTFIT	MRP -> CFZ	Recovered
5	Seo *et al* 2019[9]	67	M	Bacteremia	Acute myeloid leukaemia	Probable BTFIT	CFP	Recovered
6	Tollkuci *et al* 2021[10]	43	M	Bacteremia	-	Probable BTFIT	MRP + AMK	Recovered
7	Prasanna *et al* 2021[11]	41	F	CLABSI	B cell acute lymphoblastic leukemia	Skin	CFP -> LVFX	Recovered

A/C: amoxcicilin/clavulanic acid; AMK: amikacin, AZT: aztreonam, BTFIT: bacterial translocation from the intestinal tract; CFP: cefepime, CFZ: ceftazidima, CLABSI: central line-assofciated bloodstream infection, CLM: clindamycin, CMZ: cefmetazole, CPFX: ciprofloxacin, CTX: ceftriaxone, ERP: ertapenem, F: female, LVFX: levofloxacin, M: male, MRP: meropenem, TAZ/PIP: tazobactam/piperacillin, TBC: tobramycin

younger population with gender discrepancy than that described by Hirai J *et al*.[7] The most frequent diagnosis was bacteremia (5 of 8 cases, 62.5%) and the most frequent portal of entry was probable bacterial translocation from the intestinal tract, described in 6 (75%) of the cases. Only our patient died, but the cause of death (*C. braakii* infection or the other comorbidities) was undetermined.

In a study on the *Citrobacter* bacteremia in a Korean hospital, Lee R *et al* reported that most patients were elder, with a median age of 72 years, which was 15 years older than the average age of 55.6 years reported in the previous study by Kim *et al*, which is more compatible with our review.[1,12] In the same report, Lee R *et al* found that 90% of the patients had at least one or more comorbidities, similar to previous reports. From these comorbidities, those that cause immunosuppression such as cancer, diabetes mellitus and alcoholism are the most reported in several papers.[3,8]

Septicemia due to *C. braakii* is rare, but only one of the cases (case 7)[11] did not report it. In a previous study on the *Citrobacter* infections encountered at a tertiary university hospital, Samonis *et al* reported that the most common causative organism of septicemia was *C. freundii* (71.8%), followed by *C. koseri* (23.1%) and *C. braakii* (3.8%), and the most common types of infection were urinary tract infections (52.6%), followed by intra-abdominal (14.1%) and surgical site (7.7%).[4] In another study, when only *C. braakii* was analyzed, intra-abdominal infection was the most common site of infection with 55.8% of the cases, followed by urinary tract infection (18.6%) and central line-associated infection (9.3%).[1]

The antibiotic susceptibility results were only found in a few reports (case 3, 6, 7)[7,10,11] and, including the present case, all of them were resistant to beta-lactams and only one of them was resistant to carbapenem (case 6).[10]

To the best of our knowledge, this is the first case of a *C. braakii* bacteremia secondary to an abscess due to anastomotic dehiscence of a non-recent surgery. Several limitations should be addressed, since we were not able to drain the abscess and, therefore, confirm the presence of the same bacterium. For a better understanding of this pathogen, further reports should be published.

Conclusion

Citrobacter braakii may not be as extensively studied as other *Citrobacter* species, but it is an important microorganism in terms of understanding microbial diversity and antibiotic resistance patterns. Proper identification and antibiotic susceptibility testing are crucial for managing infections associated with this microorganism. Future research on *Citrobacter braakii* may focus on its genetic and molecular characteristics, its role in environmental microbiology, and its implications for human health. As antibiotic resistance remains a major concern, understanding the mechanisms of resistance in this bacterium can also be a focal point of research. ■

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Todos os autores aprovaram a versão final a ser publicada

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Correspondence / Correspondência:

Alexandra Machado smachado.alexandra@gmail.com
Serviço de Medicina Interna, Unidade Local de Saúde de Entre o Douro e Vouga, Santa Maria da Feira, Portugal
Rua Dr. Cândido Pinho 5, 4520-211 - Santa Maria da Feira

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