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

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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 infectioasă cu *Streptococcus gallolyticus* pe valva mitrală și aortică și vegetație de mari dimensiuni la nivelul valvei mitrale. Colonoscopia efectuată la un pacient alții 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 reținere indicată. cazul prezentat subliniază importanța constientizării 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 infectioasă, 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 transophageal, 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-
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. 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. Multiple valve involvement
is more common in Streptococcus bovis endocarditis than in other forms of endocarditis, ranging from 36-60%. In the reported case the patient had both mitral and aortic valve involvement, a pattern described in approximately 18% of S. bovis endocarditis. Some authors suggest higher embolic risk for S. bovis endocarditis due to its ability to form large vegetations. 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. In patients with Streptococcus bovis endocarditis complete evaluation of the gastrointestinal tract, particularly the colon is warranted. It is estimated that between 18 and 62% of the patients with S. bovis endocarditis have underlying colorectal tumors, 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.
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. 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.

Besides the association with colon cancer, different case series suggest also an association between *S. gallolyticus* and malignancy irrespective of site and different cases report *S. gallolyticus* bacteremia/endocarditis in patients with upper gastrointestinal tract neoplasia, gastric lymphoma or endometrial cancer. 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 ethiologies.

The pathogenesis of the association between *S. gallolyticus* endocarditis/bacteremia and colonic lesions is not yet understood, especially that *Streptococcus gallolyticus* can be found in the gastrointestinal tract in 5–16% of healthy population. 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. 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 carcinogenetic 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.

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.

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**Reference**