Bacteriémia por *Streptococcus bovis*: Correlações Clínicas numa Análise Retrospetiva

Streptococcus bovis Bacteremia: Clinical Correlates in a Retrospective Analysis

José Eduardo Mateus (https://orcid.org/0000-0003-1506-152X), Carlos Silva (https://orcid.org/0000-0003-3357-5591), Hélder Esperto (https://orcid.org/0000-0002-2344-4267), João Porto (https://orcid.org/0000-0002-3222-3511), Manuel Teixeira Veríssimo (https://orcid.org/0000-0002-2793-2129), Armando Carvalho (https://orcid.org/0000-0003-2455-8781)

Resumo

Introdução: Em 1951 foi sugerida pela primeira vez uma associação entre neoplasia colorrectal e bacteriémia por *Streptococcus bovis*. Décadas depois, continuam por esclarecer a natureza e extensão desta associação. O objetivo deste estudo foi rever todos os episódios de bacteriémia por *Streptococcus bovis* num hospital terciário.

Material e Métodos: Análise retrospetiva dos doentes internados num hospital português com bacteriémia por *Streptococcus bovis* entre janeiro de 2000 e dezembro de 2016. Resultados: Registaram-se 46 doentes com bacteriémia por *Streptococcus bovis* no período de estudo. Cerca de um terço teve endocardite. Foi realizada colonoscopia a 56,6% dos doentes e foi diagnosticada neoplasia colorrectal em 61,5% destes. Em 27 casos foi realizada identificação molecular do *Streptococcus bovis*: 19 *Streptococcus gallolyticus* subsp. *gallolyticus*, 7 *Streptococcus gallolyticus* subsp. *pasteurianus* e um *Streptococcus gallolyticus* subsp. *infantarius*. Nos doentes com bacteriémia por *Streptococcus gallolyticus* subsp. *gallolyticus* o principal foco infecioso foi endocardite (42,1%). No grupo infetado por esta subespécie, a maioria desenvolveu neoplasia colorrectal (83,3%). Contrariamente, os casos com bacteriémia por *Streptococcus gallolyticus* subsp. *pasteurianus* tiveram mais infeção do foro hepatobiliar (57,1%) e apenas 20,0% tiveram neoplasia colorrectal ($p < 0,05$).

Discussão: Apesar da relação entre bacteriémia por *Streptococcus bovis* e doença gastrointestinal ser conhecida há anos, não existe ainda nenhuma explicação satisfatória para os mecanismos fisiopatológicos subjacentes. Os indivíduos infetados com *Streptococcus gallolyticus* subsp. *gallolyticus* tiveram, na sua maioria, endocardite e alterações na avaliação do cólon.

Conclusão: São necessários mais estudos para perceber de que forma diferentes subespécies de *Streptococcus bovis* estão implicadas no desenvolvimento de neoplasia colorrectal.

Palavras-chave: Bacteriémia; Infecções Estreptocócicas; Neoplasias Colorrectais; *Streptococcus bovis*.

Abstract

Introduction: *An association between colorectal neoplasm and Streptococcus bovis bacteremia was first suggested in 1951. Decades later, the extent and nature of this association are still not completely understood. The aim of this study was to review all Streptococcus bovis bacteremic episodes documented at a tertiary-care centre.*

Material and Methods: *Retrospective analysis of patients with Streptococcus bovis bacteremia admitted to a portuguese centre from January 2000 to December 2016. Results: There were 46 patients with Streptococcus bovis bacteremia within this period. Nearly one third presented endocarditis. Colonoscopic examination was performed in 56.6% of patients, of whom 61.5% had colorectal neoplasm. Streptococcus bovis molecular identification was held in 27 of the isolates: 19 Streptococcus gallolyticus subsp. gallolyticus, 7 Streptococcus gallolyticus subsp. pasteurianus and one Streptococcus gallolyticus subsp. infantarius. In Streptococcus gallolyticus subsp. gallolyticus infection cases, endocarditis was the main source of infection (42.1%). Most of these patients developed colorectal neoplasm (83.3%). Conversely, bacteremia cases due to Streptococcus gallolyticus subsp. pasteurianus were more likely to have a hepatobiliary source (57.1%) and only 20.0% developed colorectal neoplasm ($p < 0.05$).*

Discussion: *Though the clinical relationship between Streptococcus bovis bacteremia and underlying GI diseases has been well-known for years, to date there has been no satisfactory explanation regarding the pathophysiologic mechanism for this association. Subjects infected with Streptococcus gallolyticus subsp. gallolyticus tended to present with endocarditis and to have colorectal neoplasm.*

Conclusion: *Further research is required to determine the pathogenic mechanisms in which different subspecies of Streptococcus bovis may be implicated in the development of CRN.*

Keywords: *Bacteremia; Colorectal Neoplasms; Streptococcal Infections; Streptococcus bovis.*

Serviço de Medicina Interna, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

http://revista.spmi.pt - DOI: 10.24950/rspmi/original/69/4/2018;

Introduction

Streptococcus (*S.*) *bovis* (*Sb*) is a group of gram-positive cocci that can be found as part of the human gastrointestinal microbiota in 5% to 16% of normal individuals.[1-3] However, it causes bacteremia and endocarditis, particularly in older people and in southern Europe.[1,2] *Sb* is the second most common cause of endocarditis from streptococci and is responsible for up to 15% of bacterial endocarditis.[1,3,4]

An association between colorectal neoplasm (CRN) and *Sb* bacteremia/endocarditis was first suggested in 1951.[5] Since then, this relation has been extensively established in the literature, with variable percentages.[6-10] However, the extent and nature of this association are still not completely understood.[6,7] More recent studies have highlighted the frequent association between *Sb* infection and chronic liver/biliary tract disorders as predisposing conditions.[1,3]

Streptococcal taxonomy has progressively changed over time, based on molecular characteristics. Nevertheless, current nomenclature has not been embraced by the majority of clinicians.[1,3,11,12] This lack of uniform microbiological classification in scientific literature has led to an underestimation of the relationship between *Sb* and CRN, because not all genospecies seem to be as closely related to colonic malignancies.[7,11] Several studies have shown that *S. gallolyticus* subsp. *gallolyticus* (formerly called *Sb* biotype I) is strongly related to the presence of premalignant colonic lesions and colonic cancer, up to 80%, that markedly exceeds the normal incidence of CRN in the asymptomatic population.[1,2,6,7,13] Also, it has been shown that *S. gallolyticus* subsp. *infantarius* and *S.gallolyticus* subsp. *lutetiensis* (former *Sb* biotype II/1) as well as *S. gallolyticus* subsp. *pasteurianu* (former *Sb* biotype II/2) are less often associated with endocarditis and colorectal cancer, but frequently associated with other types of infection and non-CRN.[8,13] As a matter of fact, 94% of *Sb* bacteremia associated with colorectal cancer is in fact due to *S. gallolyticus* subsp. *gallolyticus* while only 18% is associated with the other *Sb* subspecies.[7]

The incidence of CRN varies widely among countries. In the developed world, including Portugal, CRN represents a major public health problem. Several patients with *Sb* bacteremia have no clinical signs or symptoms referable to gastrointestinal (GI) tract, so CRN is solely discovered on the basis of *Sb* infection in these patients.[9] Furthermore, it is known that colonic neoplasm may arise years after the presentation of *Sb* bacteremia.[4,7] Therefore, the early detection of CRN is one of the great challenges in the battle against this disease. Nevertheless, only limited information is available as to whether any clinical characteristics of bacteremic patients are specifically associated with CRN.[8] *S. gallolyticus* subsp. *gallolyticus* related diagnostic tools may aid CRN screening programs and, thereby, contribute to a decrease in the morbidity and mortality associated with this disease.[11]

The aim of this study was to review all *Sb* bacteremic episodes documented over the last 17 years at a single tertiary-care centre, focusing on demographic and clinical associations in relation to the different subspecies.

Material and Methods

We performed a retrospective analysis of patients with *Sb* bacteremia admitted to our Internal Medicine department from january 2000 to december 2016. All *Sb* isolates recovered from blood cultures within this period were studied. Clinical charts of patients were reviewed. Coimbra Hospital and University Center (CHUC) is a tertiary-care centre and university hospital in Portugal, with a reference population of 2 million inhabitants. Hospital records were reviewed to assess their demographic ad clinical features. Diagnosis of endocarditis was based on modified Duke's criteria. Transthoracic echocardiography (TTE) was performed in all patients with suspected endocarditis. Patients with suspected intracardiac complications (abscess or pseudoaneurysm) on TTE or who had a negative TTE but high clinical suspicion of endocarditis underwent transesophageal echocardiography. Patients were considered to have undergone a colonic evaluation if they had colonoscopy during the acute hospitalization episode or within the first 24-month follow up period. CRN included both adenoma and carcinoma. The diagnosis of CRN was confirmed by the histopathological examination of colonoscopic biopsy specimens.

Subspecies identification was performed since 2009, first by the API 20 Strep system (BioMérieux, Marcy l'Etoile, France) and from 2014 on using the VITEK® MS (BioMérieux, Marcy l'Etoile, France), an automated mass spectrometry microbial identification system that uses Matrix Assisted laser desorption ionization time-of-flight (MALDI-TOF) technology.

Data are shown as median. Due to the small size of the sample, data are not normally distributed, so Fisher´s exact test and *U Mann Whitney* test were used for statistical evaluation. The threshold for statistical significance was established at a p value < 0.05. The statistical analysis was performed using SPSS, version 21.0 (SPSS Inc., Chicago, IL, USA).

This study is in line with the recommendations of the Helsinki Declaration of the World Medical Association, the International Committee of Medical Journal Editors and the Committee on Publication Ethics.

Results

Fourty-six patients with S. bacteremia were identified (range 0-10 cases per year), with a median age of 71 years, among which 33 (71.7%) were males. Endocarditis was the main source of infection (n = 14; 30.4%), followed by hepatobiliary/GI infection (n = 13; 28.3%), primary bacteremia (n = 11; 23.9%), pneumonia (n = 4; 8.7%), bone/joint infection (n = 3; 6.5%) and central nervous system (CNS) infection (n = 1; 2.2%).

Table 1: Differences between patients with bacteremia due to *S. gallolyticus* subsp. *gallolyticus* and *S. gallolyticus* subsp. *pasteurianus*.

	Age (years; median) §	Sex (male; n/%) ¶	Source of infection (n/%) ¶					
			Endocarditis	Hepatobiliary/ GI infection	Primary bacteremia	Pneumonia	Bone/Joint infection	CNS infection
S. gallolyticus subsp. *Gallolyticus* (n = 19)	75	13 (68.4)	8 (42.1)	2 (10.5)	4 (21.1)	3 (15.8)	1 (5.3)	1 (5.3)
S. gallolyticus subsp. *Pasteurianus* (n = 7)	67	7 (100)	0	4 (57.1)	1 (14,.3)	0	2 (28.6)	0
p-value	0.236	0.090	0.048	0.028	0.589	0.373	0.167	0.731

	CRN* (yes; n/%) ¶	Comorbidities (yes; n/%) ¶						Laboratory data (median) §			
		Other malignancies	Liver cirrhosis	Diabetes	Heart disease	ESRD	COPD	CRP (mg/dL)	Hb (g/dL)	Ht (%)	CEA (ng/mL)
S. gallolyticus subsp. *Gallolyticus* (n = 19)	10/12 (83.3)	2 (10.5)	2 (10.5)	8 (42.1)	5 (26.3)	5 (26.3)	4 (21.1)	8.3	10.4	30.9	3.5
S. gallolyticus subsp. *Pasteurianus* (n = 7)	1/5 (20.0)	1 (14.3)	3 (28.6)	0	4 (57.1)	1 (14.3)	2 (28.6)	6.1	9.7	29.2	5.3
p-value	0.028	0.627	0.307	0.048	0.159	0.471	0.529	0.633	0.588	0.726	0.414

§ U Mann Whitney test; ¶ Fisher's exact test; * among those who underwent colonoscopy; GI: gastrointestinal; CEA: carcinoembryonic antigen; CNS: central nervous system; CRN: colorectal neoplasm; CRP: C reactive protein; COPD: chronic obstructive pulmonary disease; ESRD: end-stage renal disease; Hb: hemoglobin; Ht: hematocrit

Of the 46 patients, 13 (28.3%) concomitantly had heart disease, 11 (23.9%) had diabetes, 10 (21.7%) had end-stage renal disease (ESLD), 9 (19.6%) had liver cirrhosis and 9 (19.6%) had chronic obstructive pulmonary disease (COPD). A history of malignancy prior to the episode of *Sb* bacteremia had been established in 9 patients (19.6%), mainly outside the gastrointestinal system.

Full colonoscopic examination was performed in 26 (56.5%) patients. Among these, 16 (61.5%) were found to have a CRN.

S. gallolyticus subsp. *gallolyticus* accounted for 19 cases (41.3%), *S. gallolyticus* subsp. *pasteurianus* for 7 cases (15.2%) and *S. gallolyticus* subsp. *infantarius* for one (2.2%). In the remaining cases (n = 19; 41.3%), molecular identification was not performed. In our study there was only one case (2.2%) of meningitis within the *S. gallolyticus* subsp. *gallolyticus* group. Gender distribution did not differ between the two main subspecies (*S. gallolyticus* subsp. *gallolyticus* and *S. gallolyticus* subsp. *pasteurianus*), as well as the median age of patients, comordities and laboratory data (Table 1, grade of liberty 18). Endocarditis was the main source of infection in patients infected with *S. gallolyticus* subsp. *gallolyticus* (n = 8; 42.1%), as opposed to the *S. gallolyticus* subsp. *pasteurianus* group in which no endocarditis case was recorded ($p < 0.05$). Bacteremia cases due to *S. gallolyticus* subsp. *pasteurianus* were more likely to have an hepatobiliary/GI source (n = 4; 57.1%) than bacteremia cases due to *S. gallolyticus* subsp. *gallolyticus* – only 2 patients (10.5%) within this group had an hepatobiliary/GI infection ($p < 0.05$). Among patients who underwent colonoscopy (n = 26), the number of cases in whom a CRN was found was significantly higher in the *S. gallolyticus* subsp. *gallolyticus* group (n = 10/12; 83.3%) than in the *S. gallolyticus* subsp. *pasteurianus* group (n = 1/5; 20.0%), $p < 0.05$. Indeed, there were important differences between patients who developed CRN and those who did not, with regard to the *Sb* subspecies and the source of infection (Table 2, grade of liberty 21). While most CRN patients had endocarditis (n = 10/16; 62.5%), no cases of this infection were found on the non-CRN group ($p < 0.05$). On the other hand, most patients who did not develop CRN had bacteremia from a hepatobiliary/GI source (n = 6/10; 60.0%) *versus*

Table 2: Multivariate analysis for categorical and continuous variables associated with a finding of CRN in patients with *Sb* bacteremia.

	Age (years; median) §	Sex (male; n/%) ¶	Source of infection (n/%) ¶					
			Endocarditis	Hepatobiliary/ GI infection	Primary bacteremia	Pneumonia	Bone/Joint infection	CNS infection
Sb bacteremia with CRN (n = 16)	71	9 (56.3)	10 (62.5)	1 (6.3)	2 (12.5)	1 (6.3)	1 (6.3)	1 (6.3)
Sb bacteremia without CRN (n = 10)	67	7 (70.0)	0	6 (60.0)	2 (20.0)	1 (10.0)	1 (10.0)	0
p-value	0.380	0.282	0.030	0.030	0.458	0.600	0.600	0.640

	Sb subspecie (n/%) ¶			
	S. gallolyticus subsp. *gallolyticus*	*S. gallolyticus* subsp. *infantarius*	*S. gallolyticus* subsp. *pasteurianus*	Non identified
Sb bacteremia with CRN (n = 16)	10 (62.5)	0	1 (6.3)	5 (31.3)
Sb bacteremia without CRN (n = 10)	2 (20.0)	1 (10.0)	4 (40.0)	3 (30.0)
p-value	0.042	0.385	0.055	0.648

	Comorbidities (yes; n/%) ¶					
	Other malignancies	Liver cirrhosis	Diabetes	Heart disease	ESRD	COPD
Sb bacteremia with CRN (n = 16)	2 (12.5)	2 (12.5)	3 (18.8)	7 (43.8)	3 (18.8)	5 (31.3)
Sb bacteremia without CRN (n = 10)	2 (20.0)	4 (40.0)	2 (20.0)	4 (40.0)	2 (20.0)	1 (10.0)
p-value	0.504	0.128	0.657	0.588	0.657	0.225

	Laboratory data (median) §			
	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
Sb bacteremia with CRN (n = 16)	6.4	9.6	29.1	4.9
Sb bacteremia without CRN (n = 10)	4.7	11.8	35.5	14.3
p-value	0.515	0.057	0.079	0.480

§ U Mann Whitney test; ¶ Fisher's exact test; * among those who underwent colonoscopy; GI: gastrointestinal; CEA: carcinoembryonic antigen; CNS: central nervous system; CRN: colorectal neoplasm; CRP: C reactive protein; COPD: chronic obstructive pulmonary disease; ESRD: end-stage renal disease; Hb: hemoglobin; Ht: hematocrit

only 1/16 cases (6.3%) of hepatobiliary/GI infection within the group of patients who developed CRN ($p < 0.05$). Also, the most frequent *Sb* subspecies found in bacteremia cases who developed CRN was *S. gallolyticus* subsp. *gallolyticus* (n = 10/16; 62.5%) *versus* only 2/10 cases (20.0%) of this subspecie within the non-CRN group ($p < 0.05$). In the latter, the most common agent was *S. gallolyticus* subsp. *pasteurianus* (n = 4/10; 40.0%).

Discussion

We observed that endocarditis was the main source of infection (30.4%). According to other investigators, the occurrence of endocarditis in patients with *Sb* bacteremia varies from 25% to 100%.[1,9,10] In our study, endocarditis was diagnosed exclusively in *S. gallolyticus* subsp. *gallolyticus* cases, which might be explained by a greater capacity of biofilm formation by this subspecies and consequently a higher risk of endocarditis.[1,13] It has been stated that the relationship between *S. gallolyticus* subsp. *gallolyticus* endocarditis and colonic tumors suggests the existence of certain adhesins on the cell wall of these bacteria allowing the colonization of both colonic and vascular tissues.[7,11]

The rate of patients undergoing colonic evaluation in our study (56,5%) did not differ much from that reported in previous literature.[1] In patients with *Sb* bacteremia, neither age, gender, pre-existing comorbidities or laboratory data were significantly associated with CRN. Only infection with *S. gallolyticus* subsp. *gallolyticus* and endocarditis were found to be associated factors. Conversely, *S. gallolyticus* subsp. *pasteurianus* infection cases were associated with hepatobiliary/GI disease.

The majority of patients infected with *S. gallolyticus* subsp. *gallolyticus* developed CRN (83.3%). At the opposite, CRN prevalence in patients infected with *S.gallolyticus* subsp. *pasteurianus* (20.0%) is similar to that found in the general asymptomatic population, which ranges between 23% and 41%.[6]

The clinical relationship between *Sb* bacteremia and underlying GI diseases has been well-known for years.[3,4,6] However, to date, there has been no satisfactory explanation regarding the pathophysiologic mechanism for this association.[3,6,13] Likewise, it remains controversial as to whether *Sb* plays an etiological role in the development of colorectal tumors or is a consequence of the disease. The relationship between *Sb/S. gallolyticus* subsp. *gallolyticus* infection and the progressive development of malignant disease in preneoplastic adenomatous polyps was supported by recent reports.[14,15] Several hypothesis have been proposed, such as the carcinogenic properties of *Sb* cell wall antigens or chronic *Sb* infection and inflammation.[4,7] Moreover, recent studies have suggested the role of hepatobiliary disorders as predisposing factors for CRN in association with *Sb* infection, by a mechanism of bacterial translocation in the setting of decreased reticuloendothelial phagocytic function and impaired secretion of intestinal luminal immunoglobulins.[6,7] Unlike other bacteria, *Sb/S. gallolyticus* subsp. *gallolyticus* is able to grow in bile, bypassing the hepatic reticulo-endothelial system and easily accessing systemic circulation.[7]

Current studies have been focusing on whether *Sb* bacteremia can be established as an independent predictor of malignancy.[4] Seroprevalence of *Sb/S.gallolyticus* subsp. *gallolyticus* is considered as a candidate practical marker for the early prediction of an underlying bowel lesion at high risk population.[7]

Our study has several limitations, including its retrospective design, the lack of control over the quality of the medical records reviewed and the fact that it was conducted in a single center. Patients approach was heterogeneous, since many did not perform colonic evaluation following the episode of bacteremia. Also, it was not possible to determine the subspecies in almost half the strains of *Sb* as only conventional methods for bacterial identification were used in the first years of study. Moreover, we did not approach the possible association of *Sb* bacteremia with nutritional factors in order to examine the role of diet in human intestinal colonization by different *Sb* species.

Conclusion

Our results suggest the existence of two clinical and microbiological patterns among patients with *Sb* bacteremia. Subjects infected with *S. gallolyticus* subsp. *gallolyticus* tended to present with endocarditis and to have positive findings in the colonic evaluation. Conversely, patients with *S. gallolyticus* subsp. *pasteurianus* bacteremia were more likely to have hepatobiliary/GI disease, which is in agreement with previous studies.

Further research is required to determine the pathogenic mechanisms in which different subspecies of *Sb* may be implicated in the development of CRN. Early diagnosis of colorectal adenomas or carcinomas via detection of *Sb/S. gallolyticus* subsp. *gallolyticus* serology seems promising in screening high risk groups for colorectal cancer.[7] ■

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Conflicts of interest: The authors have no conflicts of interest to declare.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Financing Support: This work has not received any contribution, grant or scholarship.

Direito à Privacidade e Consentimento Informado: Os autores declaram que nenhum dado que permita a identificação do doente aparece neste artigo.

Confidentiality of data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Proteção de Seres Humanos e Animais: Os autores declaram quenão foram realizadas experiências em seres humanos ou animais.

Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Correspondence/Correspondência:
José Eduardo Mateus – zeduardomateus@gmail.com
Serviço de Medicina Interna, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
Praceta Prof. Mota Pinto, 3000-075 Coimbra

Received/Recebido: 26/03/2018
Accepted/Aceite: 17/06/2018

REFERENCES

1. Fernández-Ruiz M, Villar-Silva J, Llenas-García J, Caurcel-Díaz L, Vila-Santos J, Sanz-Sanz F, et al. Streptococcus bovis bacteraemia revisited: clinical and microbiological correlates in a contemporary series of 59 patients. J Infect. 2010;61:307-13. doi: 10.1016/j.jinf.2010.07.007.
2. Olmos C, Vilacosta I, Sarriá C, López J, Ferrera C, Sáez C, et al. Streptococcus bovis endocarditis: Update from a multicenter registry. Am Heart J. 2016;171:7-13. doi: 10.1016/j.ahj.2015.10.012.
3. Romero B, Morosini MI, Loza E, Rodríguez-Baños M, Navas E, Cantón R, et al. Reidentification of Streptococcus bovis isolates causing bacteremia according to the new taxonomy criteria: still an issue? J Clin Microbiol. 2011;49:3228-33. doi: 10.1128/JCM.00524-11.
4. Gupta A, Madani R, Mukhtar H. Streptococcus bovis endocarditis, a silent sign for colonic tumour. Colorectal Dis. 2010;12:164-71. doi: 10.1111/j.1463-1318.2009.01814.x.
5. McCoy WC, Mason JM. Enterococcal endocarditis associated with carcinoma of the sigmoid: report of a case. J Med Assoc State Ala. 1951;21:162–6.
6. Corredoira JC, Alonso MP, García-País MJ, Rabuñal R, García-Garrote F, López-Roses L, et al. Is colonoscopy necessary in cases of infection by Streptococcus bovis biotype II? Eur J Clin Microbiol Infect Dis. 2014;33:171-7. doi: 10.1007/s10096-013-1940-7.
7. Abdulamir AS, Hafidh RR, Abu Bakar F. The association of Streptococcus bovis/gallolyticus with colorectal tumors: the nature and the underlying mechanisms of its etiological role. J Exp Clin Cancer Res. 2011;30:11. doi: 10.1186/1756-9966-30-11.
8. Tsai CE, Chiu CT, Rayner CK, Wu KL, Chiu YC, Hu ML, et al. Associated factors in Streptococcus bovis bacteremia and colorectal cancer. Kaohsiung J Med Sci. 2016;32:196-200. doi: 10.1016/j.kjms.2016.03.003
9. Ruoff KL, Miller SI, Garner CV, Ferraro MJ, Calderwood SB. Bacteremia with Streptococcus bovis and Streptococcus salivarius: clinical correlates of more accurate identification of isolates. J Clin Microbiol 1989;27:305-8.
10. Corredoira JC, Alonso MP, García JF, Casariego E, Coira A, Rodriguez A et al. Clinical characteristics and significance of Streptococcus salivarius bacteremia and Streptococcus bovis bacteremia: a prospective 16-year study. Eur J Clin Microbiol Infect Dis 2005;24:250-5. doi: 10.1007/s10096-005-1314-x.
11. Boleij A, van Gelder MM, Swinkels DW, Tjalsma H. Clinical Importance of Streptococcus gallolyticus infection among colorectal cancer patients: systematic review and meta-analysis. Clin Infect Dis. 2011;53:870-8. doi: 10.1093/cid/cir609.
12. Chand G, Shamban L, Forman A, Sinha P. The association of Streptococcus gallolyticus Subspecies pasteurianus Bacteremia with the detection of premalignant and malignant colonic lesions. Case Rep Gastrointest Med. 2016;2016:7815843. doi: 10.1155/2016/7815843.
13. Corredoira J, Grau I, Garcia-Rodriguez JF, Alonso-Garcia P, Garcia-Pais MJ, Rabuñal R, et al. The clinical epidemiology and malignancies associated with Streptococcus bovis biotypes in 506 cases of bloodstream infections. J Infect. 2015;71:317-25. doi: 10.1016/j.jinf.2015.05.005.
14. Abdulamir AS, Hafidh RR, Mahdi LK, Al-jeboori T, Abubaker F. Investigation into the controversial association of Streptococcus gallolyticus with colorectal cancer and adenoma. BMC Cancer. 2009;9:403. doi: 10.1186/1471-2407-9-403.
15. Kahveci A, Ari E, Arikan H, Koc M, Tuglular S, Ozener C. Streptococcus bovis bacteremia related to colon adenoma in a chronic hemodialysis patient. Hemodial Int. 2010;14:91-3. doi: 10.1111/j.1542-4758.2009.00400.x.