Streptococcus bovis endocarditis and colon cancer: myth or reality? A case report and literature review

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SUMMARY

A relationship between infective endocarditis and colon cancer was established in 1950, and *Streptococcus bovis* was successfully isolated in 1970. However, this association and its pathogenesis still remain unclear. In this paper, we describe the clinical case of a patient with a history of colon cancer and infective endocarditis caused by *Streptococcus bovis*. The role of *S bovis* as an aetiological agent in the development of colon cancer is intriguing but uncertain. *S bovis* infection should be considered a silent sign of gastrointestinal malignancy or hepatic disease. We believe that in order to demonstrate the presence of colon cancer, all patients with *S bovis* infection require an endoscopic investigation of the colon.

BACKGROUND

The American Cancer Society estimates that, in 2011, about 141 210 people will be diagnosed with colorectal cancer and about 49 380 people will die of the disease in the USA. In both men and women, colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death.[1] *Streptococcus bovis* (*S bovis*) is a Gram-positive *coccus* which belongs to group D of the Lancefield classification, as well as the category of *enterococci* bacteria. *S bovis* is a commensal microorganism in the gastrointestinal lumen of both humans and animals and it accounts for 10–15% of all cases of infective endocarditis.[2] Furthermore, most studies report that the rate of colon cancer in patients with *S bovis* infection varies between 55% and 73%.[3] The variability of these colon cancer rates is due primarily to the fact that most data were collected in retrospective studies.[2]

CASE PRESENTATION

In February 2010, a 61-year-old Caucasian man was admitted to the department of medicine of Bolognini Hospital in Seriate (Bergamo, Italy) with fever, night sweats, fatigue, myalgia (all four limbs) and a reported weight loss of 5 kg. Clinical examination was normal. Chest x-ray showed no sign of bronchopneumonia and excluded changes in the cardiac shadow. Full-body CT scan, obtained with oral and intravenous contrast material, showed wall thickening of about 4 cm in the sigmoid colon and splenomegaly (bipolar diameter of 17.7 cm). A colonoscopy confirmed the presence of a tumour in the left colon and a whole-body PET scan excluded further neoplastic lesions. CEA and CA 19.9 serum tumour markers were normal. ECG was normal while a transthoracic echocardiogram showed only mild mitral and aortic insufficiency. Blood tests documented mild-to-moderate anaemia (Hb 11.1 g/dl), thrombocytopaenia ($145\times10^3/\mu l$), with no leucocytosis or neutrophilia. Suspecting polymyalgia rheumatica, immune and thrombophilic screening tests were performed: the values of C reactive protein, erythrocyte sedimentation rate, rheumatoid factor, antineutrophil cytoplasmic antibodies, antithrombin III and B2M (β2-microglobulin) were high. These results were considered a paraneoplastic syndrome. However, complete resolution of symptoms was achieved through antibiotic therapy based on fluoroquinolones.

The patient was transferred to the department of general surgery, where he underwent laparoscopic sigmoidectomy, loco-regional lymphadenectomy and recto-colic end-to-end anastomosis. Histological examination was compatible with moderately differentiated adenocarcinoma of the large intestine invading muscularis propria and perineural space, with 15 lymph-nodes and resection margins negative; pT2pN0 (M0), stage I (TNM classification, AJCC 7th edition).

Subsequently, the patient was sent to our attention at the department of oncology and we advised no further treatment, but simply a follow-up. Further serological investigations confirmed high values of CPR, rheumatoid factor and alterations of the serum protein electrophoresis test.

On rheumatologists' recommendation, the patient underwent a bone marrow biopsy, which ruled out haematological malignancies, and he started an oral steroid therapy on suspicion of polymyalgia rheumatica disease.

In May 2010, the patient was again admitted to the medicine department of another hospital with fever and fatigue. A diagnosis of endocarditis and L3–L4 spondylodiscitis related to *S bovis* infection (confirmed by positive blood cultures) was performed. A transthoracic echocardiogram showed aortic valve vegetations (2×1 cm) with significant insufficiency.

As soon as the fever was resolved through the use of intravenous β-lactam antibiotics, the patient underwent prosthetic replacement of the aortic valve.

OUTCOME AND FOLLOW-UP

During his last visit to the department of oncology (April 2012), the patient was in good condition in prophylactic aspirin therapy (100 mg daily), with no sign of recurrence of colon cancer (recent chest x-ray, abdominal ultrasound and specific tumour markers were negative).

DISCUSSION

Several studies (mostly retrospective) and case reports published in the last 60 years have shown a

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relationship between bacterial endocarditis and colon cancer. In 1951, McCoy and Mason demonstrated a relationship between the two factors, and in 1974, *S bovis* was recognised as a possible causative agent of endocarditis. We now understand that infection caused by *S bovis* (endocarditis, sepsis, abscesses, etc) is not only related to gastrointestinal cancers, especially colon cancer, but also to liver diseases and immune deficiency syndromes (including AIDS).[3–8]

Infective endocarditis is an infection of the heart valves and mural endocardium caused by bacteria, fungi, rickettsiae and viruses. Bacterial endocarditis is the most common clinical form of endocarditis; it can occur in either acute or subacute phase and usually affects immunocompromised patients or patients with valve defects.

S bovis is the causative agent in 10–15% of all infective endocarditis.[2] Infective endocarditis is usually associated with valve vegetations, continuous bacteraemia, splenomegaly, remitting fever type and significant heart murmur (85% of cases). The endocardial involvement may lead to valve leaflets rupture with heart failure in severe forms of endocarditis.[9]

As regards our patient, it was hard to determine diagnosis of endocarditis at an early stage, primarily because of the absence of pathognomonic sign of vegetations and valvular heart murmur (subacute clinical form).

Furthermore, both antibiotic and steroid therapy, leading to fever resolution, probably masked the typical symptoms and signs of bacterial endocarditis.

Therefore, there is a link between *S bovis* infection and gastrointestinal tumours, but the exact molecular and cellular mechanisms underlying this association have not been fully clarified.

S bovis is a normal bacterial commensal microorganism of the intestinal lumen of humans and many species of vertebrate animals. However, data showing the direct involvement of *S bovis* in the development of colorectal cancer are very scarce. Some preclinical data have shown that certain components of the bacterial cell wall of *S bovis* are able to increase the production of specific cytokines promoting intestinal carcinogenesis.[10] On the other hand, the probability that a patient with colon cancer develops *S bovis* septicaemia and subsequent endocarditis is very low (about 3–6%).[11] It has been recently suggested that intestinal lesions themselves can help the overgrowth of *S bovis*. The altered permeability of the intestinal wall, further increased by specific prostaglandins secreted by the bacterium itself, would facilitate the passage of *S bovis* from the lumen to the bloodstream, resulting in bacteraemia and other infectious complications.[12]

Competing interests None.

Patient consent Obtained.

Learning points

- Evidence strongly suggests a relationship between *Streptococcus bovis* infection and colon cancer.
- This association should be considered in terms of casualness and not of causality. *S bovis* endocarditis should be considered as a potential sign of silent colon cancer. Therefore, patients with a diagnosis of *S bovis* infection should be highly recommended for an endoscopic study of the large intestine.
- It is estimated that about 50–70% of these patients already have or will develop bowel cancer. After resolution of the infection, a minimum of 2-year to 4-year follow-up with colonoscopy is recommended, as there is a higher incidence of precancerous lesions and cancer of the intestine during this period.[13]

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