CASE REPORT

Streptococcus bovis prosthetic valve endocarditis associated with silent colonic carcinomaFatehi E Elzein,¹ M Yasin Akhtar,² Hatim Khairallah,² Ali Albenmoussa³¹Department of Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia²Department of Cardiology, Prince Sultan Cardiac Center, Riyadh, Saudi Arabia³Department of Gastroenterology and Hepatology, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

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Accepted 15 May 2017

SUMMARY

A 75-year-old woman was admitted to our hospital with a 3-month history of fever. Of note, she had a bioprosthetic mitral valve replacement 1 year prior to admission. *Streptococcus bovis* was isolated from three sets of blood cultures. An echocardiogram showed a flickering mass attached to the bioprosthesis. Her blood culture became sterile by the fourth day of ceftriaxone therapy. In spite of the absence of gastrointestinal symptoms, screening colonoscopy revealed an invasive colonic adenocarcinoma. The association linking *S. bovis* endocarditis and colonic tumours is well recognised. However, despite early reports of this association by Klein *et al* in 1979, a large number of practising physicians remain unaware of this phenomenon. This lack of awareness results in lost opportunities for early diagnosis and, consequently, improved outcome in such patients. Our report emphasises this association in an area with a low incidence of *S. bovis* endocarditis.

BACKGROUND

Although *Streptococcus bovis* is a known commensal in the general population, major complications, including meningitis and infective endocarditis, that is, can occur if the bacteria translocate into the circulatory system. These bacteria account for 0.6%–1% of bacteraemia in hospitalised patients and cause 5%–14% of endocarditis cases.¹ *S. bovis* infections depend on the infecting subspecies as well as temporal and geographical factors. Based on molecular characterisations, *S. bovis* is now subdivided into biotype I, represented by *S. gallolyticus* ssp. *gallolyticus* (SGG), and biotypes II/1 and II/2, represented by *S. infantarius* subsp. *infantarius* and *S. pasteurianus*, respectively. According to the results of a systematic review and meta-analysis, endocarditis occurs in 43%–100% of patients infected with the biotype I bacteria, while it only occurs in 8%–29% of patients infected with biotype II. This can partly be explained by the increased tendency of *S. gallolyticus* to form biofilm on collagen-rich surfaces, including deformed or prosthetic cardiac valves.² Geographical location contributes to both the incidence and location of any associated complications. In the International Collaboration on Endocarditis—prospective cohort study, *S. bovis* contributed to 10% of endocarditis cases in Europe and substantially less (3%) in other areas (Africa, Asia and the Middle East).³ *S. gallolyticus* causing endocarditis could play a unique role in carcinogenesis. Alternatively, it can merely be a consequence

of colorectal cancer (CRC).⁴ CRC is postulated to facilitate the translocation of the bacteria, leading to infective endocarditis. However, in patients with underlying CRC, the chance of developing *S. gallolyticus* bacteraemia/endocarditis is only 3%–6%.⁵ On the contrary, CRC can be detected in 65%–70% of patients with *S. gallolyticus* bacteraemia/endocarditis. This association is most common in cases of endocarditis, compared with other *S. gallolyticus* infections, including septicaemia and meningitis. Here, we present a case that highlights the often-overlooked association between *S. bovis* endocarditis and CRC.

CASE PRESENTATION

A 75-year-old woman was admitted to Prince Sultan Cardiac Centre, Riyadh, with a 3-month history of fever, chills and rigours. Of note, she underwent tissue mitral valve (MV) replacement and tricuspid valve repair 1 year prior. Her medical history was significant for diabetes mellitus, hypertension, ischaemic heart disease, coronary artery bypass graft and hypothyroidism. Her general examination on admission was unremarkable, with a pulse rate of 80 beats per min, respiratory rate of 18 breaths per min, blood pressure of 107/67 mm Hg and oxygen saturation under room air of 95%. There were no peripheral signs of IE. Her fundus examination was normal, and urine was negative for haematuria. Routine laboratory investigations revealed haemoglobin of 10.7 g/dL, platelet of 141×10^9 /L and erythrocyte sedimentation rate of 114 mm/hour. Three sets of blood cultures grew *S. bovis* (figure 1). Further molecular testing to identify the species not available. A transthoracic echocardiogram and transoesophageal echo revealed a well-seated MV with thickened leaflet and a flickering mass attached to the MV bioprosthesis with trace mitral regurgitation. The repaired tricuspid valve showed moderate tricuspid regurgitation. The patient was initiated on intravenous ceftriaxone 2 g once daily. A blood culture collected 4 days later was sterile.

The patient denied any gastrointestinal symptoms; however, stool was positive for faecal occult blood (FOB). Both cancer antigen 19–9 and carcinoembryonic antigen (CEA) were high at 47 U/mL and 8.9 µg/L, respectively (normal range: 0–34 U/mL and 0.0–3.4 µg/L, respectively). Colonoscopy disclosed a large, non-circumferential and non-obstructing fungating mass 30 cm from the anal verge (figure 2). Histopathological examination revealed a moderately differentiated invasive adenocarcinoma, while CT of the abdomen, chest and pelvis revealed

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To cite: Elzein FE, Akhtar MY, Khairallah H, *et al*. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-219488

Figure 1 Gram stain showing *Streptococcus bovis* as Gram-positive cocci in chains.

a focal proximal sigmoid wall with heterogeneous thickening, measuring 3 cm in length and 1 cm in thickness, representing a primary sigmoid mass. There was evidence of direct extension to the adjacent fat superiorly, T3. Furthermore, there were adjacent lymphadenopathy/peritoneal deposits measuring up to 1.5 cm in width. In addition, a metastatic lymph node measuring 1.2 cm was noted along the superior mesenteric artery. Distant metastases were not detected.

While in the hospital, the patient developed upper respiratory tract symptoms with recurrence of fever and a nasopharyngeal swab PCR was positive for influenza A. Oseltamivir was subsequently added to her treatment regime. Minimal infiltration was

Figure 2 A large, non-circumferential and non-obstructing fungating mass 30 cm from the anal verge.

noted on the chest radiograph. Interestingly, sputum culture confirmed a heavy growth of *S. bovis*.

Six weeks following IE, she underwent an uneventful laparoscopy-assisted sigmoidectomy and primary anastomosis. The surgical specimen showed a 3.0×3.0 cm, moderately differentiated, invasive colonic adenocarcinoma. The tumour invaded through the muscularis propria into the mesenteric fat. Of 13 lymph nodes; six were positive for malignancy; largest was 1.5 cm in diameter with no extranodal extensions. However, all surgical resection margins were free of neoplasia. The tumour node metastasis classification was pT3 N2a Mx. Adjuvant chemotherapy was not given in view of poor performance status.

OUTCOME AND FOLLOW-UP

The patient completed 6 weeks of medical treatment for IE followed by colonic tumour resection. She remains stable 6 months following surgery.

DISCUSSION

Prosthetic valve endocarditis (PVE) occurs in 6%–16% of cases of *S. bovis* endocarditis.⁶ As observed in the present case, *S. bovis*-related PVE tends to affect elderly patients and poses a lower risk of systemic embolisation than native valve endocarditis. A recent study showed biotype II endocarditis to have a higher tendency to involve the prosthetic valves than SGG. However, the number of patients was too low; hence, these findings need to be confirmed in larger studies.⁶

The relationship between *S. bovis* and colorectal malignancies was initially described in 1951.⁷ Although this association was further explored by Klein *et al* in 1977, a large number of practising physicians remain unaware of this relationship.⁸ *S. gallolyticus* is associated with a higher prevalence of endocarditis (43%–100%) and colonic malignancy (70%).² However, the prevalence of CRC cases associated with biotype II streptococci (23%) is similar to that of CRC in the general population (10%–25%), raising questions regarding whether such patients should undergo screening colonoscopies.^{9 10}

Of note, many patients with CRC do not show symptoms or signs related to colorectal tumours, similar to the present case.⁸ In part, this can be explained by the non-invasive nature of such tumours. Interestingly, in various studies, the presence of antibodies against the *S. gallolyticus* antigen was thought to be correlated to the non-invasive nature of the adenocarcinoma.^{11 12} Subsequently, *S. bovis* infections were the only indicators of underlying malignancy in patients with colorectal tumours. This underscores the importance of performing colonoscopies on all patients with *S. bovis* infections. Despite the well-recognised association of CRC and *S. bovis* infection, colonoscopy remains underused.¹³ Additionally, CRC or polyps may develop years following the occurrence of SGG bacteraemia/endocarditis. Accordingly, patients with normal colonoscopy results should undergo regular follow-up colonoscopy screenings, although the time between these procedures has not yet been clearly defined. Recent reviews recommended colonoscopy every 3 years; while the European Society of Cardiology suggests annual colonoscopy; however, decisions should be individualised.^{1 14}

Our patient's stool culture was negative for *S. bovis*; in contrast, in one study, the faecal carriage rate was approximately five times greater in individuals with CRC than that in the healthy population.⁸ Conversely, in another study, 11% (2/24) of patients with CRC had *S. gallolyticus* in their faeces compared with 13% in control groups.¹⁴ On the other hand,

a recent meta-analysis revealed an increased probability of finding *S. bovis* in the stool of persons with CRC.¹⁵ Thus, more data are required before faecal carriage can be recommended as a screening test for CRC. In addition, detection of *S. gallolyticus* DNA or antibodies was suggested as a screening test in individuals at high risk for CRC.¹⁶ If shown to be effective, this screening mechanism would be of great advantage over FOB testing, which lacks sensitivity and specificity, as well as CEA, which is usually a marker of advanced disease.¹⁷

In conclusion, CRC is the second principal cause of all-cause and cancer-related mortality. Early detection of cancer can lead to a 5-year survival rate as high as 90%. Thus, because all patients with *S. bovis* endocarditis or bacteraemia have an elevated risk of developing CRC, they should undergo screening colonoscopy for the detection of such cancers. Whether serological or nucleic acid analyses of *S. gallolyticus* are effective means for the early detection of CRC remains to be determined.

Learning points

- ▶ *Streptococcus bovis* is a rare cause of bacteraemia and IE in adults.
- ▶ Both *S. bovis* endocarditis and bacteraemia are important indicators of underlying colonic neoplasm.
- ▶ Colonoscopy is mandatory in such infections.
- ▶ *S. bovis* infection can be followed by colorectal cancer years after the initial presentation. Follow-up is essential in patients with a normal screening colonoscopy.

Contributors FEE contributed to the management of the patient and writing up of the case, reviewed the literature and coordinated the submission process. MYA is the Infectious Diseases Senior Registrar. He participated in the management of the patient, gathered the investigations, and reviewed the case report. HK is the cardiologist following the patient. Arranged and performed the echocardiogram and provided the image of the echo. He had reviewed and revised the case report. AA is the gastroenterologist who performed the endoscopy and provided the images of the CT scan and endoscopic findings. He had reviewed and contributed extensively to the editing of the report.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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