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Case report

Bacteremia caused by *Veillonella dispar* in an oncological patient

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ABSTRACT

Veillonella dispar is a Gram-negative anaerobic coccus involved in only a few human diseases. We report the second case of bacteremia due to this microorganism in an elderly patient. A 72-year-old man with a history of bladder cancer presented with diarrhea, vomiting, and fever for 48 hours. After the diagnosis of septic shock, four sets of blood cultures were taken, and three of them yielded *V. dispar*. Resistance to metronidazole, penicillin, and piperacillin-tazobactam was documented. Treatment with clindamycin was started, and the patient was discharged after improvement in his general condition.

1. Introduction

Veillonella spp. are Gram-negative anaerobic cocci first described by Veillon and Zuber [1]. This pathogen is a member of the normal microbiota of the mouth and gastrointestinal tract and is also found in the urogenital area [2–4]. Among the different species of this genus, *V. parvula* has been the most frequently isolated. Identification of members of this genus at species level is hampered by the lack of discriminating phenotypic tests. We recently observed a rare case of bacteremia in pure culture in a patient with a clinical history of cancer. To our best knowledge, this is the second description of *V. dispar* obtained from blood culture.

2. Description of the case

A 72-year-old man was admitted to the Emergency Department of our hospital after 48 hours with diarrhea, vomiting, and fever (38.5 °C). His clinical history was remarkable for chronic renal disease and a bladder cancer treated 8 years earlier by bladder transurethral resection and hormone therapy. At admission no active disease was found. The physical exam showed a febrile patient (38.5 °C) with tachypnea (25 bpm), and a blood pressure of 70/40 mmHg. Blood analysis showed increased levels of urea (77 mg/dL), creatinine (3.36 mg/dL), liver cytolysis enzymes (ALT: 601 U/L, AST: 1185 U/L, γ-GT: 440/U/L), C-reactive protein (17.1 mg/L), and procalcitonin (62.56 ng/mL) and an elevated white cell blood count (17,660/mm^3). Chest X-ray and CT-scan revealed no signs of pleural effusion or lung condensation. Four sets of blood cultures were taken at different times on the same day and sent to the microbiology laboratory, while empirical treatment was started with piperacillin-tazobactam (1 gr/8 h./i.v.). The patient experienced a syncopal episode that required treatment with abundant fluids (3000 cc of crystalloids), and his blood lactate level at that time was 5 meQ/L. He was then admitted to the ICU due to septic shock requiring treatment with vasoactive drugs. The result of a polymerase chain reaction test for SARS-Coronavirus 2 was negative.

In the microbiology laboratory, samples were inoculated onto the BACTEC FX 40 (Becton Dickinson, Franklin Lakes, NY) monitorization system for culture. On day 2 of incubation, the two anaerobic bottles from two blood culture sets were positive. The samples were subcultured on aerobic or anaerobic blood agar (BD Columbia Agar with 5% Sheep Blood, Becton Dickinson, Franklin Lakes, NY). All media were incubated at 37 °C. The AnaeroGen Compact anaerobic system (Oxoid Ltd, Wide Road, Basingstoke,

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England) was used. Gram staining of the blood cultures revealed abundant Gram-negative cocci; on day 2 of incubation, abundant colonies of these microorganisms were observed in pure culture on anaerobic blood agar alone. MALDI-TOF MS version 9 (8468 msp) (Bruker Biotyper, Billerica, MA) was employed, identifying the strain as *V. dispar* (score 2.13). However, the MALDI-TOF MS pattern was not consistent, because there was also a matching pattern with *V. parvula* and *V. atypica*. The strain was sent to the Centre of Genomic and Oncologic Research (GENYO, Granada, Spain) for 16S rRNA gene sequence analysis using a previously reported method [5]. A fragment of 1498 bp was obtained, yielding 99.59% similarity with the V. dispar type strain ATCC 17748 GenBank sequence (Accession number NR 115355.1). The 16S sequence was submitted to the GenBank (accession number: MT586631.1).

The E-test was used for antimicrobial susceptibility testing based on 2020 EUCAST criteria [6]. Because there are no EUCAST resistance breakpoints for moxifloxacin, susceptibility test results for this antibiotic were based on 2019 CLSI criteria [7]. The following MIC values were obtained: penicillin (1.5 mg/L), amoxicillin-clavulanate (0.75 mg/L), piperacillin-tazobactam (16 mg/L), clindamycin (0.5 mg/L), meropenem (0.19 mg/L), imipenem (0.25 mg/L), ertapenem (0.094 mg/L), moxifloxacin (2 mg/L), and metronidazole (12 mg/L).

Antimicrobial treatment was changed to clindamycin (300 mg/8 h) for 14 days. The patient had a new episode of diarrhea with abdominal pain 10 days after his initial admission, and a colonoscopy revealed multiple several intestinal polyps. These were excised, and the patient slowly improved. His general condition remains good at 2 months of follow-up.

3. Discussion

Veillonella spp. are non-motile anaerobic Gram-negative cocci. They are commonly described as contaminants with limited pathogenicity and are usually associated with polymicrobial infections. Among species of the genus *Veillonella* that have been isolated in human infections, *V. parvula* is the most frequently implicated; however, it is uncommon as a cause of bloodstream infections [8–10], although these have been associated with non-identified species of *Veillonella* [11,12]. Another species, *V. dispar*, was isolated in pure culture from a patient with prosthetic valve endocarditis and from another with prosthetic joint infection [13,14]. To date, only one case of bloodstream infection by *V. dispar* has been described in the literature, and the method used to confirm the species identification was not reported [15]. Hence, to our best knowledge, we present the second case of bacteremia due to this anaerobic microorganism isolated in pure culture.

The possible sources of infection with this anaerobe are not well known, although *Veillonella* is often implicated in periodontal disease. The present patient had no history of periodontal disease and showed only an abdominal focus of the infection, with diarrhea and vomiting. The most likely source of infection was therefore the gut, taking into account that *Veillonella* spp. form part of the normal microbiota of the gastrointestinal tract.

MALDI-TOF MS offers a rapid approach for the routine analysis of bacteria in clinical laboratories. It can be highly useful for the final identification at both genus and species level and may help to detect new species of anaerobes. Nevertheless, this technique should be applied with care, evaluating the version of the database used, the log score obtained, and the consistency of the identification. When the log score indicates high confidence but the consistency is low (as in the present case), molecular methods should be used to confirm the result and avoid misidentification.

Most *in vitro* studies suggest that *Veillonella* spp. remain susceptible to a wide range of commonly used drugs. Among case reports, several did not perform antimicrobial susceptibility testing [8,10,15] and three found that *Veillonella* isolates were susceptible to all antimicrobials tested, although there was a high heterogeneity [11,13,14]. High resistance to metronidazole (MIC > 128 mg/L) was described in one report [9] and resistance to penicillin and metronidazole in another 12], whereas metronidazole was found to be active against 100% of *Veillonella* isolates in another study [16]. A study of 83 isolates of *Veillonella* (52 isolates of *V. parvula*) showed resistance to penicillin in 59% and resistance to clindamycin in 7% of them. In the present study, no resistance to metronidazole or imipenem was detected [17]. In a very recent study of *Veillonella* isolates (n = 17) in Greece [18], 29.4% were resistant to penicillin and 35.3% to ampicillin, with a beta-lactamase production rate of 29.4%, and 17.6% were resistant to piperacillin-tazobactam, 11.8% to clindamycin, and 5.9% to moxifloxacin; no resistance to metronidazole was observed. However, a study in Taiwan found that 20% of Veillonella spp. isolates were resistant to metronidazole [19]. In the present case, the strain was resistant to penicillin, piperacillin-tazobactam, and metronidazole.

Taken together, the above findings indicate an increased resistance of *Veillonella* spp. to penicillin, clindamycin, and piperacillin-tazobactam. Overall, the resistance of *Veillonella* spp. to metronidazole remains low, although some resistant strains have been reported in different countries. Susceptibility testing of these strains is essential to develop the optimal therapeutic strategy against these infections.

In conclusion, this is the second report of *V. dispar* isolated in pure culture and confirmed by 16S rRNA gene sequencing as a cause of bacteremia, indicating that this pathogen can be responsible for severe infections. This case report and recent observations of antimicrobial susceptibility among *Veillonella* spp. highlight an increased resistance to various antimicrobials and emphasize the need for antimicrobial susceptibility testing of all isolates.

Conflict of interest

Authors declare no conflict of interest.

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