

Human disease caused by *Streptococcus alactolyticus*: a case report of native valve infective endocarditis and review of the literature

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Abstract

Streptococcus alactolyticus, a member of the *Streptococcus bovis*/*Streptococcus equinus* complex, is primarily hosted in the gastrointestinal tract of animals and rarely of humans, with only scarce reports relating to human disease. We herein present a case

of subacute infective endocarditis (IE) caused by *S. alactolyticus* in a 64-year old male with pre-existing mitral prolapse. Despite a 10-month history of low-grade fever and weight loss, the diagnosis of IE was triggered by left quadrant abdominal pain which revealed splenic infarcts on computed tomography. A definitive diagnosis of IE was subsequently established by four consecutive blood cultures positive for *S. alactolyticus* plus demonstration of a vegetation on the mitral valve by trans-esophageal ultrasound. Further workup revealed multiple embolic phenomena including brain and spine. A dental abscess was identified as the most probable origin of the bacteraemia, while colonoscopy revealed no evidence of cancer. Although rare, IE caused by *S. alactolyticus* may be severe and of obscure origin; oral cavity should not be overlooked as a possible origin. Attention should be given in patients with preexisting risk factors.

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Keywords: Infective endocarditis; Bacterial endocarditis; *Streptococcus bovis*; *Streptococcus alactolyticus*.

Authors' contributions; CM, conceptualization, writing-original draft; GG, literature review, writing-review and editing; GP, literature review, writing-critical revision; EM, literature review, writing-review and editing; KS, writing-review and editing, supervision. All authors have approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: The authors report no conflict of interest.

Funding: None.

Ethics approval and consent to participate: No ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: The patient gave his written consent to use his personal data for the publication of this case report and any accompanying images.

Acknowledgments: None

Received for publication: 3 June 2020.
Accepted for publication: 21 August 2020.

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Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2020; 90:1428
doi: 10.4081/monaldi.2020.1428

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Introduction

Streptococcus bovis/*Streptococcus equinus* complex (SBSEC) is a group of non-enterococcal Group D *Streptococcus* species mainly isolated from animal gastrointestinal tracts and fermented dairy products [1]. The current classification of SBSEC includes seven (sub)species, which are grouped into four branches (clusters) based on sequences identities: the *Streptococcus gallolyticus*, the *Streptococcus equinus*, the *Streptococcus infantarius* and the *Streptococcus alactolyticus* branch [2]. While mostly acting as commensals, members of this complex sometimes act as opportunistic pathogens [1]. The most notorious association within the literature is between SBSEC bacteremia and colorectal cancer [3]. More specifically, *S. gallolyticus subsp. gallolyticus* (initially referred as *S. bovis*) bacteremia is associated with colorectal neoplasia in approximately 60% of cases [4]. Interestingly, other members of the SBSEC complex have failed to demonstrate such a correlation. *S. alactolyticus* (sometimes erroneously referred as *S. intestinalis*) is the solitary member of cluster IV of SBSEC [1]. It has been isolated from the intestinal flora of pigs, chickens, pigeons, and dogs, but is infrequently isolated from humans and is rarely associated with human diseases [5,6].

Case Report

A 64-year old man, with a history of diabetes mellitus type 2, arterial hypertension and mitral valve prolapse, presented to the emergency department with worsening left upper quadrant

abdominal pain, which started two days ago. He neither had alteration in bowel habits, nor blood in his stool. When asked further, he reported loss of weight, low-grade fever during the last 10 months and lumbar pain during the last two months. He had visited an orthopedic surgeon and had been through a magnetic resonance imaging (MRI) of the spine 10 days before his admission in our Department, which demonstrated edema of the L4 vertebra, the endplates of L4-L5 spinal segment and the paraspinal soft tissue of the lumbar spine. Moreover, there were hernias of the intervertebral discs L3-L4, L4-L5 and L5-S1. The patient was administered no specific treatment except for nonsteroidal anti-inflammatory drugs (NSAIDs).

At the Emergency Department the patient was afebrile, tachycardic (124 bpm) and with elevated blood pressure (160/100 mmHg). The abdomen was nondistended, but it was rigid and tender at the palpation of the left upper quadrant with rebound tenderness. Bowel sounds were normal. The clinical examination of the chest revealed a holosystolic murmur best heard at the cardiac apex. The lab tests showed: white blood cells = 19,130 cells/ μ l, 85% polymorphonuclear type, glucose = 261 mg/dl, C-reactive protein = 3.5 mg/dl (normal range <0.7), erythrocyte sedimentation rate 94 mm/h and troponin=7000 pg/ml (normal range <0.017). The electrocardiogram (ECG) had ST segment elevations at II, III and aVF leads, ST segment depression in aVL lead, and Q waves in III and aVF. The patient was submitted to an emergent computed tomography (CT) of the abdomen, which was notable for multiple splenic infarcts (Figure 1).

An admission to the internal medicine department of the hospital was decided and after cardiologic consultation the patient was placed on a double antiplatelet treatment, a beta-blocker, an angiotensin-converting-enzyme inhibitor and a statin, while a percutaneous coronary intervention performed during his hospital stay revealed no clinically significant stenosis in the coronary arteries. A transthoracic echocardiogram demonstrated vegetations and severe regurgitation of the mitral valve. The findings were consistent with the trans-esophageal echocardiogram, which revealed a vegetation on the front flap of the mitral valve with imaging features of chronicity (Figure 2). In the next days, Gram positive cocci in chains were recovered from four consecutive blood cultures. The patient fulfilled two major plus two minor Duke's criteria, thus establishing the diagnosis of definitive

infective endocarditis (IE) [7]. Based on this, antibiotic therapy was started with gentamicin (3 mg/kg divided in three daily doses), ciprofloxacin (600 mg twice daily) and daptomycin (10 mg/kg) as empiric treatment of sub-acute endocarditis, while the blood cultures were pending [8]. The organism was identified as *S. alactolyticus*, by automated system Vitek2 (BioMerieux). Based on the antibiogram (Table 1), antibiotic treatment was de-escalated to ceftriaxone (2 g once daily) and the patient completed four weeks of intravenous antibiotic treatment. Serial troponin measurements showed a reduction until normalization of the value, and later ECGs showed only Q waves in leads III and aVF. During the hospital stay, the glucose levels were well regulated with the sole use of basic insulin.

Table 1. Antibiotic sensitivities of *Streptococcus alactolyticus* isolated from the blood cultures.

Antibiotic	Sensitivity
Penicillin	(MIC <0.064 g/ml)
Ampicillin	Sensitive
Amoxicillin and clavulanic acid	Sensitive
Cephalothin	Sensitive
Cefuroxime	Sensitive
Cefotaxime	Sensitive
Ceftriaxone	Sensitive
Tetracycline	Sensitive
Gentamycin	Resistant
Streptomycin high potency	Sensitive
Erythromycin	Sensitive
Levofloxacin	Sensitive
Lincomycin	Sensitive
Imipenem	Sensitive
Chloramphenicol	Sensitive
Teicoplanin	Sensitive
Vancomycin	Sensitive
Tigecycline	Sensitive



Figure 1. Abdominal CT scan showing multiple splenic infarcts.

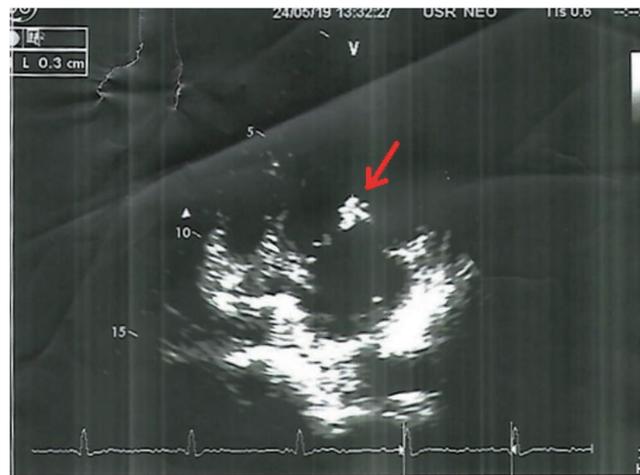


Figure 2. Trans-esophageal echocardiogram depicting a vegetation (arrow) on the front flap of the mitral valve.

As for the patient's presenting complaint, the abdominal pain subsided the very next day of the patient's admission, attributed probably to a new splenic infarct. The work-up was extended to examine for possible embolic complications of IE. A chest CT did not reveal abnormal findings, whereas a brain CT revealed multiple hypodense areas in the cerebellar hemispheres, consistent with chronic infarcts. A subsequent brain MRI reconfirmed the multiple chronic lesions along with new ones, without imaging evidence of mycotic aneurysms. A repeat abdominal CT demonstrated a new splenic infarct along with the previously shown. Moreover, the CT imaging of the spine revealed hypodense lesions on O4 and O5 vertebrae raising suspicion of spondylodiskitis. However, technetium-99m (^{99m}Tc) scintigraphy, ordered to clarify this issue did not confirm the diagnosis of spondylodiskitis. Paradoxically, the patients' lumbar pain improved during his hospital stay. Also, during his stay at the hospital, the patient complained for toothache. A dental examination revealed poor hygiene and a dental abscess in a previously endodontically-treated tooth thus recommending repair after the completion of the antibiotic therapy, in an outpatient basis.

The patient completed four weeks of intravenous antibiotic therapy with ceftriaxone and was then discharged from the hospital with an additional two week-course of oral treatment with amoxicillin/clavulanate for probable spondylodiskitis. He underwent a colonoscopy as an outpatient, which was negative for neoplastic lesions. After restoring his dental health, he uneventfully underwent a mitral valve replacement in another hospital. He had several follow-up visits at the outpatient clinic of our Department, where blood cultures were sent every 15 days for two months post-discharge and were all negative.

Discussion

We herein present a rare case of subacute infective endocarditis of probable oral cavity origin, in an adult male caused by *S.*

alactolyticus, one of the four taxonomic branches of the SBSEC group. *S. alactolyticus*, is mainly associated with animal pathogenicity [5,6]. Our literature review retrieved four case reports of human disease caused by *S.alactolyticus* (Table 2). Two cases of IE are reported, one in a patient with preexisting heart valve disease [9] and another in a patient with recent coronary artery bypass grafting [10]. Furthermore, there is one case of severe diabetic ketoacidosis caused by *S.alactolyticus* bacteraemia [11] and one fatal case of fulminant neonatal sepsis caused by the same pathogen [12]. In our case, the patient had a history of mitral valve prolapse, a risk factor for IE [13,14].

SBSEC accounts for 6% of all native valve IE cases in developed countries according to recent epidemiological studies, ranking after *Staphylococcus aureus* (31%), *Viridans* group streptococci (17%), Coagulase- negative staphylococci (11%) and Enterococci (10%). The frequency of SBSEC-associated IE is relatively higher in Europe and South America compared to other regions [13,15]. Notably, *S. gallolyticus subsp. gallolyticus* is the subspecies predominantly associated with IE in the context of underlying colorectal neoplasia compared to other members of the SBSEC. Approximately 70% of this subspecies' bacteremias were complicated by IE [4]. In our case however, we presume that a dental abscess was the probable source of bacteremia. The niche of SBSEC bacteria is generally considered the human gastrointestinal tract and secondarily the upper respiratory tract; however, particularly for *S. alactolyticus* we only found one study having isolated this species from mouth samples [16]. Moreover, post-discharge colonoscopy, did not reveal any evidence of colonic malignancy. Although the origin of the bacteremia was not proven, the patient restored his dental health prior to undergoing mitral valve replacement.

Infective endocarditis is a disease associated with serious and potentially lethal complications [13-15]. Despite the relatively benign clinical course of our patient's disease, the findings of the brain CT and MRI confirmed the presence of multiple yet asymptomatic brain emboli although no mycotic aneurysm was

Table 2. Case reports of human infections caused by *S. alactolyticus*.

Author (year)	Patient (age/ gender)	Case presentation	Source of infection	Antimicrobial therapy	Outcome
Toepfner <i>et al.</i> (2014)	Neonate/ NA	Early onset neonatal sepsis, rds. <i>S. alactolyticus</i> cultured from nasopharyngeal and endotracheal Smears	Probable peripartal chorioamnionitis or birth canal transmission	Piperacillin / tobramycin (empiric treatment)	Death
Almeida <i>et al.</i> (2016)	65/female	IE with renal, splenic and brain septic emboli and intracerebral mycotic aneurysm	Presumed dental	Vancomycin/gentamicin/ penicillin-g (empiric treatment), Ceftriaxone (de-escalation treatment)	Recovery Cardiac surgery
Idrees <i>et al.</i> (2018)	35/female	<i>S. Alactolyticus</i> bacteremia Diabetic ketoacidosis	Probably lower abdomen/upper pelvis	Vancomycin (empiric), ceftriaxone (de-escalation)	Recovery
Cekmen <i>et al.</i> (2019)	64/male	IE No embolic events	Not identified	Vancomycin/gentamicin penicillin-g (empiric), ceftriaxone (de-escalation)	Recovery Cardiac surgery
Current report	64/male	IE with splenic, brain, spine septic emboli	Probably dental abscess	Gentamycin/ciprofloxacin/ daptomycin (empiric), ceftriaxone (de-escalation)	Recovery Cardiac surgery

NA, not available; IE, infective endocarditis.

recognized. Moreover, the ECG and laboratory findings consistent with acute myocardial ischemia could also be explained by a septic embolus, maybe of a transient nature, provided that no significant stenosis were documented in the percutaneous coronary intervention. Other possible explanations could include a type 2 myocardial infarction or an acute nonischemic myocardial injury [17]. Spondylodiskitis elucidated by spine imaging completes the clinical range of embolic phenomena. Interestingly, left upper quadrant abdominal pain attributed to a recent splenic infarct triggered the diagnosis of infective endocarditis in this patient with non-specific symptoms starting 10 months earlier. Finally, severe mitral regurgitation prompted surgical repair which was uneventfully performed a few weeks later.

Conclusions

We report an unusual case of subacute infective endocarditis caused by *S. alactolyticus* complicated by multiple embolic phenomena including brain, spleen and spine, which escaped attention and diagnosis despite a 10-month history of low grade fever and weight loss. Our case shows that even though human infections by *S. alactolyticus* are rare, they can be associated with multiple and potentially life-threatening complications. Although most commonly associated with colon pathology, oral cavity should not be overlooked as a possible origin of *S. alactolyticus* bacteremia. Particular attention should be given in patients with preexisting risk factors, as early recognition could be the key to successful treatment.

References

- Jans C, Meile L, Lacroix C, Stevens MJ. Genomics, evolution, and molecular epidemiology of the *Streptococcus bovis*/*Streptococcus equinus* complex (SBSEC). *Infection, genetics and evolution*. *Infect Genet Evol* 2015;33:419-36.
- Dekker JP, Lau AF. An Update on the *Streptococcus bovis* group: Classification, identification, and disease associations. *J Clinical Microbiology*. 2016;54:1694-9.
- Dahmus JD, Kotler DL, Kastenber DM, Kistler CA. The gut microbiome and colorectal cancer: a review of bacterial pathogenesis. *Journal Of Gastrointestinal Oncology*. 2018;9:769-77.
- Boleij A, van Gelder MM, Swinkels DW, Tjalsma H. 2011. Clinical importance of *Streptococcus gallolyticus* infection among colorectal cancer patients: systematic review and meta-analysis. *Clin Infect Dis* 53:870-878.
- Rinkinen ML, Koort JM, Ouwehand AC, et al. *Streptococcus alactolyticus* is the dominating culturable lactic acid bacterium species in canine jejunum and feces of four fistulated dogs. *FEMS Microbiol Lett* 2004;230:35-9.
- Devriese LA, Vandamme P, Pot B, et al. Differentiation between *Streptococcus gallolyticus* strains of human clinical and veterinary origins and *Streptococcus bovis* strains from the intestinal tracts of ruminants. *J Clin Microbiol* 1998;36:3520-3.
- Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994;96:200-9.
- Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;36:3075-28.
- Almeida P, Railsback J, Gleason JB. A rare case of *Streptococcus alactolyticus* infective endocarditis complicated by septic emboli and mycotic left middle cerebral artery aneurysm. *Case Rep Infect Dis* 2016;2016:9081352.
- Cekmen N, Baysan O, Disbudak E, Gunt C. A rare case of bacterial infective endocarditis caused by *Streptococcus alactolyticus*. *Heart Vessels Transplant* 2019;3:109-13.
- Idrees S, Gupta S, Mantilla M, et al. Unusual cause of severe diabetic ketoacidosis precipitated by *Streptococcus bovis/equinus* (SBSEC) bacteremia: Case report and review of literature. *IDCases* 2018;11:53-5.
- Toepfner N, Shetty S, Kunze M, et al. Fulminant neonatal sepsis due to *Streptococcus alactolyticus* - A case report and review. *APMIS* 2014;122:654-6.
- Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med* 2009;169:463-73.
- Katan O, Michelena HI, Avierinos JF, et al. Incidence and predictors of infective endocarditis in mitral valve prolapse: A population-based study. *Mayo Clin Proc* 2016;91:336-42.
- Jamil M, Sultan I, Gleason TG, et al. Infective endocarditis: trends, surgical outcomes, and controversies. *J Thorac Dis* 2019;11:4875-85.
- Damian M, Palade AM, Băltoiu M, et al. Phenotypic and molecular methods used for identification of oral streptococci and related microorganisms. *Roum Arch Microbiol Immunol* 2010;69:85-9.
- DeFilippis AP, Chapman AR, Mills NL, et al. Assessment and treatment of patients with type 2 myocardial infarction and acute nonischemic myocardial injury. *Circulation* 2019;140:1661-78.