Lock, stock, and *Leuconostoc*: an unusual presentation of a rare pathogen

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ABSTRACT

Leuconostoc mesenteroides *is a Gram-positive bacterium in the Lactobacillaceae family. This species is rarely encountered clinically and in the past was regarded as a contaminant when cultured. Recently it is being recognized as a pathogen responsible for opportunistic infections in immunocompromised patients. Compared to other Gram-positive cocci,* Leuconostoc *spp. carry intrinsic resistance to vancomycin. It is not common for clinical microbiology laboratories to isolate this organism and instead incorrectly report enterococcus and streptococcus organisms. Here, we present a case of bacteremia resulting in febrile illness and pneumonia in an 81-year-old woman with a history of rheumatoid arthritis and a notable lapse between immunomodulator therapy exposure. She was successfully treated when this organism was identified, and her antibiotic therapy was switched from vancomycin to ampicillin-sulbactam. This case highlights the importance of considering* L. mesenteroides *as a source of infection in patients predisposed to an immunocompromised state despite this organism's being a rare pathogen.*

Keywords: *Leuconostoc mesenteroides*, rheumatoid arthritis, immunomodulators; vancomycin resistance

INTRODUCTION

Infections with rare pathogens can be both a diagnostic and therapeutic challenge for physicians. Particularly challenging is the use of specialized diagnostic methods to identify the pathogen and inherent resistance patterns that may not be anticipated by those unfamiliar with the organisms. *Leuconostoc mesenteroides* is such a bacterium, often requiring advanced culture techniques, historically mistaken for other organisms, and inherently resistant to vancomycin. Infections attributed to this organism are rare and usually occur in patients who have undergone transplants, have indwelling catheters, take immunomodulator therapy, or received vancomycin.[1] However, a wide variety of presentations have been reported, including endocarditis, urinary tract infections, intrabdominal infections, meningitis, empyema, and catheter-associated bloodstream infections.[1] Furthermore, although *L. mesenteroides* is frequently associated with oncology patients,[2–4] infections may occur in patients with other forms of immunocompromise. We present a case of bacteremia caused by this organism in an 81-year-old woman with severe immunodeficiency as a result of her immunomodulator therapies for rheumatoid arthritis.

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CASE

An 81-year-old woman presented to the emergency department for a near syncopal episode after arising from a seated position. Her past medical history included hypertension, seropositive rheumatoid arthritis (RA), and osteopenia. Her RA was diagnosed in 2012 with a positive cyclic citrullinated peptide (CPP) antibody, and she has been treated with multiple disease-modifying antirheumatic drugs (DMARDs), including methotrexate,

hydroxychloroquine, leflunomide, adalimumab, certolizumab, golimumab, abatacept, tocilizumab, and sulfasalazine. Prior to her admission, she was recently treated with rituximab for 7 years but stopped 7 months ago and switched to hydroxychloroquine. Evaluations by a rheumatology consultant had discovered persistent lymphopenia and hypogammaglobinemia, which was considered residual effects of rituximab.

The patient was initially found to be orthostatic and treated with conservative measures but subsequently developed a febrile illness and hypoxic respiratory failure with radiographic evidence of pneumonia. Treatment was initiated with ceftriaxone and azithromycin for community-acquired pneumonia. Despite treatment, she remained febrile (101–102°F), and treatment was broadened to cefepime and metronidazole. The following day, blood cultures grew a Gram-positive organism in pairs and chains. Polymerase chain reaction testing was negative for multiple organisms, including *Staphylococcus*, *Streptococcus*, *Listeria*, and *Enterococcus*. Subsequent send-out testing identified *L. mesenteroides* as the organism with susceptibility to all antimicrobials tested (penicillin, ampicillin, chloramphenicol). She was switched to ampicillin-sulbactam and underwent a transesophageal echocardiogram, which was negative for vegetations. She completed a 14-day course of ampicillin-sulbactam with defervescence and clearance of blood cultures and was discharged with a plan for follow-up in pulmonology and rheumatology clinics.

Discussion

Leuconostoc mesenteriodes is a Gram-positive, nonmotile, catalase-negative, lactic acid-producing bacterium found on plant and vegetable matter and is used in the food industry for dairy product fermentation.[5] It is a rare and typically opportunistic pathogen in humans, with the first pathogenic case identified in 1985.[6] Risk factors include an immunocompromised immune status, indwelling catheters, bacteremia, pre-mature birth weight, underlying enteric disease, parenteral nutrition, compromised gastrointestinal mucosa, and previous vancomycin exposure.[1,7–9] *Leuconostoc* spp. are often associated with patients with underlying malignancy,[10] likely secondary to immunocompromised host defenses and indwelling catheters. *L. mesenteroides* are also variable biofilm producers, which may allow their colonization of indwelling catheters.[11] Hospital outbreaks of *L. mesenteroides* have been reported. In one such outbreak, parenteral nutrition was the suspected source.[9] *L. mesenteroides* can also colonize the human gastrointestinal tract, with disruption of the GI mucosal membrane as the proposed means of entry.[12,13] In one case, a patient with poor dentition consumed unpasteurized milk resulting in *L. mesenteroides* bacteremia.[14] In this case, no definitive source was determined. The most likely source was the lungs, given her pneumonia, but sputum cultures did not grow *L. mesenteroides*.

Leuconostoc spp. may result in a variety of presentations, such as endocarditis,[15] prosthetic joint infection,[16] urinary tract infection,[17] empyema,[18] meningitis,[19] brain abscess,[13] odontogenic infection,[20] osteomyelitis,[21] and endophthalmitis;[22] bacteremia and catheter infection are usually the most common.[9] Identification of *L. mesenteroides* can be challenging. They may be misidentified as *Streptococcal*, *Enterococcus,* or *Lactobacillus* species.[23] Identification of a vancomycin-resistant streptococcal species should prompt testing for other bacterial species such as *Leuconostoc*,[20] which may include advanced microbiological testing or molecular methods, such as 16S rRNA sequencing.[13] Microbiological criteria include catalase-negative organism, resistance of vancomycin, negative for pyrolidonyl arylamidase production, negative leucine aminopeptidase production, dioxide production from glucose, and no growth in broth with 6.5% NaCl.[3,10,24] Treatment for *Leuconostoc* spp. includes penicillin, clindamycin carbapenems, ampicillin, and aminoglycosdies.[25] Central venous catheters should be removed.[2,26] Echocardiography should be considered given the potential for *Leuconostoc* spp. to cause endocarditis.[15,24,27–29] In one single-center study, fatalities related to *L. mesenteroides* was 7.1%, but many of the patients in this study had significant underlying disorders.[9]

Immunosuppression is a known risk factor for *L. mesenteroides* infection, as is the case here with hydroxychloroquine use and recent rituximab use. Immune reconstitution after stopping rituximab usually begins at six months and is completed at 9 to 12 months;[30] her persistent lymphopenia and hypogammaglobinemia are consistent with this. However, *Leuconostoc* infection in patients with rheumatological diseases is infrequent. Indeed, there are only 3 cases of *L. mesenteroides*

infection in rheumatoid arthritis patients. Patients with rheumatological diseases, such as rheumatoid arthritis receiving immunosuppressive therapy, are at risk for a variety of infections.[31] The global disease burden of rheumatoid arthritis is projected to increase to 31.7 million by 2050 (from 17.6 million in 2020). Furthermore, the increasing prevalence of immunosuppression,[32] including increased use of disease-modifying anti-rheumatic drugs (DMARDs),[33] means physicians may encounter infections with unusual bacteria, such as *L. mesenteroides,* in patients without malignancy, active chemotherapy, or indwelling ports.

In conclusion, *L. mesenteroides* is a rare cause of human infection. While often associated the malignancy, it can also be associated with other forms of immunocompromised host defenses. In this case, we report the third instance of *L. mesenteroides* infection in a patient with RA. Immunosuppression was not readily apparent given her discontinuation of rituximab, though it is possible her immune system was not fully reconstituted at the time of infection. With an increase in the use of immune-modulating agents to treat cancers and autoimmune diseases, more patients could be susceptible to infection from traditionally rare pathogens like *L. mesenteroides*. Physicians should consider *Leuconostoc* infection in patients with known risk factors and isolation of a vancomycin-resistant *Streptococcus.*

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References

1. Menegueti MG, Gaspar GG, Laus AM, et al. Bacteremia by *Leuconostoc mesenteroides* in an immunocompetent patient with chronic Chagas disease: a case report. *BMC Infectious Diseases* 2018/11/03 2018;18(1):547. doi:10.1186/s12879-018-3452-7
2. Caso JM, Recio R, Ruiz-Ruigómez M, et al. Bacteremia due to *Leuconostoc* species: A 13-year single-center case series. *Enfermedades infecciosas y microbiologia clinica (English ed)* 2024/03/01/ 2024;42(3):149–51. doi:https://doi.org/10.1016/j.eimce.2023.01.007
3. Ishiyama K, Yamazaki H, Nakao S, et al. *Leuconostoc* bacteremia in three patients with malignancies. *J Infection and Chemotherapy* 2011/01/01/ 2011;17(3):412–18. doi:https://doi.org/10.1007/s10156-010-0123-z
4. Cuervo S, Cortes J, Rodríguez E, et al. *Leuconostoc* sp in cancer patients: A descriptive study. *Revista chilena de infectología: órgano oficial de la Sociedad Chilena de Infectología* 07/01 2008;25:184–8.
5. Holland R, Liu SQ. Lactic Acid Bacteria | *Leuconostoc* spp. In: Fuquay JW, ed. *Encyclopedia of Dairy Sciences (Second Edition)*. Academic Press; 2011:138–42.
6. Buu-Hoi A, Branger C, Acar J. Vancomycin-resistant streptococci or *Leuconostoc sp. Antimicrobial agents and chemotherapy* 1985;28(3):458–60.
7. Barletta J, Estrada T, Rolón MJ, et al. Meningitis due to *Leuconostoc mesenteroides* associated with central nervous system tuberculosis: a case report. *Ann Clin Case Rep 2017; 2*. 2017;1228.
8. Scano F, Rossi L, Cattelan A, et al. *Leuconostoc* species: a case-cluster hospital infection. *Scandinavian J Infectious Diseases* 1999/01/01 1999;31(4):371–3. doi:10.1080/00365549950163815
9. Bou G, Luis Saleta J, Sáez Nieto JA, et al. Nosocomial outbreaks caused by *Leuconostoc mesenteroides subsp. mesenteroides*. *Emerg Infect Dis* Jun 2008;14(6):968–71. doi:10.3201/eid1406.071095
10. Lee MR, Huang YT, Lee PI, et al. Healthcare-associated bacteraemia caused by *Leuconostoc* species at a university hospital in Taiwan between 1995 and 2008. *J Hospital Infection* 2011/05/01/ 2011;78(1):45–9. doi:https://doi.org/10.1016/j.jhin.2010.11.014
11. Leathers TD, Bischoff KM. Biofilm formation by strains of *Leuconostoc citreum* and *L. mesenteroides*. *Biotechnology Letters* 2011/03/01 2011;33(3):517–23. doi:10.1007/s10529-010-0450-2
12. Haslam DB, St. Geme JW. Chapter 124 – Other Gram-Positive, Catalase-Negative Cocci: Leuconostoc and Pediococcus Species and Other Genera. In: Long SS, Prober CG, Fischer M, eds. *Principles and Practice of Pediatric Infectious Diseases (Fifth Edition)*. Elsevier; 2018:746–7.e1.
13. Albanese A, Spanu T, Sali M, et al. Molecular identification of *Leuconostoc mesenteroide*s as a cause of brain abscess in an immunocompromised patient. *J Clinical Microbiology* 2006;44(8):3044–5. doi:10.1128/jcm.00448-06

14. Immel S, Widmer K. *Leuconostoc mesenteroides* bacteremia in a patient with exposure to unpasteurised raw milk. *BMJ Case Rep* Mar 22 2023;16(3). doi:10.1136/bcr-2022-252034

15. Vázquez E, Carazo I, Martín A, et al. [Infectious endocarditis caused by *Leuconostoc mesenteroides*]. *Enferm Infecc Microbiol Clin* 1998/05/ 1998;16(5):237–8.

16. Franco-Cendejas R, Colín-Castro CA, Hernández-Durán M, et al. *Leuconostoc mesenteroides* periprosthetic knee infection, an unusual fastidious Gram-positive bacteria: a case report. *BMC Infectious Diseases* 2017/03/23 2017; 17(1):227. doi:10.1186/s12879-017-2315-y

17. Taneja N, Rani P, Emmanuel R, et al. Nosocomial urinary tract infection due to *Leuconostoc mesenteroides* at a tertiary care centre in north India. *Indian J Medical Research* 2005;122(2):178.

18. Usta-Atmaca H, Akbas F, Karagoz Y, et al. A rarely seen cause for empyema: *Leuconostoc mesenteroıdes*. *J Infect Dev Ctries* Apr 15 2015;9(4):425–7. doi:10.3855/jidc.5237

19. Friedland IR, Snipelisky M, Khoosal M. Meningitis in a neonate caused by *Leuconostoc* sp. *J Clin Microbiol* Sep 1990; 28(9):2125–6. doi:10.1128/jcm.28.9.2125-2126.1990

20. Wenocur HS, Smith MA, Vellozzi EM, et al. Odontogenic infection secondary to *Leuconostoc* species. *J Clinical Microbiology* 1988;26(9):1893–4. doi:10.1128/jcm.26.9.1893-1894.1988

21. Zaoui A, Brousse C, Bletry O, et al. *Leuconostoc* osteomyelitis. *Joint Bone Spine* 2005/01/01/ 2005;72(1):79–81. doi:https://doi.org/10.1016/j.jbspin.2004.05.004

22. Damasceno NP, Horowitz SA, Damasceno EF. *Leuconostoc* as a cause of endophthalmitis post-intravitreal injection of ranibizumab. *Ocul Immunol Inflamm* 2016;24(1):118–9. doi: 10.3109/09273948.2014.898073

23. Cappelli EA, Barros RR, Camello TC, et al. *Leuconostoc pseudomesenteroides* as a cause of nosocomial urinary tract infections. *J Clinical Microbiology* 1999;37(12):4124–6. doi:10.1128/jcm.37.12.4124-4126.1999

24. Starr JA. Leuconostoc species—associated endocarditis. *Pharmacotherapy: The J Human Pharmacology and Drug Therapy* 2007/05/01 2007;27(5):766–70. doi:https://doi.org/10.1592/phco.27.5.766

25. Han H, Gandhi SA, Manthani K. *Leuconostoc mesenteroides* bacteremia in a patient with lower extremity cellulitis. Infectious Diseases Consultant. published online September 12, 2019.

26. Karbuz A, Kocabaş BA, Yalman A, et al. Catheter related *Leuconostoc mesenteroides* bacteremia: a rare case and review of the literature. *The J Pediatric Research* 2017; 4(1):35.

27. Valencia D, Valencia V, Fershko A. Leuconostoc species endocarditis in an intravenous drug user. *J Cardiol Cases* Jul 2018;18(1):37–41. doi:10.1016/j.jccase.2018.04.002

28. García-Granja PE, López J, Ladrón R, et al. Infective endocarditis due to *Leuconostoc* species. *Revista Española de Cardiología (English Edition)* 2018;71(7):592–4. doi:10.1016/j.rec.2017.04.013

29. Sarmiento-Ortiz EA, Oliveros-Andrade OA, Rojas-Hernández JP. Endocarditis caused by *Leuconostoc lactis* in an infant. Case report. *Revista de la Facultad de Medicina* 2020; 68(3):467–70.

30. Worch J, Makarova O, Burkhardt B. Immunreconstitution and infectious complications after rituximab treatment in children and adolescents: what do we know and what can we learn from adults? *Cancers (Basel)* Jan 29 2015;7(1):305–28. doi:10.3390/cancers7010305

31. Mehta B, Pedro S, Ozen G, et al. Serious infection risk in rheumatoid arthritis compared with non-inflammatory rheumatic and musculoskeletal diseases: a US national cohort study. *RMD Open* 2019;5(1):e000935. doi:10.1136/rmdopen-2019-000935

32. Martinson ML, Lapham J. Prevalence of immunosuppression among US adults. *JAMA* 2024; Mar 12;331(10):880–2. doi: 10.1001/jama.2023.28019

33. Peasah SK, Swart ECS, Huang Y, et al. Disease-Modifying Medications in Patients with Rheumatoid Arthritis in the USA: Trends from 2016 to 202. *Drugs – Real World Outcomes* 2024/02/18 2024;doi:10.1007/s40801-024-00416-3