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A curious case of *Lactococcus garvieae* bacteremia associated with adenocarcinoma

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Keywords:	<i>Lactococcus garvieae</i> is a pathogen typically acquired from the consumption of raw seafood or unpasteurized dairy products. Here, we present the unique case of a middle-aged gentleman who presented with back pain, originally thought to be muscle spasms due to poor posture and heavy lifting. Initial radiological imaging showed evidence of a lumbar epidural abscess and lung nodule. Upon further work-up, <i>L. garvieae</i> was isolated in blood and abscess cultures. It was later hypothesized that the <i>L. garvieae</i> bacteremia might have an association with adenocarcinoma of the lung.
Lactococcus Garvieae	
Adenocarcinoma Raw fish Cancer	

Introduction

L. garvieae is a gram-positive, catalase-negative, anaerobic cocci bacteria species that can exist in chains, pairs or even as a single unit. *Lactococcus* organisms were originally part of the *Streptococcus* genus, but only distinguished by their ability to ferment carbohydrates and produce lactic acid [1]. In 1985, the *Lactococcus* organisms were officially separated from the *Streptococcus* genus and given their own genus based on 16 s rRNA sequencing data and DNA-DNA relatedness [2]. The *Lactococcus* genus is now classified as 5 species and 3 subspecies including *L. garvieae*, *L. piscium*, *L. plantarum*, *L. raffinolactis*, *L. xyloses*, *L. lactis* ser Lactis, *L. lactis* ser Cremoris, and *L. lactis* ser Hordniae [1,3]. Although most species and subspecies are not associated with human disease; recently, *L. garvieae* has been seen as one of the emerging pathogens affecting humans [4].

Case presentation

A 52-year-old male presented to the emergency department with complaints of back pain that started after approximately one hour of heavy lifting. He stated that the pain was located in his lower back, characterized it as dull, and specified that it did not radiate. The back pain was said to have had an insidious onset and progressively worsened. The patient denied noticing any aggravating or relieving factors, as well as having similar pain in the past. He had not experienced any trauma to the affected area prior to the onset of symptoms, nor did he have a history of associated fever, numbness, tingling, weakness of his extremities, constipation, or urine retention. Additionally, he complained of chest pain that started roughly the same time as the back pain. Although, he endorsed previously experiencing the same type of chest pain recurrently for several months. The chest pain was described as sharp, pleuritic in nature, moderate severity, and had no known relieving factors. He denied chest pain with exertion, cough, sputum production, and shortness of breath.

The patient's past medical history was notable for hypertension, schizophrenia, hepatitis C, questionable COPD/asthma, and alcohol abuse. He had a 30 pack-year smoking history and was still smoking at the time of presentation. His medications included amlodipine, hydro-chlorothiazide, lisinopril, and naproxen for pain, and he had no known drug allergies. He was unemployed at the time of presentation but had worked as a mechanic previously. His diet consisted mainly of well-cooked meats, potatoes, and beans. Notably, the patient had no history of eating raw fish or fishing.

Physical examination at time of arrival was significant for low grade fever and tachycardia. No obvious neurological deficits were appreciated. Laboratory tests collected included a complete blood count, a comprehensive metabolic panel, and blood cultures. A computerized tomography (CT) scan of the lumbar spine was obtained and revealed an L3-L5 epidural abscess with L5-S1 discitis. A CT scan of the thorax showed a right upper lobe pulmonary nodule measuring 4.2×3.2 cm.

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Case report





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This nodule was seen a year earlier and measured about 1.7 \times 0.9 cm, but the patient had elected against further surveillance/workup at that time. Other, less characterized, findings on the CT scan included a small liver nodule and a small mass in the pancreatic head (imaging not published per patient's family request). General serum tests including blood cultures, inflammatory markers, complete blood count, and metabolic profile were collected. They were significant for elevated values of ESR (78 mm/h), CRP (33 mg/dl), and white blood count (17.1 \times 10^[9]/L).

Overnight, the two sets of blood cultures grew with 4 of 4 bottles showing Enterococcus species. Subsequently, the patient was started on intravenous (IV) vancomycin, and L3-L5 hemi-laminectomies were performed for evacuation of the abscess and culture of aspirate. An acidfast bacillus concentration and smear with mycobacterium tuberculosis by polymerase chain reaction (PCR) came back negative. The remaining laboratory results were unremarkable. Over the next 2 days, blood cultures further speciated to L. Garvieae (identified by MALDI-TOF). In addition, the epidural abscess culture also grew L. garvieae, likely from hematologic seeding. Susceptibility testing showed it was susceptible to penicillin (MIC 0.8 µg/ml), ceftriaxone (MIC 0.6 µg/ml), vancomycin (MIC 0.8 µg/ml) and levofloxacin (MIC 2.2 µg/ml). The patient's antibiotic regimen was then switched to IV ceftriaxone and azithromycin and repeat blood cultures returned no growth. A transthoracic echocardiogram was obtained and was negative for any vegetation. In view of the spinal involvement, the patient was prescribed a total of 6 weeks of antibiotics to be completed outpatient as recommended by the infectious disease team.

CT guided biopsy of the lung nodule was also performed, and pathology results showed invasive adenocarcinoma of the lung. Upon discharge, the patient was scheduled for a PET scan with further treatment recommendations to be provided based on imaging results. In view of the *L. garvieae* bacteremia, an outpatient colonoscopy was scheduled to rule out colon cancer, as the patient had never been scoped, and the organism had been reported in numerous patients with occult colon cancer [5–8]. However, shortly after being discharged to complete antibiotics outpatient, the patient unfortunately and unexpectedly passed away from unrelated causes before further workup could be obtained.

Discussion

L. garvieae has been documented as the causative organism of major outbreaks in fish farms growing rainbow trout, giant freshwater prawn, and gray mullet [9]. There has been an overwhelming association between pathogen introduction into the human body and the consumption of raw or fresh fish, most commonly rainbow trout [9].

Although aquatic species are the most common host for *L. garvieae*, the organism has also been found in sausages, pig processing plants, dog and cat tonsils, poultry, cows with subclinical intramammary infections, water buffaloes with subclinical mastitis, and unpasteurized dairy milk [9].

Our literature review points towards some similarities among patient cases infected by L. garvieae. Although many cases had presented as infective endocarditis, abscesses of the liver, spondylitis, peritonitis, diverticulitis, urinary tract infections, or multiorgan dysfunction, most of the cases involved bacteremia [7,8,10–17]. The published data most likely underestimates the prevalence and incidence of disease caused by L. garvieae due to misidentification with Enterococcus species. Phenotypically, Lactococcus and Enterococcus share many features such as gram-positive staining, short chains and pairs morphology, facultative anaerobic growth, catalase negativity, susceptibility to vancomycin, and growth at 10 degrees Celsius [1,14]. Although testing for metabolism of different carbohydrates can differentiate the two genuses, automated phenotypic systems used in clinical settings are better equipped to differentiate the common human pathogenic species E. faecalis and E. faecium, rather than less common Enterococcus species and Lactococcus, resulting in misidentification [18-20]. When automated identification systems fail to isolate an Enterococcus species, molecular testing should be considered to confirm whether Lactococcus is responsible.

Even though the exact pathogenesis of *L. garvieae* is unclear, some similarities have been shown amongst published cases. Many of the reported cases had an underlying gastrointestinal disturbance such as diverticulosis, gastric ulcer, previous gastrointestinal surgery, or chronic gastric acid suppressant use that may have increased susceptibility to infection [11]. Once the patients were bacteremic, the organism most likely infected body systems with predisposing anomalies such as: valvular lesions or abnormalities resulting in endocarditis, diverticulosis resulting in diverticulitis, degenerative spine resulting in infective spondylitis, or ruptured bowel resulting in peritonitis.

What is striking about this particular case is that the patient had no known history of seafood ingestion, valve disease, or gastrointestinal disturbance. Per literature review, it is the only case where *L. garvieae* infection was potentially associated with adenocarcinoma of the lung.

Conclusion

The presentation of *L. garvieae* associated disease has been reported to include a wide range of pathology, yet there is no recorded data with links of the pathogen to adenocarcinoma. Although our case is unique, as the patient passed away before further testing could be completed to determine the likely source and possible association with adenocarcinoma and *L. garvieae*, it would be important to keep this pathogen in mind even in patients without any risk factors for such disease. Further investigation and studies in exploring the possible association patterns related to *L. garvieae* would be highly beneficial.

Consent

Written informed consent was obtained from the patient's family for publication of this case report excluding images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

S.N. Amarasinghe, A.L. Fontenot, M.W. Khan, A. Hasan: Conception and design of study. M.W. Khan: Acquisition of data. S.N. Amarasinghe, A.L. Fontenot, M.W. Khan, A. Hasan: Analysis and/or interpretation of data. S.N. Amarasinghe, A.L. Fontenot, M.W. Khan, A. Hasan: Drafting the manuscript. S.N. Amarasinghe, A.L. Fontenot, M.W. Khan, A. Hasan: Revising the manuscript critically for important intellectual content. S.N. Amarasinghe, A.L. Fontenot, M.W. Khan, A. Hasan: Approval of the version of the manuscript to be published.

Conflicts of interest

No conflicts of interest to disclose.

Data availability

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References

- Facklam R, Elliott JA. Identification, classification, and clinical relevance of catalase-negative, gram-positive cocci, excluding the streptococci and enterococci. Clin Microbiol Rev 2022;8(4):479–95. (https://pubmed.ncbi.nlm.nih.gov/8 665466/).
- [2] Schleifer KH, Kraus J, Dvorak C, Kilpper-Bälz R, Collins MD, Fischer W. Transfer of Streptococcus lactis and related Streptococci to the genus Lactococcus gen. nov. Syst Appl Microbiol 1985;6(2):183–95.
- [3] Pu ZY, Dobos M, Limsowtin GKY, Powell IB. Integrated polymerase chain reactionbased procedures for the detection and identification of species and subspecies of the Gram-positive bacterial genus Lactococcus. J Appl Microbiol 2022;93(2): 353–61. (https://pubmed.ncbi.nlm.nih.gov/12147085/).
- [4] von Bubnoff A. Next-generation sequencing: the race is on. Cell 2022;132(5): 721–3. (https://pubmed.ncbi.nlm.nih.gov/18329356/).
- [5] Ortiz C, López J, del Amo E, Sevilla T, García PE, San Román JA. Lactococcus garvieae infective endocarditis: report of 2 cases and review of the literature. Rev Esp Cardiol 2022;67(9):776–8. (https://pubmed.ncbi.nlm.nib.gov/25172081/).
- [6] Fleming H, Fowler S v, Nguyen L, Hofinger DM. Lactococcus garvieae multi-valve infective endocarditis in a traveler returning from South Korea. Travel Med Infect Dis 2022;10(2):101–4. (https://pubmed.ncbi.nlm.nih.gov/22397769/).
- [7] Vinh DC, Nichol KA, Rand F, Embil JM. Native-valve bacterial endocarditis caused by Lactococcus garvieae. Diagn Microbiol Infect Dis 2006;56(1):91–4.
- [8] Bazemore TC, Maskarinec SA, Zietlow K, Hendershot EF, Perfect JR. Familial adenomatous polyposis manifesting as Lactococcus endocarditis: a case report and review of the association of Lactococcus with underlying gastrointestinal disease. Case Rep Infect Dis 2022;2016:1–5. Available from: /pmc/articles/PMC5080505/.
- [9] Vendrell D, Balcázar JL, Ruiz-Zarzuela I, de Blas I, Gironés O, Múzquiz JL. Lactococcus garvieae in fish: a review. Comp Immunol Microbiol Infect Dis 2006; 29(4):177–98.
- [10] Mofredj A, Baraka D, Cadranel JF, LeMaitre P, Kloeti G, Dumont JL. Lactococcus garvieae septicemia with liver abscess in an immunosuppressed patient. Am J Med 2022;109(6):513–4. (https://pubmed.ncbi.nlm.nih.gov/11184774/).

- [11] Chan JFW, Woo PCY, Teng JLL, Lau SKP, Leung SSM, Tam FCC, et al. Primary infective spondylodiscitis caused by Lactococcus garvieae and a review of human L. garvieae infections. Infection 2022;39(3):259–64. (https://pubmed.ncbi.nlm. nih.gov/21424437/).
- [12] Wang CYC, Shie HS, Chen SC, Huang JP, Hsieh IC, Wen MS, et al. Lactococcus garvieae infections in humans: possible association with aquaculture outbreaks. Int J Clin Pract, 61; 2022. p. 68–73. https://doi.org/10.1111/j.1742-1241.2006.00855.x.
- [13] James PR, Hardman SMC, Patterson DLH. Osteomyelitis and possible endocarditis secondary to Lactococcus garvieae: a first case report. Postgrad Med J 2022;76 (895):301. Available from: /pmc/articles/PMC1741591/?report=abstract.
- [14] Fefer JJ, Ratzan KR, Sharp SE, Saiz E. Lactococcus garvieae endocarditis: report of a case and review of the literature. Diagn Microbiol Infect Dis 2022;32(2):127–30. (https://pubmed.ncbi.nlm.nih.gov/9823537/).
- [15] Fihman V, Raskine L, Barrou Z, Kiffel C, Riahi J, Berçot B, et al. Lactococcus garvieae endocarditis: identification by 16S rRNA and sodA sequence analysis. J Infect 2022;52(1). (https://pubmed.ncbi.nlm.nih.gov/15936823/).
- [16] Yiu KH, Siu CW, To KKW, Jim MH, Lee KLF, Lau CP, et al. A rare cause of infective endocarditis; Lactococcus garvieae. Int J Cardiol 2022;114(2):286–7. (https://p ubmed.ncbi.nlm.nih.gov/16618510/).
- [17] Li WK, Chen YS, Wann SR, Liu YC, Tsai HC. Lactococcus garvieae endocarditis with initial presentation of acute cerebral infarction in a healthy immunocompetent man. Intern Med 2022;47(12):1143–6. (https://pubmed.ncbi.nlm.nih.gov/18 552475/).
- [18] Zlotkin A, Eldar A, Ghittino C, Bercovier H. Identification of Lactococcus garvieae by PCR. J Clin Microbiol 2022;36(4):983–5. https://doi.org/10.1128/ JCM.36.4.983-985.1998.
- [19] Poyart C, Quesnes G, Trieu-Cuot P. Sequencing the gene encoding manganesedependent superoxide dismutase for rapid species identification of enterococci. J Clin Microbiol 2022;38(1):415–8. https://doi.org/10.1128/JCM.38.1.415-418.2000.
- [20] Navas ME, Hall G, el Bejjani D. A case of endocarditis caused by Lactococcus garvieae and suggested methods for identification. J Clin Microbiol 2022;51(6): 1990.