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Case Report

Pancytopenia associated with *Weissella confusa* septicemia

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Abstract

Introduction: *Weissella spp.* are facultative gram-positive bacteria. They are also part of the human microbiota and can cause opportunistic infections. There are very few case reports in the literature describing bacteremia caused by *W. confusa*.

Case presentation: A 74-year-old male patient presented to the Internal Medicine Department of Ankara Etlik City Hospital with complaints of fever, chills, nausea, and vomiting. Laboratory tests revealed pancytopenia. Etiological investigation identified *W. confusa* in blood cultures using MALDI-TOF MS, and other potential causes of pancytopenia were excluded. The patient had chronic kidney disease and was undergoing hemodialysis three times a week.

Conclusions: *W. confusa* should be considered among opportunistic pathogens, especially in patients with end-stage renal disease. This case is presented as a rare clinical report due to the association of pancytopenia with *W. confusa* septicemia.

Key words: Septicemia; *Weissella confusa*; pancytopenia; Case Report.

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Introduction

Weissella spp., members of the *Lactobacillaceae* family, are commonly found in the human microbiome, often as harmless commensals but rarely as opportunistic pathogens. Reports of bacteremia caused by these organisms—typically colonizing the genitourinary and gastrointestinal tract—are scarce. *W. confusa*, a gram-positive, catalase-negative coccobacillus, was reclassified from the *Leuconostoc* genus by Collins *et al.* in 1993 [1]. Formerly known as *Lactobacillus confusus*, it has been isolated from raw milk, feces, saliva, urine, and meat products. It may act as an opportunistic pathogen, particularly in individuals with altered intestinal flora, those receiving vancomycin therapy, carrying central venous catheters, or in immunocompromised or recently operated patients. It has been implicated in cases of bacteremia and septicemia [2–4].

Studies investigating the antimicrobial susceptibility of *Weissella spp*. are limited. These organisms are intrinsically resistant to vancomycin [5], and while they demonstrate low minimum inhibitory concentrations (MICs) against penicillin, ampicillin, tetracyclines, carbapenems, and quinolones, they are resistant to ceftazidime, rifampin, and co-trimoxazole [6]. Successful treatments have included daptomycin, amoxicillin-clavulanate, piperacillin/tazobactam with teicoplanin or gentamicin, and combinations such as metronidazole with levofloxacin, cefoperazone-sulbactam, meropenem, aztreonam, cefoxitin, or teicoplanin [7].

Pancytopenia is defined as the reduction of all three hematologic cell lines below normal reference ranges. Although *W. confusa* has been implicated in bacteremia, septicemia, meningitis, and endocarditis, to our knowledge, no cases associating it with pancytopenia have been reported. We present this case as a novel contribution to the literature.

Case Report

A 74-year-old male with a history of type 2 diabetes mellitus, hypertension, and end-stage renal disease (ESRD), receiving hemodialysis three times weekly, presented to the emergency department with fever, chills, vomiting, and weight loss. Pancytopenia was detected, and he was admitted to the internal medicine clinic for further etiological evaluation.

Initial laboratory findings revealed hemoglobin 10.4 g/dL, leukocyte 3900/mm^3, and platelets 93000/mm^3. Prior blood test results from September 4, 2023, showed hemoglobin 13.8 g/dL, leukocyte 8930/mm^3, and platelets 219000/mm^3. A previous blood test from March 3, 2023, was also within normal limits, confirming that pancytopenia developed acutely.

Given the deterioration of clinical condition and elevated inflammatory markers (CRP and procalcitonin), along with a fever of 38.7°C, blood and urine cultures were obtained. On October 3, 2023, four

blood culture sets (two aerobic, two anaerobic) were collected, all of which grew *W. confusa*. Identification was performed using the matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) directly from blood agar. A polymicrobial pattern was observed. *W. confusa* had a score value of 2.20 (+++), indicating reliable identification. *Streptococcus salivarius* was also isolated, but due to a lower score of 1.89 (+), it was considered a contaminant.

As no species-specific breakpoints for *W. confusa* exist in the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, antibiotic susceptibility was assessed using non-species-specific pharmacokinetic/pharmacodynamic (PK/PD) breakpoints. The organism was found to be susceptible to meropenem, imipenem, and levofloxacin, but resistant to piperacillin-tazobactam, ceftazidime, ceftriaxone, and vancomycin. Meropenem was initiated in accordance with these results and in line with Spiegelhauer *et al.*'s therapeutic recommendations [7].

Before treatment, pancytopenia and leukopenia worsened. By day 6, the leukocyte count had dropped to 1590/mm^3, with neutrophils at 500/mm^3. Figure 1 shows trends in leukocyte count and inflammatory markers.

An extensive workup was conducted to exclude other causes of pancytopenia. Serologies for *Brucella* spp., Herpes simplex virus (HSV), Ebstein-Barr virus (EBV), Parvovirus B19, *Toxoplasma gondii*, Cytomegalovirus (CMV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and *Mycobacterium tuberculosis* were negative (Table 1). Autoimmune screening, including anti-nuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), extractable nuclear antigen (anti-ENA) panel, rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP), was also negative.

Peripheral blood smear revealed no atypical cells but did show a left shift and toxic granulation, which was consistent with bacteremia. Bone marrow aspiration and biopsy were normocellular, with no atypia or findings suggestive of leukemia. Investigations for lymphoproliferative disorders and aplastic anemia revealed no pathological findings. Serum free kappa and lambda light chain levels and ratio, serum protein electrophoresis, and immunoglobulin G, A, and M levels—conducted to screen for plasma cell dyscrasias—were within normal limits. No monoclonal gammopathy was detected on serum immunofixation electrophoresis.

Due to the patient's ESRD and immunosuppressed status, as well as the presence of fever, a transthoracic echocardiogram was performed to evaluate for possible cardiac vegetation and infective endocarditis, but no findings consistent with infective endocarditis were observed.

Following meropenem therapy, there was a marked decrease in acute phase reactants, accompanied by clinical improvement and resolution of fever. Pancytopenia also resolved, with all hematologic parameters returning to normal reference ranges (Figure 1). Post-treatment blood cultures were negative for microbial growth. Thus, pancytopenia was attributed to *W. confusa* septicemia.

Table 1. Tests performed for infectious parameters involved in the etiology of pancytopenia.

Test	Result
Anti-CMV IgM	0.205, Negative
COVID-19 Reverse Transcriptase	Negative
Brucella Agglutination Test (Rose Bengal)	Negative
Quantiferon TB-Gold	Negative
Anti-HIV	0.302, Negative
EBV-VCA IgM	0.22, Negative
HSV-1 / HSV-2 IgM	Negative
Parvovirus B19 IgM	0.1, Negative
Anti-Toxoplasma IgM	0.171, Negative
Anti-Rubella IgM	0.243, Negative

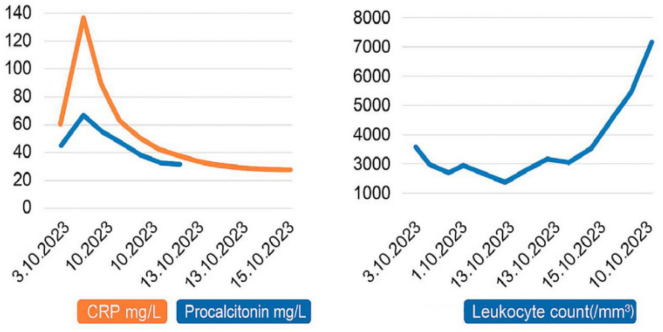
CMV: *Cytomegalovirus*; Ig: Immunoglobulin; EBV-VCA: *Epstein-Barr Virus* Viral Capsid Antigen; HSV: *Herpes Simplex Virus.*

Discussion

Infections caused by *Weissella* and *Lactobacillus spp.,* both part of the normal gastrointestinal and vaginal flora, are rare and typically occur in immunocompromised individuals. Clinical conditions such as ESRD, diabetes, malignancy, and recent surgery increase susceptibility to such infections [8]. Although *W. confusa* has been proposed as a probiotic and is commonly found in fermented foods, it has also been implicated in serious infections in immunocompromised individuals.

W. confusa is a recognized opportunistic pathogen that poses diagnostic challenges in clinical laboratories.

Figure 1. Temporal decrease in leukocyte counts and increase in acute phase reactants during the clinical course.



Its identification can be difficult using conventional commercial systems, which may misidentify or fail to detect the organism. However, matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) has demonstrated reliability in accurately identifying *W. confusa*, as evidenced by the findings of Fairfax *et al.* [9].

W. confusa, a vancomycin-resistant gram-positive bacterium. In the absence of organism-specific EUCAST breakpoints for this bacterium, antibiotic susceptibility was interpreted using non-species-related PK/PD breakpoints. Based on these criteria, the isolate was susceptible to levofloxacin, meropenem, and imipenem, and resistant to piperacillin-tazobactam, ceftazidime, ceftriaxone, and vancomycin. Given the patient's immunocompromised status and comorbidities, and in accordance with the recommendation by Spiegelhauer *et al.,* meropenem was initiated [7]. After initiating meropenem, the patient's septic response and acute phase reaction subsided. Our isolate was successfully treated with meropenem, consistent with Spiegelhauer *et al.*'s case [7].

In our review of the literature on *W. confusa* as an opportunistic pathogen in immunocompromised individuals, we identified case reports describing *W. confusa* septicemia in a renal transplant recipient, a patient who had undergone allogeneic bone marrow transplantation, and another with adenocarcinoma of the gastroesophageal junction [4–10]. Our patient was similarly immunocompromised due to end-stage renal disease and was receiving hemodialysis three times per week. Both his age and chronic conditions presenting possible risk factors for *W. confusa* septicemia.

A comprehensive evaluation excluded hematological, rheumatological, and other infectious etiologies. Bone marrow was normocellular, and no alternative explanation for pancytopenia was identified.

Conclusions

To the best of our knowledge, this is the first reported case of pancytopenia secondary to *W. confusa* septicemia. Therefore, our case is particularly valuable as the first case report to describe this condition, and also raises awareness about considering *Weissella* group bacteria in the evaluation of opportunistic pathogens in patients with ESRD and also with immunocompromised states. This case highlights the need for caution in the use of *W. confusa* as a probiotic, given the unclear true incidence of its role as an opportunistic pathogen and its potential to cause infections in immunocompromised individuals.

Authors' contributions

Akkus C. First author, literature review, writing, correction, and editing; Arslan A. Collection of data, writing, and literature review.

Statement of informed consent

The authors have obtained written informed consent from the patient.

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Conflict of interest

No conflict of interest is declared.

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