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Colon cancer presenting as *Streptococcus gallolyticus* infective endocarditis

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ABSTRACT

A 58-year-old Chinese man presented with a three-week history of fever. He had a background history of rheumatic heart disease, hypertension, and thalassaemia. He was found to have infective endocarditis of the aortic valve due to *Streptococcus gallolyticus*. During the hospital stay, he developed a few episodes of haematochaezia and was subsequently found to have colonic carcinoma-in-situ. He completed appropriate antibiotic treatment for his infective endocarditis and underwent a left hemicolectomy with primary anastomosis. The association between *Streptococcus gallolyticus* infective endocarditis and colonic neoplasm is well documented. This case report stresses the importance of performing routine colonoscopy to look for colonic neoplastic change in patients diagnosed to have *Streptococcus gallolyticus* infective endocarditis. The early diagnosis of the colonic neoplasm has enabled our patient to have a curative surgery without compromising his quality of life.

Keywords: bacterial endocarditism, colonoscopy, colorectal neoplasm, gastrointestinal haemorrhage, infective endocarditis, *Streptococcus bovis*, *Streptococcus gallolyticus* infective endocarditis

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INTRODUCTION

More than 50% of native valve infective endocarditis (IE) in patients without a history of intravenous drug use is due to *Streptococcus*. Clinically, streptococcal IE is more likely to affect the aortic, then mixed aortic and mitral valves, then mitral valve alone.[1] There are numerous reports suggesting the possible association between Streptococcal IE and malignant colorectal neoplasm.[2-7] This report illustrates the importance of recognising this association and its potential benefit.

CASE REPORT

A 58-year-old Chinese man presented to our department in December 2005 with a three-week history of fever, chills, sore throat, and headache. Background medical history included hypertension, thalassaemia minor, possible rheumatic heart disease involving the mitral and aortic valves on follow-up with another hospital, and lower limb eczema. He denied any intravenous drug use in the past. There was no significant contact or travel history, or any recent dental procedures. Physical examination revealed a temperature of 38.4°C and a pansystolic murmur at apex and a diastolic murmur over the left lower sternal edge. His other vital signs were stable. Examination was otherwise unremarkable.

Initial investigations showed a white cell count of 16.23 × 10^9/L with a neutrophil count of 80%, haemoglobin of 8.9 g/dL, mean corpuscular volume of 57.2 fL, platelet count of 504 × 109/L, erythrocyte sedimentation rate of 119 mm/h, C-reactive protein of 143.2 mg/L, sodium of 134 mmol/L, alanine aminotransferase of 55 U/L, gamma glutamyltranspeptidase of 116 U/L. Other liver function markers, creatinine, creatinine kinase, and troponin T levels were normal. Electrocardiogram showed sinus rhythm, left ventricular hypertrophy and first degree heart block without any ST or T wave changes. His chest radiograph was unremarkable. An urgent transthoracic echocardiogram, followed by a transoesophageal echocardiogram, were performed and showed vegetation on the non-coronary aortic cusp with moderate aortic regurgitation, anterior mitral leaflet prolapse with mild mitral regurgitation. There was no para-valvular abscess. The left ventricular systolic function was normal. Standard antibiotic regime for left-sided IE was administered after septic work-up, with good response clinically.

Two out of three sets of blood culture yielded Gram-positive cocci in chains after one day of incubation. Subculture on blood agar plates revealed catalase negative, esculin positive, non-haemolytic streptococci sensitive to penicillin and vancomycin, but resistant to tetracycline, erythromycin, and clindamycin. No pyrrolidonyl arylamidase was demonstrated, ruling out enterococci. A commercial identification system (API 20 Strep, bioMérieux, Marcy-l'Etoile, France) incorrectly identified the organism as *Leuconostoc* spp., a species that is intrinsically resistant to vancomycin. The isolate was later subjected to 16s

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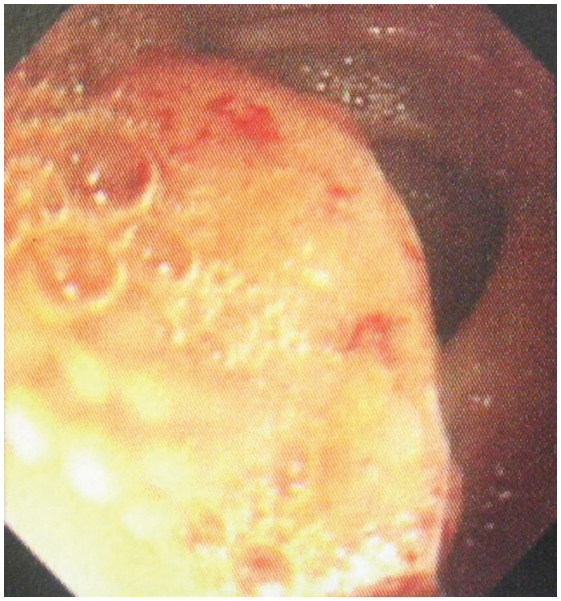

Fig. 1 Photograph taken during colonoscopy shows a colonic polyp with ulcer.

RNA sequencing to reach the species diagnosis, *Streptococcus gallolyticus (S. gallolyticus)*, which is a member of the *Streptococcus bovis (S. bovis)* complex. While the laboratory markers were showing signs of improvement, the patient sustained episodic haematochaezia on days 17 and 18.

Colonoscopy revealed multiple haemorrhoids and a large polypoid lesion near the splenic flexure (Fig. 1). Only a superficial biopsy was obtained due to technical difficulty, which showed tubular adenoma with focal high grade dysplasia. An uneventful curative left hemicolectomy with primary anastomosis was performed on day 25. No intra-abdominal lymphadenopathy or ascites was noted. Histology of the resected specimen confirmed colonic carcinoma-in-situ. The carcinoembryonic antigen was normal. He recovered steadily and was discharged two weeks after the operation.

DISCUSSION

The association between streptococcal IE and colonic cancer was first postulated by McCoy and Mason in 1951.[2] The prevalence of this association has been reported between 25%–80%.[2-7] Besides IE, case reports have suggested the possibility of streptococcal infections in various sites such as osteomyelitis, discitis, and neck abscess could be linked to colonic malignancy or malignancies in other locations.[8,9] Although most European studies suggested IE was the commonest manifestation of streptococcal infection, it has been reported that cholecystitis, cholangitis, and biliary tract diseases were commoner manifestations in other geographical areas, such as in Hong Kong.[10]

In terms of pathogenesis, as *S. bovis* is a transient normal flora in the gut, researchers have postulated that increased bacterial load in the colon might be responsible. However, studies have showed inconsistent results.[5,11,12] Some extracted antigens from the *S. bovis* cell wall and demonstrated that these antigens could stimulate inflammatory cytokines productions and promote pre-malignant lesions in animal models.[3,13,14] *S. bovis* is considered to be a low-grade pathogen, and capable of causing a chronic inflammation in the colon. Chronic inflammatory states are associated with malignant changes such as Barrett's oesophagitis, chronic gastritis secondary to *Helicobacter pylori* infection leading to gastric carcinoma, inflammatory bowel disease in colonic cancer, and chronic hepatitis B or C infection causing hepatoma. More studies are needed to ascertain the detailed pathogenesis of malignancy from *S. bovis* infection.

The microbiological diagnosis of *S. bovis* is usually straightforward. Many laboratories also use commercial identification systems, but sometimes the result from these systems can be unreliable. Most isolates belonging to biotypes I and IIa of the *S. bovis* species have been reclassified as *S. gallolyticus*.[15] The resistance pattern of our isolate is in line with previous reports that isolates frequently are resistant to macrolides and tetracycline.[4] Therefore, for patients presenting with IE, attempts should be made to confirm the causative organism. For those who have *S. gallolyticus* IE or bacteraemia, colonoscopy should be routinely performed to look for early malignant changes including colonic polyps. This is important as early diagnosis of colon cancer may greatly improve the prognosis and quality of life of the patients. Such as in our patient, we were able to diagnose and perform a curative surgery for his colon cancer. Repeat colonoscopy should be arranged for those who have a normal colonoscopy initially, as there is no temporal knowledge on this association at present. Surveillance on malignancy in other locations should be considered in this group of patients if clinically indicated.

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