CASE REPORT

Second look at *Streptococcus sanguinis* and the colonRobert Thomas,¹ Vineet Gupta,¹ Brian Kwan^{1,2}¹Medicine, University of California San Diego Health System, San Diego, California, USA²Medicine, VA San Diego Healthcare System, San Diego, California, USA**Correspondence to**
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SUMMARY

Although the link between *Streptococcus bovis* bacteraemia and colon cancer is well established, bacteraemia from other viridans group streptococci that commonly colonise colonic mucosa may also herald occult malignancy. We present a case of *Streptococcus sanguinis* bacteraemia in an elderly man with new anaemia that led to the detection and removal of a high-grade colon neoplasm. This case contributes to a growing body of literature contending that unexplained streptococcal bacteraemia merits a thorough workup that may include relatively invasive procedures such as endoscopy. Diagnostic colonoscopy provides an opportunity to prevent invasive malignancy that may outweigh bleeding and perforation risks in elderly patients.

BACKGROUND

Gastrointestinal neoplasms are occasionally heralded by bacteraemia. The relationship between colon cancer and endocarditis with *Streptococcus bovis/gallolyticus* species was initially described in 1951.¹ Subsequently, the association between these species and colon cancer has been well documented.² The literature reveals that 25%–80% of patients with *S. bovis/gallolyticus* bacteraemia harbour underlying colonic neoplasm. These species are also associated with extracolonic cancers including gallbladder, pancreatic, ovarian and lung disease.³ Although less well characterised, other streptococcal species are common colonic commensals and have been linked to occult gastrointestinal tumours in case reports. We present a case of an elderly male with uncommon streptococcal bacteraemia that served as a sentinel event for an undiscovered colonic lesion.

CASE PRESENTATION

An elderly man with medical history significant for severe aortic stenosis status post tissue aortic valve, sick sinus syndrome with permanent pacemaker and renal cell carcinoma with partial nephrectomy presented with 4 days of lethargy, weakness and subjective fever. He also described intermittent chest discomfort reproducible with palpation and unintentional 10-pounds weight loss over the prior 2 weeks. The review of systems was negative for sore throat, cough, shortness of breath, nausea, vomiting, abdominal pain, dysuria, melena and haematochezia. He reported no recent travel or sick contacts. His last dental cleaning was 6 months prior to admission with appropriate antibiotics prophylaxis.

Initial vital signs were temperature 97.4°F, blood pressure 99/67 mm Hg, pulse 55/min, respirations 17/min and O₂ saturation 98% on room air. Head and neck examination demonstrated no conjunctival haemorrhages, rare palatal petechiae, dry mucus membranes and excellent dentition with no caries or gum tenderness. Examination of extremities revealed no stigmata of endocarditis including erythematous macules, tender subcutaneous nodules or splinter haemorrhages. He had a soft 2/6 systolic ejection murmur at the right upper sternal border. Rectal examination showed haemorrhoids and brown stool that was positive for occult blood.

INVESTIGATIONS

Pertinent laboratory data revealed new-onset anaemia and elevated inflammatory markers. Blood cultures (two aerobic and two anaerobic cultures) from hospital day 1 grew gram-positive cocci within 24 hours of incubation. *Streptococcus sanguinis* was identified after 5 days of incubation by means of VITEK2 microbial identification system using advanced calorimetry (bioMérieux, Marcy l'Etoile, France). No other bacterial species were isolated from the blood cultures (table 1).

Transthoracic echocardiogram demonstrated no macroscopic vegetations. Transesophageal echocardiogram was not performed due to the patient's advanced age and comorbidities.

DIFFERENTIAL DIAGNOSIS

Respiratory, urinary, gingival and colonic sources were considered during the patient's workup for *S. sanguinis* bacteraemia. The patient's benign urinalysis and absence of pulmonary symptoms increased suspicion for a potential gastrointestinal lesion.

TREATMENT

Based on blood culture sensitivities, the patient was empirically treated for endocarditis with intravenous penicillin G (2 million units every 4 hours) and gentamycin (120 mg every 48 hours) given his artificial valve. Further investigation pursuing the source of bacteraemia included a positron emission tomography scan showing increased metabolic uptake in the descending colon and rectum. Subsequent colonoscopy revealed two large polyps in the ascending and sigmoid colon consistent with tubular adenomas (figure 1). The patient was discharged home to complete 6 weeks of intravenous antibiotics. However, he was readmitted 1 week later with haematochezia with haemoglobin

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Table 1 Laboratory data on presentation

Test	Value (normal range)
White blood count	6.1 K/ μ L (4.8–10.8)
Haemoglobin	11.4 g/dL (12.4–17.4)
Baseline Haemoglobin	13.6 g/dL (2 months prior to admission)
Iron	20 μ g/dL (36–160)
Iron saturation	10% (20–50)
Total iron binding capacity	203 μ g/dL (228–428)
Ferritin	81 ng/mL (30–400)
Sedimentation rate (ESR)	55 mm/hour (0–10)
C-Reactive Protein- High Sensitivity (CRP-HS)	7.03 mg/dL (<0.8)
Blood cultures	4/4 bottles positive for <i>Streptococcus sanguinis</i>

drop to 7.3 g/dL. Repeat colonoscopy revealed a 4 cm rectal mass verified as tubular adenoma on biopsy (figure 2).

After the patient's bleeding resolved, the patient was discharged to continue outpatient treatment for endocarditis. Three months later, repeat endoscopic ultrasound and resection of the rectal mass revealed a 2.8 cm tubulovillous adenoma with focal high-grade dysplasia and low-grade adenomatous epithelium at the cauterised edge (figure 2).

OUTCOME AND FOLLOW-UP

Seven months after initial presentation, the patient's haemoglobin was 10.0 g/dL, consistent with resolution of gastrointestinal blood loss. A final colonoscopy the following month removed residual tubular adenoma at the resection site, and further colonic surveillance was discontinued.

DISCUSSION

Although classically considered to be of low virulence, viridans group streptococci can lead to significant infections including bacteraemia and endocarditis in the setting of underlying malignancy. In this case report, the discovery of *S. sanguinis* bacteraemia led to the discovery and removal of a large colonic mass with high-grade dysplasia. While colonoscopy has become the standard of care for *S. bovis/gallolyticus* bacteraemia, several authors have made the case that other viridans species merit similar vigilance.⁴ Eight cases of *S. sanguinis* bacteraemia associated with occult gastrointestinal malignancy have been previously reported. The source of *S. sanguinis* bacteraemia is notoriously difficult to identify and often requires extensive workup.^{5–11} While *S. sanguinis* is commonly isolated from gingival crevices, it may also be isolated from colonic mucosa. Prior case reports reveal that some cases initially attributed to gingival inflammation

Figure 2 Rectal mass discovered during second colonoscopy. Left: Polypoid 4 cm mass located 10 cm from the anal verge; Right: Close-up image showing semipedunculated morphology of the same mass.

were subsequently revealed to be secondary to advanced colon carcinoma. In a case study of 14 782 admissions over 3 years, *S. sanguinis* was the most common cause of streptococcus bacteraemia in patients with malignancy, and oral and colonic sites seeded *S. sanguinis* bacteraemia with roughly equal frequency.¹² By disrupting intestinal mucosa, gastrointestinal neoplasms facilitate translocation of bacteria into the blood. Although the source of this patient's bacteraemia was confounded by the presence of his bovine valve, the combination of new anaemia, heme-positive stool and streptococcal bacteraemia supported further investigation for gastrointestinal pathology. In combination with other reported cases, our observations indicate internists should seriously consider underlying gastrointestinal neoplasm in any patient who develops viridans group streptococcal bacteraemia without clear aetiology.

USPSTF guidelines recommend against screening colonoscopy in patients over 85 years old due to risks of perforation and major bleeding.¹³ However, epidemiological studies indicate the incidence of colorectal cancer more than doubles from age 50–64 (120/100 000) to age 85 (290 per 100 000). Additionally, in patients who are symptomatic, colorectal cancer is identified in 3.7%–14.2% of cases.^{14 15} A recent meta-analysis comparing younger versus older cohorts argues colonoscopy is relatively well tolerated with comparable completion rates and adverse outcomes including perforation (1.0 events/1000 for patients over 65 vs 1.5 events for patients over 80) and major bleeding (6.3 events/1000 for patients over 65 vs 2.4 events for patients over 80).¹⁶ These data suggest that advanced age is not necessarily a contraindication for diagnostic endoscopy, especially in those who are symptomatic with a high pretest probability of gastrointestinal pathology. In our case, endoscopy identified and removed a high-grade dysplastic lesion that may have developed into an invasive adenocarcinoma within the patient's natural lifespan. Based on this presentation and similar cases in

Figure 1 Polyps from first colonoscopy. Left: sessile 10 mm polyp in the ascending colon; Right: pedunculated 14 mm polyp in the sigmoid colon.

Learning points

- The source of viridans group streptococcus bacteraemia is difficult to identify and requires thorough diagnostic investigation.
- *Streptococcus sanguinis* bacteraemia can be traced to colonic mucosal disruption with the same frequency as oral sources.
- *S. sanguinis* bacteraemia in the setting of new anaemia provides strong indication for colonoscopy to check for underlying malignancy.
- Diagnostic colonoscopy provides an opportunity to prevent invasive malignancy that may outweigh bleeding and perforation risks in elderly patients.

the literature, *S. sanguinis* bacteraemia of unclear origin should prompt an individualised risk assessment and treatment plan that may include endoscopic workup to detect occult neoplasms and provide definitive therapy.

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REFERENCES

- 1 McCoy WC, Mason JM. Enterococcal endocarditis associated with carcinoma of the sigmoid; report of a case. *J Med Assoc State Ala* 1951;21:162–6.
- 2 Boleij A, van Gelder MM, Swinkels DW, et al. Clinical Importance of Streptococcus gallolyticus infection among colorectal cancer patients: systematic review and meta-analysis. *Clin Infect Dis* 2011;53:870–8.
- 3 Abdulmir AS, Hafidh RR, Abu Bakar F. The association of Streptococcus bovis/gallolyticus with colorectal tumors: the nature and the underlying mechanisms of its etiological role. *J Exp Clin Cancer Res* 2011;30:11.
- 4 Mulita A, Ajayi T. Streptococcus viridians bacteraemia and colonic adenocarcinoma. *BMJ Case Rep* 2014;2014:bcr2014203695.
- 5 Nijjer S, Dubrey SW. Streptococcus sanguis endocarditis associated with colonic carcinoma. *BMJ Case Rep* 2010;2010.
- 6 Marinella MA. Streptococcus sanguis bacteremia associated with cecal carcinoma: case report and review of the literature. *Am J Gastroenterol* 1997;92:1541–2.
- 7 Macaluso A, Simmang C, Anthony T. Streptococcus sanguis Bacteremia and Colorectal Cancer. A case report. *Med Pediatr Oncol* 1995;24:67–8.
- 8 Fass R, Alim A, Kaunitz JD. Adenocarcinoma of the colon presenting as Streptococcus sanguis bacteremia. *Am J Gastroenterol* 1995;90:1343–5.
- 9 Kampe CE, Vovan T, Alim A, et al. Streptococcus sanguis bacteremia and colorectal cancer: A case report. *Med Pediatr Oncol* 1995;24:67–8.
- 10 Siegart CE, Overbosch D. Adenocarcinoma of the colon presenting as Streptococcus sanguis bacteremia. *Am J Gastroenterol* 1995;90:1528–9.
- 11 Chen FL, Jean SS, Ou TY, et al. Streptococcus sanguis bacteremia complicating endocarditis associated with colonic adenocarcinoma. *J Microbiol Immunol Infect* 2017;50:399–400.
- 12 Awada A, van der Auwera P, Meunier F, et al. Streptococcal and enterococcal bacteremia in patients with cancer. *Clinical Infectious Diseases* 1992;15:33–48.
- 13 Bibbins-Domingo K, et al; Screening for colorectal cancer: us preventive services task force recommendation statement. *JAMA* 2016;315:2564–75.
- 14 Lin OS. Performing colonoscopy in elderly and very elderly patients: Risks, costs and benefits. *World J Gastrointest Endosc* 2014;6:220–6.
- 15 Loffeld RJLF, Liberov B, Dekkers PEP. Yearly diagnostic yield of colonoscopy in patients age 80 years or older, with a special interest in colorectal cancer. *Geriatr Gerontol Int* 2012;12:298–303.
- 16 Day LW, Kwon A, Inadomi JM, et al. Adverse events in older patients undergoing colonoscopy: a systematic review and meta-analysis. *Gastrointest Endosc* 2011;74:885–96.

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