



Case report

A case of silent colonic lesions associated with streptococcus gallolyticus, bacteremia and endocarditis

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Abstract

We present a clinical case of synchronous colonic lesions, histologically different, associated with streptococcus gallolyticus subsp. gallolyticus (Sgg)/ Streptococcus bovis biotype I, bacteremia and infective endocarditis. A 53-year-old female, without history of CRC in her family, known with total hysterectomy for uterine fibromatosis, presents to Emergency Department for marked asthenia, nausea, weight loss (10 kgs in the last month), febrile episode associated with severe anemia, symptomatology that has increased in the last two weeks. The patient was admitted in the Internal Medicine Department for further investigations, under the suspicion of sepsis of unknown cause. On blood cultures grew Sgg bacteria. Both transthoracic echocardiography and transesophageal echocardiography were performed and diagnosed infective endocarditis with vegetations of the mitral and aortic valves. Antibiotics treatment was initiated, with ceftriaxone and gentamycin, according to antibiogram results. Severe hypochromic, microcytic anemia, and lack of an infective origin site required digestive endoscopic evaluation, and showed gastritis, ulcerovegetative tumor of the ascending colon and polyp in the rectosigmoid. Resection of rectosigmoid polyp was performed through colonoscopy, and, also, right hemicolectomy with ileo-transverse anastomosis for the ascending colon cancer. Post-operative evolution was favorable. Histological result showed mucinous adenocarcinoma of the ascending colon and tubulovillous adenoma, with moderate dysplasia, in the rectosigmoid. At 6-month, endoscopic evaluation showed normal aspect of anastomosis without presence of other colonic lesions.

Keywords

: colorectal cancer, streptococcus gallolyticus, polyp colon, infective endocarditis

Highlights

- ✓ This case illustrates a direct link between Sgg and colorectal cancer; the presence of Sgg bacteremia/ infective endocarditis, requires evaluation of gastrointestinal tract, even in the absence of any digestive clinical signs.
- ✓ Following an episode of Sgg bacteremia/endocarditis, endoscopic colonic monitoring is recommended to detect the progression of possible new lesions.

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Introduction

Colorectal cancer (CRC) development is a complex multi-factorial process, including genetic and environmental factors. Both can influence the progression of CRC, from dysplastic lesions to carcinoma invasive. As a tumoral microenvironment factor, the gut microbiota can play a critical role in several biological processes, such as barrier, immunity and metabolic functions.

The colorectal disorders comprise polymorph lesions, benign, premalignant and malignant conditions. In the development of this lesions, and furthermore in progression, colonic microflora is large debated in recent studies, as having an important role (1, 2). *Streptococcus gallolyticus* subsp. *gallolyticus* (Sgg) belongs to the Group D streptococci, also known as the *S. bovis*/*S. equinus* complex (SBSEC) with seven subspecies, in the recent nomenclature: *Streptococcus equinus*, *Streptococcus infantarius* subsp. *infantarius*, *Streptococcus lutetiensis*, *Streptococcus alactolyticus*, *Streptococcus gallolyticus* subsp. *gallolyticus* (Sgg), *Streptococcus gallolyticus* subsp. *macedonicus* (Sgm) and *Streptococcus gallolyticus* subsp. *pasteurianus* (Sgp) (3). Of all, Sgg has been regularly related to CRC (2). Moreover, in different case reports, Sg bacteremia was linked to benign colonic lesions (diverticulosis, inflammatory bowel disease, polyps) (4) and several other malignancies like gastric carcinoma (5), gastric lymphoma (6), pancreatic carcinoma (7), esophageal carcinoma (8), Kaposi sarcoma (9) and endometrial cancer (10). We highlight a case of a patient with infective endocarditis, Sgg bacteremia and two different histological types of colonic lesions, without any digestive signs.

Case report

A 53-year-old female, without history of inherited CRC in her family, known with total hysterectomy for uterine fibromatosis, presents to Urgent Compartment for marked asthenia, nausea, weight loss (10 kgs in the last month), febrile episode associated with severe anemia, symptomatology that has increased in the last two weeks. The patient was admitted in the Internal Medicine Department for Sepsis with unknown cause as diagnosis, for further investigations.

On physical examination, she was febrile (39.1 °C), blood pressure was 147/80 mm Hg with pulse rate 89 beats/min and diastolic blast in the aortic outbreak. Had supple, painless abdomen and normal rectal tact. Laboratory values showed an important inflammatory syndrome (WBC, 16200/ml with 89.2% neutrophils, ESR, 96 mm/h, CRP, 9.5 mg/dl) and severe hypochromic, microcytic anemia (Hb, 6,5 g/dl) with seric Fe, 18.4 ug/dl. Liver functions tests and coagulation parameters were found to be within normal limits. Urinalysis revealed rare white and red blood cells, cloudy look and positive culture for *Escherichia coli*. Chest radiography was normal. Two sets of blood cultures were drawn and both were positive for Sgg bacteria. Both transthoracic echocardiography and transesophageal echocardiography were performed and diagnosed infective endocarditis with vegetation in the mitral and aortic valves. Antibiotics treatment was initiated, with ceftriaxone (2 x 1 g/day) and gentamycin (2 x 80 mg/day), systemic therapy, according to infectious diseases specialist and to antibiogram results, followed by normal body temperature.

To identify the infectious focus of disseminations, a computer tomographic (CT) scan of the brain, thoracic and abdomen was requested. Images of CT-scan revealed normal bone structure and no pathological lesions. In this circumstance, the presence of severe anemia and lack of an infective focus determined gut endoscopic evaluation, and showed gastritis, ulcerovegetative tumor of the ascending colon and polyp in the rectosigmoid. Resection of rectosigmoid polyp was performed through colonoscopy (Figure 1; A, B, C), associated with right hemicolectomy, with ileo-transverse anastomosis for the ascending colon cancer.

Post-operative evolution was favorable. Further, the patient was referred to the Department of Cardiac Surgery for the valvuloplasty intervention. Histological result showed mucinous adenocarcinoma of the ascending colon and tubulovillous adenoma, with moderate dysplasia, in the rectosigmoid. At 6-month, endoscopic evaluation showed normal aspect of anastomosis without presence of other colonic lesions (Figure 2; A, B).



Figure 1- A, B, C. Resection of rectosigmoid polyp through colonoscopy

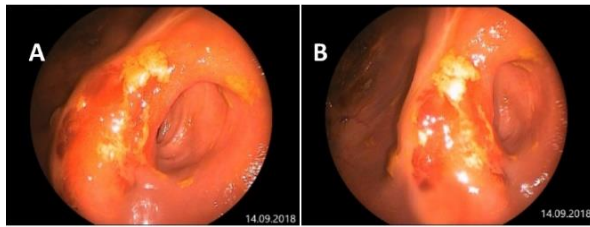


Figure 2- A, B. At 6-month, endoscopic evaluation showed normal aspect of ileo-transverse anastomosis.

Discussions

CRC is a common and lethal disease, with a high mortality rate (11). The American Cancer Society estimates that about 1 in 21 men and 1 in 23 women in the USA will develop colorectal cancer during their lifetime. In its development and progression, both genetic and environmental factors play an important role. Since 1951 (12), when the association between CRC and group D endocarditis was reported, and later in 1977 (13), 1989 (14), 2005 (15), other studies highlighted this, and still the role of gut microflora in colorectal disorders is debated. Following these reports, *Streptococcus gallolyticus* subsp. *gallolyticus* (bovis biotype D) is becoming the model bacteria for the SBSEC due to its implication in CRC, bacteremia and infective endocarditis. In a recent paper (2017) (16), the advanced and non-advanced colonic adenomas and tumors, associated with Sgg, were mostly located in the distal colon (65.6%), cecum/ascending colon (23.4%) and transverse colon (10.9%). Furthermore, in patients with Sgg bacteremia and/or infective endocarditis is correlated with the presence of villous or tubulovillous adenomas (17, 18). Our case, due to the synchronous colonic lesions presented, the mucinous adenocarcinoma of the ascending colon and tubulovillous adenoma in the rectosigmoid, associated with Sgg endocarditis, supports the hypothesis that Sgg can play a role CRC (19).

At the moment, is very debated if Sgg plays an etiological role in the development of colorectal tumors or it is only a consequence of CRC (20). In sustaining the etiological role of Sgg in CRC, the first experimental evidence that *S. bovis* could stimulate cancer development was reported by Ellmerich et al. (2000) (21). They showed that Sg may have carcinogenic activity in colonic mucosa, when preneoplastic lesions are already present. Also, in 2010, a molecular study revealed a higher presence of Sgg in human neoplastic tissues compared with normal adjacent tissue from the same patient (4), and in a recent study (2017) (16), it was

demonstrated that Sgg promotes colorectal tumors development through an increase of cell proliferation in a β -catenin dependent manner. Although these studies demonstrated the etiological role of Sgg in promoting CRC development (16), Sgg initially has to colonize the colon, process that might require the presence of independent mutations in the oncogenic signaling pathways, together with chronic inflammatory conditions (22).

Sgg is an important cause of bacteremia and endocarditis (23). It uniquely can translocate in a paracellular manner across malignant gut epithelium, in the absence of an important immune response. Too, it may disseminate to the bloodstream through premalignant/malignant colonic lesions and then adhere to the collagen-rich surfaces (such as surfaces of cardiac valves) and form biofilms (24). Compared to other related streptococci or other bacterial species inhabiting the gut, this microorganism is able to grow in bile (25) and can cross the hepatic reticulo-endothelial system and get into the systemic circulation, that could explain the association between colonic lesions and Sgg bacteremia/infective endocarditis (26).

A striking correlation between Sgg bacteremia, infective endocarditis and CRC was revealed by numerous studies (14, 27). Except infective endocarditis, the *S. gallolyticus* may also determinate infections in other sites, like osteomyelitis, discitis (28) and neck abscess (29) that can be associated with colonic malignancy. In our case, we did not find other infectious lesions, on the CT-scan images. Were found only the two colonic lesions: a small ulcerovegetative adenocarcinoma of the ascending colon that was clearly the way of Sgg infection dissemination, and a tubulovillous adenoma polyp, with moderate dysplasia, in the rectosigmoid, that suggests its development and progression begun in the colonic mucosa colonized with Sgg. Regarding the necessary time required for monitoring and diagnose a new colonic lesion, following Sgg bacteremia/infective endocarditis, was considered to be within 2 to 4 years (30). At 6-month, our endoscopic evaluation showed normal aspect of anastomosis, without presence of other colonic lesions.

Conclusions

This case shows a direct link between Sgg and colorectal cancer and also the potential of this microorganism to disseminate in other organs. The presence of Sgg bacteremia/infective endocarditis, requires always the evaluation of gastrointestinal tract,

even in the absence of any digestive clinically signs. After a such episode of Sgg bacteremia/endocarditis, endoscopic colonic monitoring is recommended to detect the progression of a new lesion. Furthermore, in the screening process feces cultures must be considered, as it can reveal the presence of colonic recolonization with Sgg.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article, and there was no financial support that could have influenced the outcomes. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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