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Alloscardovia omnicolens, AN UNUSUAL PATHOGEN CAUSING BACTEREMIA: A CASE REPORT AND LITERATURE REVIEW

Yoleidys Martínez-Ysasis

Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Raúl Altaba

Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Daniela de-Minac

Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Ferran Navarro

Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain Genetics and Microbiology Department. Universitat Autònoma de Barcelona, Spain Sant Pau Institute of Biomedical Research (IIb Sant Pau), Barcelona, Spain

Alba Rivera

Microbiology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain Genetics and Microbiology Department. Universitat Autònoma de Barcelona, Spain Sant Pau Institute of Biomedical Research (IIb Sant Pau), Barcelona, Spain



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Abstract: Background: Bloodstream infections by Alloscardovia omnicolens are extremely rare, most of the bacteremia cases reported to date have been found in immunocompromised patients and were secondary to urinary tract infections. Case presentation: An 82-year-old male presented to the emergency department with jaundice, generalized pruritus and choluria. He had several comorbidities including diabetes mellitus, chronic kidney disease, dyslipidemia, chronic obstructive pulmonary disease, and cardiac insufficiency. Laboratory findings showed altered liver function and a cholangiopancreatography revealed findings suggestive of cholangiocarcinoma. During admission the patient developed fever and blood cultures were performed. Alloscardovia omnicolens, a facultative anaerobic gram-positive rod belonging to the family Bifidobacteriaceae, grew on aerobic bottles of two blood culture sets. The patient was treated with piperacillin-tazobactam for two weeks and died four weeks after admission. Conclusion: This case highlights the importance of early recognition and effective management of this rare complication caused by this microorganism.

Keywords: *Alloscardovia*; *omnicolens*; Cholangiocarcinoma; Bacteremia

CASE PRESENTATION

An 82-year-old male presented to the emergency department with two weeks of jaundice accompanied by generalized pruritus and choluria. The patient's past medical history was significant for hypertension, type 2 diabetes mellitus, chronic kidney disease, dyslipidemia, chronic obstructive pulmonary disease (COPD) GOLD 3, and cardiac insufficiency. The patient was vaccinated against SARS-CoV-2 (2 doses). Physical examination reveals no fever, normal blood pressure (132/65 mmHg) and 94% room air oxygen saturation. Lung sounds were present, and no

rales, wheezing or rhonchi were appreciated. The patient had no abdominal pain, presented with slight abdominal distention and no peripheral edema was observed. Neurologic examination showed that patient was alert and oriented to person, place, but not and time, he was otherwise normal. The patient denied cough, diarrhea, nauseas, fever or vomiting.

Recent laboratory findings showed elevated glucose 510,84mg/dl, and 10U of insulin was administered. Liver function markers were altered including total bilirubin 318 µmol/L, (18,63 mg/dL), conjugated bilirubin 214 µmol/L, (12,54 mg/dL), aspartate aminotransferase 320 U/L, alanine aminotransferase 588 U/L, and alkaline phosphate 1043 U/L. The patient showed normal C reactive protein (5,5 mg/L), low hemoglobin (104 g/L), and leukocytosis (white blood cells 18,57 x109/L).

Chest X-ray and abdominal ultrasound results were within normal limits. Given the persistence of symptoms, it was decided to perform cholangiopancreatography that showed mild dilation of the intrahepatic bile duct secondary to the thickening of the parietal bifurcation of the common hepatic duct, which suggested cholangiocarcinoma. Due to these findings, the patient was admitted.

During the admission, the patient developed fever (38.5°C), two sets of blood cultures were obtained (BioMerieux, France), and empirical antimicrobial therapy with intravenous piperacillin/tazobactam was initiated. Blood culture bottles were incubated in a BacT/Alert Virtuo (bioMerieux, France) and aerobic bottles from two sets were positive after 28 hours of incubation. Gram stain reveal Gram-positive bacilli (Figure 1) and culture on sheep blood agar plates (bioMerieux, France) grew small gray alpha-hemolytic colonies after 24 h incubation at 35°C with 5% CO₂ (Figure 2). The isolate was identified by MALDI--TOF MS (Bruker, Germany) as Alloscardovia omnicolens (score 2,40). A urine sample obtained for microbiological study showed no pyuria on microscopic sediment examination and no culture was carried out. No follow-up blood cultures or additional urine cultures were performed.

The antimicrobial susceptibility testing was performed by the gradient diffusion method (Liofilchem, Italy) in Mueller-Hilton F (Bio-Merieux, France). MIC values were determined for penicillin, vancomycin, ciprofloxacin, linezolid and piperacillin/tazobactam. Interpretation was performed according to EU-CAST breakpoints for Corynebacterium spp. except for piperacillin-tazobactam which was interpreted according PK-PD (Non-species related) breakpoints (1) and also according to CLSI breakpoints for Corynebacterium spp. (2)in vitro antimicrobial susceptibility testing of the isolated organism may be indicated. Susceptibility testing is particularly necessary in those situations in which the etiological agent belongs to a bacterial species for which resistance to commonly used antimicrobial agents has been documented, or could arise. A variety of laboratory techniques can be used to measure the in vitro susceptibility of bacteria to antimicrobial agents. Clinical and Laboratory Standards Institute document M45— Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria describes the standard microdilution and agar disk diffusion methods. It also includes a series of procedures designed to standardize test performance. The performance, applications, and limitations of the current CLSI-recommended methods are described. Clinical and Laboratory Standards Institute (CLSI. The isolate was susceptible to all antimicrobial agents tested (Table 1).

During admission the patient had hyperglycemic decompensation in the context of type 2 diabetes mellitus and progressive worsening of liver function, leukocytosis secondary to corticosteroid treatment, persistence of jaundice and appearance of pruritus probably secondary to obstruction of the intrahepatic bile duct. Due to the poor general condition of the patient, palliative measures are decided.

After 2 weeks admission the patient was released from the hospital as per family's request, and antibiotic treatment was changed from intravenous piperacillin/tazobactam to oral levofloxacin. The patient passed away 12 days after discharge.

DISCUSSION

The genus *Alloscardovia* includes facultative anaerobic gram-positive rods, nonmotile, non–sporing-forming, catalase and oxidase negative and belongs to the family *Bifidobacteriaceae*. To date five species have been described including *Alloscardovia omnicolens* (3), *Alloscardovia macacae* (4), *Alloscardovia criceti* (4), *Alloscardovia venturai* (5) and *Alloscardovia theropitheci* (6) originally isolated mainly from the oral cavity and gastrointestinal tract of different mammals.

Alloscardovia omnicolens was first described by Geer Huys in 2007 after analysis of 12 isolates originated from human clinical samples including urine, blood, urethra, oral cavity, amygdala, pulmonary abscess, and aortic valve collected in Belgium, Norway, and Sweden from 1978 to 2005 (3). The origin of its bacterial name, comes from omnis every, colens dwelling; omnicolens "dwelling everywhere in the human body" (3).

This microorganism can be isolated in culture, growing better under anaerobic conditions after 24 h at 37°C on blood agar, but when incubated in CO2 atmosphere small, pinpoint, alpha-hemolytic colonies are also observed (7). Currently Molecular testing by MALDI-TOF and 16S rRNA sequencing has increased accurate identification and raised awareness of *A. omnicolens* as a potential cause of infection (8).

At present there is controversy about the pathogenicity and significance of this microorganism, due in part to the difficulties in distinguishing these organisms from other genera such as Actinomyces (9). Mahlen (9) in 2009 analyzed the clinical significance of 15 A. omnicolens and Bifidobacterium (4 A. omnicolens, 4 B. scardovii, 2 B. longum, 4 B. breve) isolates identified by 16S rRNA gene sequencing from a clinical laboratory in order to determine the potential disease-causing role of these organism. While not all of the A. omnicolens isolates in this study were implicated as causative agent of disease, these organisms might be considered as potential contributing pathogens (9).

A. omnicolens can be found in the gastrointestinal tract, oral cavity and urinary tract are as part of the normal human microbiota (3,9). Has been described as a possible causative agent in premature rupture of membranes and urinary tract infections (10-12). Recently, a case of thoracic empyema caused by A. omnicolens, Bifidobacterim dentium, and Prevotella loescheii in a patient with no significant past medical history, with pleural tuberculosis has been described (12). Bloodstream infections by this pathogen are extremely rare, and bacteremia secondary to urinary tract infection have been reported in immunocompromised patients (13). In recent years, the progress of metagenomic sequencing has allowed the study of the human microbiota and its relationship with several diseases. A predominance of A. omnicolens along with Clostridium butyricum, Clostridium disporicum, and Veillonella montpellierensis have been described in patients with endometriosis/ adenomyosis-associated chronic pelvic pain (14). The authors concluded that these vaginal microorganisms may be considered as potential contributing pathogens and potential biomarkers for the diagnosis of this diseases. In a study characterizing the gut microbiota and bile acid metabolism, higher prevalence

of *Alloscardovia*, *Lactobacillus*, *Actinomyces* and *Peptostreptococcaeae* were found in patients with intrahepatic cholangiocarcinoma compared to patients with hepatocellular carcinoma, liver cirrhosis or healthy individuals (15). Our patient was affected by a possible cholangiocarcinoma and had bacteremia without presenting any symptoms of sepsis, the isolation of *A. omnicolens* in blood culture was probably associated to the translocation from the digestive tract.

Antimicrobial susceptibility of A. omnincolens has not been extensively studied. To date no CLSI or EUCAST breakpoints have been defined for this species, the criteria for anaerobic Gram-positive bacilli has been used in one study (16). In our work Corynebacterium breakpoints were used, since they are available in both committees. Isnard et al analysed the in vitro antimicrobial susceptibility of 31 A. omnicolens isolates and reported low minimum inhibitory concentrations (MICs) for β-lactams, glycopeptides, linezolid, tetracycline, tigecycline, cotrimoxazole and rifampin (17). In contrast, they found high MICs values for gentamicin metronidazole, nitrofurantoin and fosfomycin.

A diversity of agents has been used for the antimicrobial management of *A. omnicolens* infections. A case of thoracic empyema was treated with intravenous ampicillin/sulbactam and oral amoxicillin/clavulanate with favorable results (12). A case of urinary tract infection caused by *A. omnicolens* was resolved with intravenous cefmetazole (13). Intravenous azithromycin, ampicillin, and gentamicin were used for the treatment of a premature membrane rupture case caused by this bacterium with successful recovery (16).

In our case, the patient received intravenous piperacillin-tazobactam and the treatment was changed to oral levofloxacin when the patient was discharged with palliative measures. The patient died 12 days later as a consequence of his oncological process.

CONCLUSION

The first case of bacteremia by *A. omnicolens* associated with digestive pathology (cholangiocarcinoma) is reported. This pathogen showed susceptibility to several antibiotics, especially beta-lactams, which provides a great advantage in terms of treatment. The pathological and epidemiological importance of *A. omnicolens* should be considered.

DECLARATIONS

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Not applicable.

AUTHOR CONTRIBUTIONS

YM, AR: manuscript writing, literature review, manuscript revision, RA, DM: data collection, literature review. FN: manuscript revision.

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The authors declare no financial relationships that could influence the findings or interpretation of this research manuscript.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Consent for publication was obtained. The clinical case was approved by the Clinical Research Ethics Committee of the Hospital de la Santa Creu i Sant Pau.

COMPETING INTERESTS

All authors report no potential conflicts of interest.

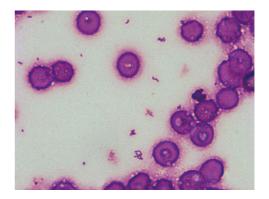


Figure 1. Gram stain of isolate *A. omnicolens*.

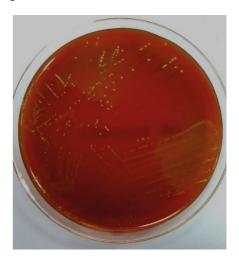


Figure 2. Small, pinpoint, alpha-hemolytic colonies of *A. omnicolens* on sheep blood agar.

Drugs	MICs	EUCAST breakpoints ¹	CLSI Breakpoints ²
Penicillin	0.125	S	S
Piperacillin/ tazobactam	2	S	-
Cefotaxime	0.5	S	S
Vancomycin	0.38	S	S
Ciprofloxacin	1	I	S
Linezolid	0.5	S	S

Table 1: Antimicrobial susceptibility of *A. om-nicolens* according to EUCAST and CLSI breakpoints.

¹Interpretation according to EUCAST *Coryne-bacterium* breakpoints for penicillin, van-comycin, ciprofloxacin and linezolid and to PK-PD (Non-species related) breakpoints for piperacillin/tazobactam and cefotaxime. ²Interpretation according to CLSI *Corynebacterium* breakpoints.

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