

PREZENTĂRI DE CAZ

Endocarditis due to *Streptococcus gallolyticus* and colonic high grade dysplasia – a case report

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Articol primit la data de 23 noiembrie 2011. Articol acceptat la data de 28 noiembrie 2011.

Abstract: Endocarditis due to *Streptococcus bovis* is frequently associated with colorectal carcinoma. In recent bacteriological nomenclature *Streptococcus bovis* type I has been renamed *Streptococcus gallolyticus*. In patients with *Streptococcus gallolyticus* endocarditis evaluation of the lower digestive tract through colonoscopy is warranted. We report the case of a 51-year old patient with *Streptococcus gallolyticus* endocarditis with aortic and mitral valve involvement and large mitral vegetation. Colonoscopy performed in an otherwise asymptomatic patient revealed multiple polypoid colonic lesions - three pedunculated and two sessile, which were endoscopically resected. Histopathological examination revealed in one of pedunculated polypoid lesions high grade dysplasia occupying 40% of the polyp surface with multiple epithelial misplacement areas of low grade dysplasia. The polyp presented safe margins of resection. The case underlines the importance of the new bacteriologic nomenclature and stresses the significance of the association between *Streptococcus gallolyticus* endocarditis and colorectal premalignant and malignant lesions. It also suggests epithelial misplacement as a possible cause of bacteremia.

Keywords: *Streptococcus gallolyticus*, infective endocarditis, colonic cancer

Rezumat: Endocardita determinată de *Streptococcus bovis* este frecvent asociată cu carcinomul colorectal. În nomenclatura microbiologică recentă biotipul I al *Streptococcus bovis* a fost redenumit *Streptococcus gallolyticus*. În cazul pacienților cu endocardită cu *Streptococcus gallolyticus* este necesară evaluarea tubului digestiv inferior prin colonoscopie. Prezentăm cazul unui pacient de 51 de ani, cu endocardită infecțioasă cu *Streptococcus gallolyticus* pe valva mitrală și aortică și vegetație de mari dimensiuni la nivelul valvei mitrale. Colonoscopia efectuată la un pacient altfel asimptomatic din punct de vedere digestiv a evidențiat mai multe leziuni polipoide ce au fost excizate endoscopic. Examenul histopatologic a evidențiat la nivelul unei formațiuni polipoide pediculate displazie de grad înalt și arii de „*epithelial misplacement*” cu displazie de grad jos. Polipul a fost excizat cu o margine de rezecție indemnă. Cazul prezentat subliniază importanța conștientizării asocierii între endocardita infecțioasă cu *Streptococcus gallolyticus* și leziunile maligne sau premaligne colorectale și a noii nomenclaturi microbiologice. De asemenea, sugerează asocierea dintre leziunile de tip „*epithelial misplacement*” și prezența bacteriemiei.

Cuvinte cheie: *Streptococcus gallolyticus*, endocardită infecțioasă, cancer colonic

CASE REPORT

We report the case of a 51-year old patient, admitted for dyspnea on moderate exertion after the completion of a 6-week antibiotic cure for *Streptococcus gallolyticus* infective endocarditis in another clinic. Prior to the diagnosis of endocarditis the patient complained of low grade fever and malaise for approximately two months. He had no previous history of valvular heart disease and no medical maneuver with bacteremic risk could be identified.

Physical examination revealed grade III apical systolic murmur and diastolic murmur in the aortic area, with no signs of pulmonary or systemic congestion and

no fever. ECG (**Figure 1**) showed sinus rhythm, normal QRS complex and no ST-T abnormalities. Blood tests in our clinic were unremarkable for inflammatory parameters (leukocytes 8520/mm³, ESR 19 mm/h, fibrinogen 400 mg/dl). At this moment blood cultures were negative after the antibiotic treatment (ceftriaxone and gentamicine for 6 weeks).

Echocardiography, both transthoracic and transeophageal, revealed severe mitral regurgitation, moderate-severe aortic regurgitation and the presence of a long, mobile vegetation on the posterior mitral valve measuring approximately 2.2 cm (**Figure 2, 3**). The left ventricle was slightly enlarged, with preserved left ven-

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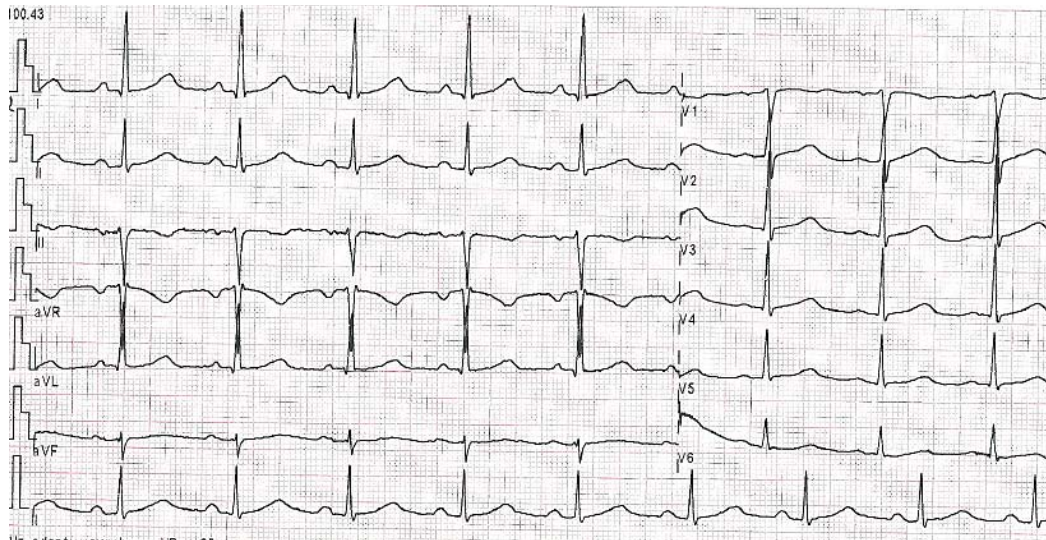


Figure 1. ECG: sinus rhythm, normal QRS complex and no ST-T abnormalities.

tricular ejection fraction. Moderate pulmonary hypertension was noted.

Due to the etiology of the endocarditis and the known association between *Streptococcus gallolyticus* endocarditis/bacteraemia and colonic lesions, colonoscopy was performed. Five colonic polypoid lesions were found, three pedunculated (1.5 cm, 1.5 cm and 5 mm respectively) and two sessile (5 mm) which were endoscopically resected by endoscopic mucosectomy, after submucosal injection of 1:10000 Adrenaline solution (**Figure 4**). The histopathological analysis revealed in one of the three pedunculated polyps, located in the sigmoid colon (1.5 cm in size) 40% of mucosal surface with high grade dysplasia and multiple areas of epithelial misplacement, with low grade dysplasia (**Figure 5**). All the lesions were endoscopically resected with safe

resection margins. The polypectomy site was tattooed using SPOT for colonoscopic surveillance.

Taking into account the presence of heart failure symptoms in a patient with two significant regurgitations and the large, mobile mitral valve vegetation, heart surgical intervention was considered. The patient underwent uneventful aortic and mitral valve replacement with mechanical prosthesis.

DISCUSSION

Endocarditis due to *Streptococcus bovis* is frequently associated with colorectal disease, multiple valve involvement and embolic risk.¹ *Streptococcus bovis* is the etiological agent in 6% of the infective endocarditis cases, varying from 2% in North America to 10% in Europe in a large database.² Multiple valve involvement

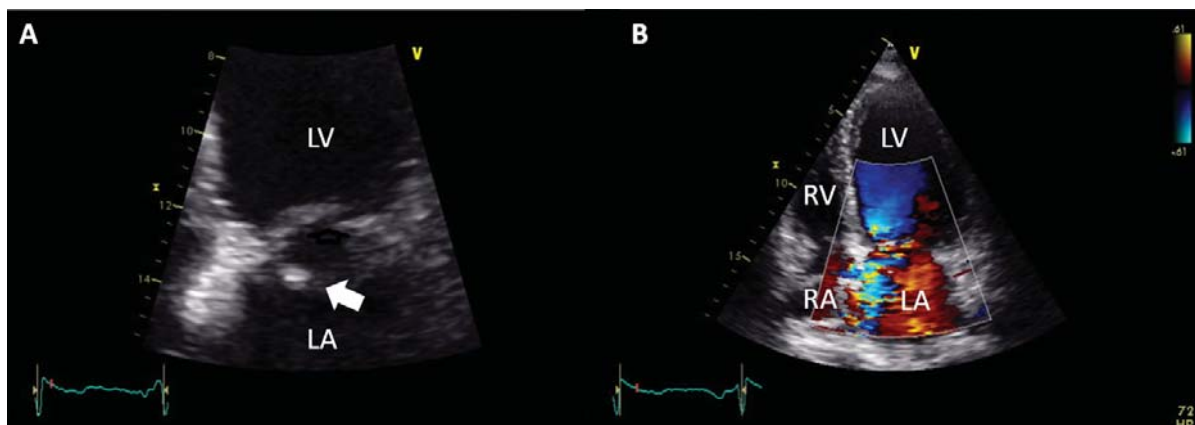


Figure 2. Transthoracic echocardiography. **A.** Apical 4 chamber view, zoom on the mitral valve. A mobile hyperechogenic mass (arrow) is attached on the atrial side of the mitral valve. **B.** Color Doppler imaging reveals severe mitral regurgitation with eccentric jet towards the interatrial septum. LA left atrium, LV left ventricle, RA right atrium, RV right ventricle.

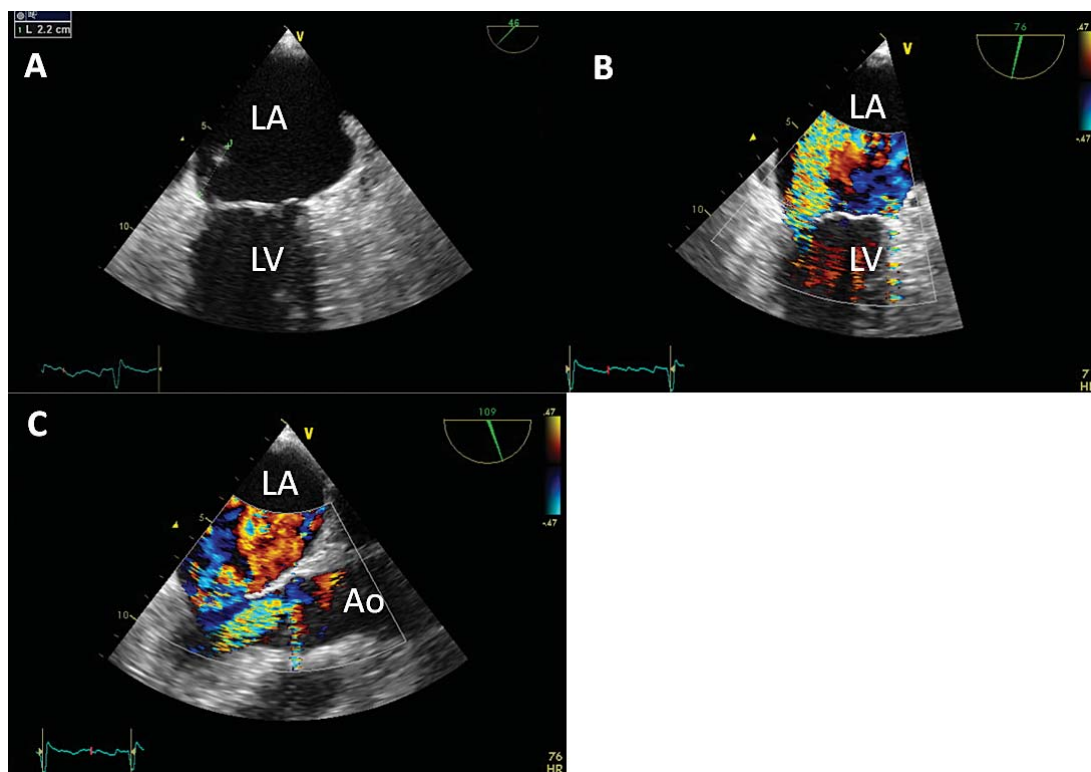


Figure 3. Transesophageal echocardiography - midesophageal 2 chamber view (A,B) and long axis view (C) **A.** 2.2 cm long, mobile, hyperechogenic mass attached on the atrial side of the mitral valve. The echocardiographic appearance is suggestive for vegetation. **B.** Severe mitral regurgitation is revealed by the color Doppler examination **C.** Color Doppler imaging shows moderate-severe aortic regurgitation. LA left atrium, LV left ventricle, Ao ascending aorta.

is more common in *Streptococcus bovis* endocarditis than in other forms of endocarditis, ranging from 36-60%.^{3,4} In the reported case the patient had both mitral and aortic valve involvement, a pattern described in approximately 18% of *S. bovis* endocarditis.⁴ Some authors suggest higher embolic risk for *S. bovis* endocarditis due to its ability to form large vegetations.⁵ Our patient had a long, mobile vegetation on the mitral valve, consistent with this description, however, no embolic event could be detected clinically. The embolic risk due to vegetation size, together with the presence of heart failure symptoms in a patient with two significant valvular regurgitations were the indication for mitral and aortic valve replacement in this case. The patient had no previous history of valve disease, a pattern consistent with *S. bovis* ability to infect normal valves. However, the presence of only mild symptoms of heart failure under these circumstances is a particularity of this case.

The association between *Streptococcus bovis* endocarditis and colonic lesions, both benign or malignant, has been well recognized.⁶⁻⁹ In patients with *Streptococcus bovis* endocarditis complete evaluation of the gastrointestinal tract, particularly the colon is warranted.¹⁰ It is estimated that between 18 and 62% of the pa-

tients with *S. bovis* endocarditis have underlying colorectal tumors¹¹, sometimes with no signs or symptoms referable to gastrointestinal disease. Moreover, colonic neoplasia may appear years after a diagnosis of *S. bovis* endocarditis or bacteraemia, suggesting the need of colonoscopic surveillance in the patients with normal initial colonoscopy.



Figure 4. Colonoscopy: pedunculated polypoid lesion in the descending colon.

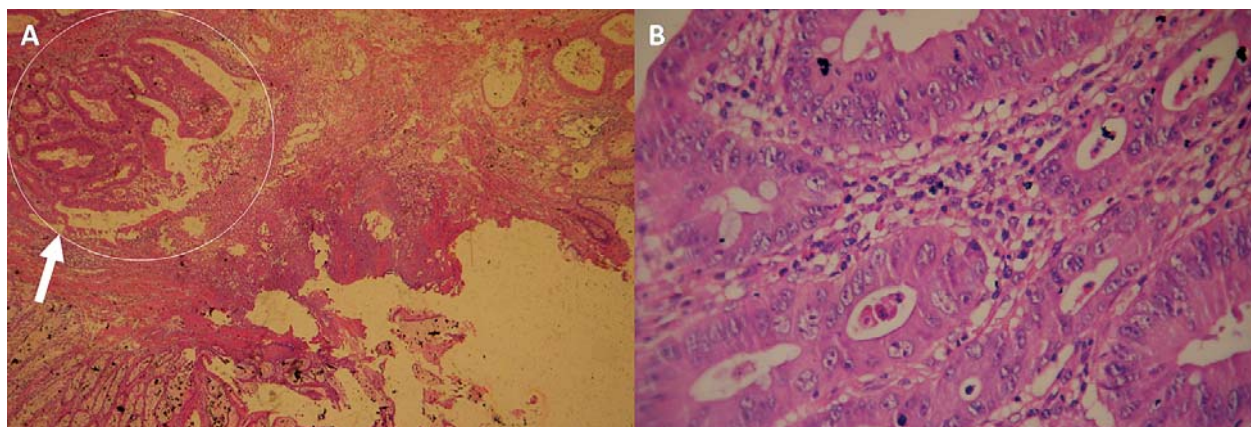


Figure 5. Histopathological examination of one of the resected pedunculated polyps – optic microscopy, haematoxylin-eosin staining (HE). **A.** Epithelial misplacement (low grade dysplasia in the encircled area) – 2 mm distance from the resection margin (HE 10X). **B.** High grade dysplasia (HE 40X).

Three *Streptococcus bovis* biotypes I, II/1 and II/2 have been described. Most of the cases of *S. bovis* bacteremia associated with colorectal cases were actually proven to be due to *S. bovis* biotype I. In an attempt to modernize molecular classification of *S. bovis* subspecies, these biotypes have been recently renamed.¹² Based on molecular characteristics *Streptococcus bovis* biotype I has been renamed as *Streptococcus gallolyticus* subsp. *gallolyticus* and biotype II/2 was renamed *S. gallolyticus* subsp. *pasteurianus* while *Streptococcus infantarius* subsp. *infantarius* and *S. infantarius* subsp. *coli* are the former *S. bovis* II/1. However, proper distinction between the *Streptococcus bovis* strains belonging to *Streptococcus gallolyticus* and *Streptococcus infantarius* has not been uniformly included in studies or cardiological literature and practice, and it has been suggested that lack of awareness of the new bacteriological nomenclature may lead to involuntary underdiagnosis of serious underlying conditions, including colon carcinoma.¹³

Besides the association with colon cancer, different case series suggest also an association between *S. gallolyticus* and malignancy irrespective of site¹⁴ and different cases report *S. gallolyticus* bacteraemia/endocarditis in patients with upper gastrointestinal tract neoplasia, gastric lymphoma or endometrial cancer.¹¹ It appears that there is also a link between *Streptococcus gallolyticus* endocarditis and liver disease, the prevalence of chronic liver disease in patients with this type of endocarditis being significantly higher than in patients with endocarditis of other etiologies.¹⁵

The pathogenesis of the association between *S. gallolyticus* endocarditis/bacteraemia and colonic lesions is not yet understood, especially that *Streptococcus gallolyticus* can be found in the gastrointestinal tract in

5-16% of healthy population.^{11,16} The etiological versus non-etiological nature of the association is also not clearly defined. Several possible mechanisms have been described. While ulceration of a neoplastic lesion can provide a pathway for the bacteria to enter the bloodstream this hypothesis does not explain the case of association between *Streptococcus gallolyticus* and non-ulcerated colonic adenoma or polyps. Some authors suggest a bacterial translocation without the need for mucosal disruption due to vascular changes in the context of several gastrointestinal diseases.¹⁶ The association between *Streptococcus bovis* bacteremia and liver disease suggests that an altered hepatic function may also play a role in the changes of colonic flora and bacterial translocation. On the other site, a direct carcinogenic role of *Streptococcus gallolyticus* has been considered possible due to the potential of this bacteria to promote preneoplastic colonic lesions progression in a rat model.^{16,17}

However, no matter of the mechanism of the association, the clinical importance of adequate screening for gastrointestinal malignancy in cases of *Streptococcus gallolyticus* endocarditis should be underlined, especially as lesions can be identified in early premalignant stages.

In the above reported case, proper acknowledgement of *Streptococcus gallolyticus* as a subspecies of *S. bovis* led to the evaluation of the lower digestive tract in a patient with otherwise no gastrointestinal signs or symptoms and to the early diagnosis and treatment of a colonic premalignant lesion. The histopathological assessment raised the question of differential diagnosis between invasive adenocarcinoma and the epithelial misplacement lesion. Epithelial misplacement is due to the traction of polyp mucosa by the torsion of peduncle,

especially in pedunculated polyps located in the left colon. In our patient it was certified by the presence of low grade dysplasia at the site of epithelial misplacement, and a positive Pearls staining surrounding that area. To our knowledge there are no current reports suggesting epithelial misplacement as a possible cause of *Streptococcus gallolyticus* endocarditis in patients at risk.

Funding

This work was partially supported by 42-119/2008 grant PARTENERIATE funded by UEFISCDI – Ministry of Education and Research, Romania.

Reference

1. Habib G, Hoen B, Tornos P, et al. Guidelines on the prevention, diagnosis and treatment of infective endocarditis (new version 2009). *Eur H Jour* 2009;30:2369-2413.
2. Murdoch DR, Corey R, Hoen B, et al. Clinical presentation, etiology and outcome of infective endocarditis in the 21st century. *Arch Intern Med* 2009;169:463-473.
3. Kupferwasser I, Darius H, Mueller AM, et al. Clinical and morphological characteristics in *Streptococcus bovis* endocarditis: a comparison with other causative microorganisms in 177 cases. *Heart*; 1998: 276-280.
4. Ballet M, Gevigney G, Gare JP, et al. Infective endocarditis due to *Streptococcus bovis*. A report of 53 cases. *Eur H Jour* 1995;16:1975-1980.
5. Pergola V, Di Salvo G, Habib G, et al. Comparison of clinical and echocardiographic characteristics of *Streptococcus bovis* endocarditis with that caused by other pathogens. *Am J Cardiol* 2001;88:871-875.
6. Hoppes WL, Lerner PI. Nonenterococcal group-D streptococcal endocarditis caused by *Streptococcus bovis*. *Ann Intern Med* 1974;81: 588-593.
7. Klein RS, Recco RA, Catalano MT, et al. Association of *Streptococcus bovis* with carcinoma of the colon. *N Engl J Med* 1977;297:800-802.
8. Klein RS, Catalano MT, Edberg SC, et al. *Streptococcus bovis* septicemia and carcinoma of the colon. *Ann Intern Med* 1979;91:560-562.
9. Murray HW, Roberts RB. *Streptococcus bovis* bacteremia and underlying gastrointestinal disease. *Arch Intern Med* 1978;138:1097-1099.
10. Karchmer AW. Infective Endocarditis. In Braunwald's Heart Disease. 8th Edition. Saunders Elsevier 2008;1713-1738.
11. Abdulmir 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.
12. Schlegel L, Grimont F, Ageron E, et al. Reappraisal of the taxonomy of the *Streptococcus bovis/Streptococcus equinus* complex and related species: description of *Streptococcus gallolyticus* subsp. *gallolyticus* subsp. nov., *S. gallolyticus* subsp. *macedonicus* subsp. nov. and *S. gallolyticus* subsp. *pasteurianus* subsp. nov. *Int J Syst Evol Microbiol* 2003; 53:631-45.
13. Van't Wout JW, Bijlmer HA. Bacteremia due to *Streptococcus gallolyticus*, or the perils of revised nomenclature in bacteriology. *Clin Infect Dis*. 2005;40:1070-1071.
14. Gold JS, Batar S, Salem RR. Association of *Streptococcus bovis* bacteremia with colonic neoplasia and extracolonic malignancy. *Arch Surg* 2004;139:760-765.
15. Tripodi MF, Adinolfi LE, Ragone E, et al. *Streptococcus bovis* endocarditis and its association with chronic liver disease: an underestimated risk factor. *Clin Infect Dis* 2004;38:1394-1400.
16. Ferrari A, Botrugo I, Bombelli E, et al. Colonoscopy is mandatory after *Streptococcus bovis* endocarditis: a lesson still not learned. Case report. *World J Surg Oncol* 2008; 6:49.
17. Ellmerich S, Scholler M, Duranton B, et al. Promotion of intestinal carcinogenesis by *Streptococcus bovis*. *Carcinogenesis* 2000;21:753-756.