CASE REPORT

Streptococcus gallolyticus: a single bacteria, two different conditionsCristiano Silva Cruz,¹ Catarina Machado,^{1,2} André Almeida,¹ Rita Barata Moura¹¹Department of Internal Medicine, Centro Hospitalar de Lisboa Central, EPE—Hospital de Santa Marta, Lisbon, Portugal²Department of Internal Medicine, Hospital de Santo Espírito da Ilha Terceira, Angra do Heroísmo, Portugal**Correspondence to**
Dr Catarina Machado,
machado.cat@gmail.com

Accepted 8 June 2015

SUMMARY

The authors describe the case of a 48-year-old woman presenting with fever, joint pain and migratory skin lesions. She had no other symptoms or medical history. After an extensive and inconclusive work up, she was admitted to the hospital for further study. This patient was ultimately found to have *Streptococcus gallolyticus* subsp *gallolyticus* bacteraemia. This finding led to the diagnosis of mitral valve infective endocarditis related to an underlying rectum adenocarcinoma. This article points out diagnostic difficulties related to an unusual presentation of the underlying disease. Furthermore, the authors reinforce the need of keeping a high level of suspicion and a systematic approach in every case of fever of unknown origin. This case highlights the importance of performing a colonoscopy in the event of *S. gallolyticus* subsp *gallolyticus* bacteraemia, as it may provide an opportunity for detecting colonic lesions at an earlier stage.

BACKGROUND

The human gastrointestinal tract is colonised by different commensal bacterial species. Among these, *Streptococcus bovis* is emphasised by its prevalence (2.5–15% of the population)¹ and its well-known correlation with bacteraemia, infective endocarditis, colonic malignancies and other benign gastrointestinal lesions.^{2–4}

All the taxonomy related to group D streptococci, particularly to *S. bovis*, has been reviewed over the last two decades. Despite this fact, many studies did not distinguish between the different biotypes, bringing some variability and inconsistency to the current literature.

S. bovis biotype I, recently renamed *S. gallolyticus* subsp *gallolyticus*, has particular interest due to the previously mentioned associations, making colonoscopic evaluation of the gastrointestinal tract mandatory for patients infected by this organism.⁵ Infection caused by other biotypes or subspecies seems to be associated with colonic conditions as well. Furthermore, these bacteria also seem to be linked to biliary tract disease and infections in infants and neonates.^{6–8}

CASE PRESENTATION

A 48-year-old woman presented with a 7-week long history of fever (38°C), headache, and right ankle and left hand metacarpophalangeal joint pain. Moreover, she reported migratory tender erythematous nodular and maculopapular skin lesions. On examination, she was tachycardic and presented two nodular skin lesions on her left leg. Besides

being a current smoker, she had no other relevant history of medical conditions or regular drug habits.

INVESTIGATIONS

This patient had several previous observations in the emergency department and general practitioner, where a thorough investigation was pursued. Blood and urine tests, viral serologies, chest X-ray, CT scan and abdominal and pelvic ultrasound were all unremarkable, except for an elevated C reactive protein (CRP; 51 mg/L) and erythrocyte sedimentation rate (ESR; 41 mm/h). Repeated blood work up requested in our outpatient clinic revealed rising levels of CRP and ESR, positive rheumatoid factor (RF; 48.3 UI/mL) and positive IgM antibodies for *Borrelia burgdorferi*.

After antibiotic treatment with doxycycline 100 mg two times per day was started, erythema appeared in the neckline, face and arms, and the patient had no resolution of fever or of the other symptoms for over 5 days. She was then admitted to our medical ward, where doxycycline was interrupted and blood cultures were obtained. Her RF rose to 273 UI/mL and *B. burgdorferi* IgM and IgG were negative on reassessment. Two separate blood cultures were positive for *S. gallolyticus* subsp *gallolyticus*. The presence of mitral vegetations was suggested by transthoracic echocardiogram, and confirmed by transoesophageal echocardiogram, comprising a very mobile one (14×5 mm) on the anterior leaflet, and another on the posterior leaflet (6×4 mm; figure 1, video 1).

A colonoscopy was later performed, revealing a polypoid lesion on the rectosigmoid transition, occupying 50% of the intestinal lumen (figure 2). Histology documented a villous adenoma with areas of well-differentiated adenocarcinoma.

For tumour staging purposes, a CT of the thorax, abdomen and pelvis, a pelvic MRI and a rectal endoscopy, were carried out, ultimately classifying the rectum adenocarcinoma as T3N+M0.

DIFFERENTIAL DIAGNOSIS

Lyme disease was the original diagnostic hypothesis in this patient, as she was living in an endemic area, and manifested symptoms and skin lesions compatible with early disseminated disease. As IgM antibody for *B. burgdorferi* was positive, doxycycline was begun, but suspicion about this diagnosis mounted as there was failure to improve on treatment. Serology was therefore repeated, and turned out to be negative for IgM as well as IgG antibodies.

CrossMark

To cite: Silva Cruz C, Machado C, Almeida A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-208998

Figure 1 Vegetations of the anterior and posterior leaflet of the mitral valve.

Given the fever of unknown origin, two sets of blood cultures were obtained during the initial course of the investigation. As *S. gallolyticus* subsp *gallolyticus* was isolated on these samples, a transthoracic echocardiogram was anticipated in order to assess endocardiac involvement, which was indeed encountered.

The presence of a colonic neoplasm should always be investigated when *S. gallolyticus* subsp *gallolyticus* bacteraemia is identified. Even considering this patient was 48 years old with no gastrointestinal symptoms, a colonoscopy was planned immediately after the results of the blood cultures were available, and the examination was carried out in the last week of antibiotic treatment.

Chronic liver disease, a condition that might be associated with *S. gallolyticus* subsp *gallolyticus* bacteraemia, was ruled out, as liver function tests were unremarkable.

TREATMENT

According to antibiotic sensitivity test (penicillin minimum inhibitory concentration of 0.094 µg/mL), treatment with

Video 1 Vegetations of the anterior and posterior leaflet of the mitral valve.

ceftriaxone and gentamicin was started, and maintained for 6–2 weeks, respectively.

Afebrile, resolution of all symptoms and inflammatory marker (CRP, ESR) decrease occurred within the first 48 h of treatment. Blood cultures were repeated twice during the final stage of treatment, with negative results. No significant changes of vegetation size or features were seen on repeated transoesophageal and transthoracic echocardiograms but an asymptomatic small-to-moderate mitral valve insufficiency was documented.

Consultation by cardiac surgery excluded indication for surgical treatment at this point.

After presentation, the patient's care was transferred to the multidisciplinary colon and rectal cancer team, which then established a treatment plan.

OUTCOME AND FOLLOW-UP

After completion of the antibiotic course, the patient was discharged with scheduled follow-up appointments of internal medicine, cardiac surgery, colorectal surgery and oncology.

Two weeks after discharge, the patient developed flu-like symptoms, fever (38–38.5°C) and productive cough. She maintained fever for over 72 h and three large nodular skin lesions, similar to those previously documented, appeared on the extensor surface of the right forearm. These were very swollen and tender, producing pain along the whole upper limb during movement. She also presented with several small red and violaceous, tender warm nodules, some of which had a suppurative centre, on the terminal phalanges of fingers and toes. They were considered to be Osler nodes (figures 3 and 4).

The patient was admitted again for surveillance and investigation at our medical ward. No antibiotic treatment was initiated. Blood cultures were collected at two different times with negative results. Transthoracic echocardiogram revealed reduction of the width, without length change, of the vegetations.

The patient's condition improved, fever resolved after the first 24 h and the skin lesions rapidly decreased in size, became painless and resolved in a few days. She was discharged with the advice to maintain surveillance at home.

To date, no other similar episodes have occurred. The patient is currently undergoing chemotherapy and radiotherapy with good tolerance and will later be planned for rectal surgery.

DISCUSSION

More than half of all cases of native valve infective endocarditis in patients without known-specific risk factors are caused by

Figure 2 Colonoscopy image showing a polypoid vegetating mass of the rectosigmoid transition.

Figure 3 Osler nodes on the second finger of the right hand.

Staphylococcus and *Streptococcus* spp, with the mitral being the most frequently affected valve (alone or in association with aortic valve infection).^{9 10} An age of over 50 years, an insidious presentation and larger vegetations are aspects that usually hint towards the latter species.¹¹ *S. gallolyticus* subsp *gallolyticus* is the second greatest cause of endocarditis from *Streptococcus* spp, being responsible for 5–25% of all patients with bacterial endocarditis.^{12 13} The mortality rate of infection due to this pathogen is estimated to be 2–4%. This condition has been linked mainly to lower gastrointestinal pathology aforementioned,^{2–4} but some authors suggest that presence of an upper gastrointestinal tract malignancy must also be considered.

The association between *S. bovis* endocarditis and gastrointestinal disease has been often well documented in the literature since its first description in 1951.^{14–16} The real incidence of colorectal malignancy with *S. gallolyticus* subsp *gallolyticus* (or former *S. bovis*) endocarditis or bacteraemia is difficult to estimate as figures vary between 6% and 80%.^{2 5 17}

Faecal carriage of *S. gallolyticus* subsp *gallolyticus* is common and in healthy colons it ranges between 2.3% and 13.0%. Significant differences in the rate of colonisation between these and patients with colorectal malignancies are yet to be proved.^{16 18 19} It is not clear whether the presence of the bacteria was the cause or merely an incidental finding in patients with colorectal cancer.²⁰

Figure 4 Osler nodes on the first and second toe of the left foot.

This case report shows that correct identification of a fever's origin and source of infection is not always straight-forward. Isolation of *Streptococcus* spp is essential considering its associated pathologies. The data also demonstrate the importance of colonoscopic exploration when *S. gallolyticus* subsp *gallolyticus* endocarditis is diagnosed. Some authors reported the emergence of tumours years after an episode of endocarditis.²¹ Therefore, patients with normal colonoscopy should still be considered a group at risk for developing colonic cancer and repeated colonoscopies are advised.²²

Physicians' daily practice is frequently filled with intricate clinical pictures and diagnosis of more than one disease is common. When the complex interaction between two pathologies carries a high rate of morbidity and mortality, a multidisciplinary and a personalised treatment approach should be the rule.

Learning points

- ▶ Diagnosing an infective endocarditis is not always straightforward; a high level of suspicion and a systematic approach are essential.
- ▶ *Streptococcus gallolyticus* subsp *gallolyticus* bacteraemia may provide an early opportunity for screening patients and detecting colonic lesions at a premalignant stage; colonoscopic exploration must be carried out.
- ▶ Further report of cases and case series is desirable to step up the management of these conditions, and improve their final outcome.

Contributors All the authors were attending physicians involved in the management of the patient and read and approved the final manuscript and RBM was additionally involved in the outpatient assessment and follow-up. CSC, CM and AA were involved in the drafting of the manuscript and RBM revised it critically for design and important intellectual content.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hooper LV, Gordon JI. Commensal host-bacterial relationships in the gut. *Science* 2011;292:1115–18.
- 2 Sharara AI, Abou Hamdam T, Malli A, et al. Association of *Streptococcus bovis* endocarditis and advanced colorectal neoplasia: case-control study. *J Dig Dis* 2013;14:382–7.
- 3 Gonzalez-Quintela A, Martinez-Rey C, Castroagudin JF, et al. Prevalence of liver disease in patients with *Streptococcus bovis* bacteraemia. *J Infect* 2011;42:116–19.
- 4 Reynolds JG, Silva E, McCormack WM. Association of *Streptococcus bovis* bacteremia with bowel disease. *J Clin Microbiol* 1983;17:696–7.
- 5 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.
- 6 Corredoira JC, Alonso MP, Coira A, et al. Characteristics of *Streptococcus bovis* endocarditis and its differences with *Streptococcus viridans* endocarditis. *Eur J Clin Microbiol Infect Dis* 2008;27:285–91.
- 7 Corredoira JC, Alonso MP, Garcia JF, et al. Clinical characteristics and significance of *Streptococcus salivarius* bacteremia and *Streptococcus bovis* bacteremia: a prospective 16-year study. *Eur J Clin Microbiol Infect Dis* 2005;24:250–5.
- 8 Klatte JM, Claridge JE, Bratcher D, et al. A longitudinal case series description of meningitis due to *Streptococcus gallolyticus* subsp. *pasteurianus* in infants. *J Clin Microbiol* 2012;50:57–60.
- 9 Fowler VG Jr, Miro JM, Hoen B, et al. *Staphylococcus aureus* endocarditis: a consequence of medical progress. *JAMA* 2005;293:3012–21.

- 10 Murdoch DR, Corey GR, Hoen B, *et al.* Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Pro prospective Cohort Study. *Arch Intern Med* 2009;169:463–73.
- 11 Pergola V, Di Salvo G, Habib G, *et al.* Comparison of clinical and echocardiographic characteristics of *Streptococcus* bovis endocarditis with that caused by other pathogens. *Am J Cardiol* 2001;88:871–5.
- 12 Delahaye F, Goulet V, Lacassin F, *et al.* Characteristics of infective endocarditis in France in 1991. A 1-year survey. *Eur Heart J* 1995;16:394–401.
- 13 Hoen B, Alla F, Selton-Suty C, *et al.* Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA* 2002;288:75–81.
- 14 McCoy CW, Mason JM. Enterococcal endocarditis associated with carcinoma of the sigmoid; report of a case. *J Med Assoc Ala* 1951;21:162–6.
- 15 Hoppes WL, Lerner PI. Nonenterococcal group-D streptococcal endocarditis caused by *Streptococcus* bovis. *Ann Intern Med* 1974;81:588–93.
- 16 Klein RS, Recco RA, Catalano MT, *et al.* Association of *Streptococcus* bovis with carcinoma of the colon. *N Eng J Med* 1977;297:800–2.
- 17 Gupta A, Mandani R, Mukhtar H. *Streptococcus* bovis endocarditis, a silent sign for colonic tumour. *Colorectal Dis* 2010;12:164–71.
- 18 Burns CA, McCaughery R, Lauter CB. The association of *Streptococcus* bovis fecal carriage and colon neoplasia: possible relationship with polyps and their premalignant potential. *Am J Gastroenterol* 1985;80:42–6.
- 19 Potter MA, Cunliffe NA, Smith M, *et al.* A prospective controlled study of the association of *Streptococcus* bovis with colorectal carcinoma. *J Clin Pathol* 1998;51:473–4.
- 20 Boleij A, Muijtens CM, Bukhari SI, *et al.* Novel clues on the specific association of *Streptococcus* gallolyticus subsp gallolyticus with colorectal cancer. *J Infect Dis* 2011;203:1101–9.
- 21 Robbins N, Klein RS. Carcinoma of the colon 2 years after endocarditis due to *Streptococcus* bovis. *Am J Gastroenterol* 1983;78:162–3.
- 22 Beeching NJ, Christmas TI, Ellis-Pegler RB, *et al.* *Streptococcus* bovis bacteraemia requires rigorous exclusion of colonic neoplasia and endocarditis. *Q J Med* 1985;56:439–50.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow