Reminder of important clinical lesson

Getting to the heart of rectal bleeding: subacute bacterial endocarditis presenting as anaemia and a GI bleed

Whitney Cesari,¹ Christy Stewart,² Mukta Panda³¹Department of Medicine, University of Tennessee, Memphis, Chattanooga, Tennessee, United States;²Department of Medicine, University of Tennessee, Chattanooga, Hixson, Tennessee, United States;³Department of Medicine, University of Tennessee, Chattanooga, Chattanooga, Tennessee, United States**Correspondence to** Dr Christy Stewart, christy.stewart@erlanger.org**Summary**

In this case report, the authors demonstrate a case of subacute bacterial endocarditis presenting with anaemia. It is the first of its kind to describe a delay in diagnosis due to an initial patient investigation for a bleed rather than a cardiac evaluation. Astute clinicians need to be aware of the causes of anaemia in patients with endocarditis and consider that in *Streptococcus bovis* (*S bovis*) infection can be related to gastrointestinal polyps or malignancy resulting in bleeding. Although patients with *S bovis* endocarditis should undergo full gastrointestinal investigation after endocarditis is diagnosed, it should not delay medical treatment. In this article, the authors discuss the consequences of failing to achieve timely recognition of endocarditis along with common systemic complications. The authors also outline current recommendations for surgical intervention as heart valve replacement surgery was warranted in the patient to prevent fatal outcome.

BACKGROUND

Subacute bacterial endocarditis (SBE) is characterised by the presence of a vegetation on a cardiac valve. The aetiology can be attributed to infection, malignancy, autoimmunity or hypercoagulability. Infectious endocarditis, the focus of this case, is caused by an inflammatory response to bacteria that result in deposition of fibrin, inflammatory cells and organisms on a heart valve.¹ Aortic and mitral valves are most commonly involved, the exception being intravenous drug misusers in whom the tricuspid valve is most commonly affected.¹ SBE is differentiated from acute bacterial endocarditis (BE) in that it typically causes mortality over a span of weeks versus days. SBE is clinically defined by the modified Duke's criteria.² Following these criteria is central to timely diagnosis—especially considering that SBE, as opposed to acute BE, typically presents with non-specific symptoms such as anorexia, weight loss, night sweats, anaemia and petechiae (figure 1). One study of 72 patients with SBE between 2005 and 2007 showed that 82% of patients presented with fever, 74% with anaemia, 33% with haematuria and 23% with leukocytosis.³ Classic lesions of endocarditis, such as Roth spots, splinter haemorrhages, Janeway lesions and Osler nodes are only found in 20–25% of cases.⁴ Some helpful patterns have been established to aid in the clinical recognition of SBE. For instance, 85% of documented cases of SBE occurred following a dental or other procedure.⁵ A murmur is present in 99% of people with SBE, a majority that should cause clinicians to seriously doubt a diagnosis of SBE if no murmur is present.⁵ After the initial weeks of presenting with constitutional symptoms, SBE progresses with complications such as septic emboli, heart failure and immune complex disease. These can present in a manner that may divert the clinical investigation, such as dyspnoea, glomerulonephritis and anaemia. Recognition is important given that SBE is fatal if left untreated, possibly causing death after 6 weeks.

This case focuses on recognising the common subtlety of the presentation of SBE. The possible cause of anaemia in SBE will be discussed, as well as special consideration of causes of anaemia in those with *S bovis* endocarditis. The importance of a full gastrointestinal (GI) investigation in patients with *S bovis* endocarditis will also be discussed. However, GI investigation should not occur before diagnosis of SBE, as any delay in diagnosis predisposes to complications such as congestive heart failure (CHF), stroke, splenic and kidney pathology. Surgery is supported as a preventive measure of complications of SBE.

CASE PRESENTATION

A 51-year-old healthy male was admitted to our hospital with 'trouble breathing' for 1 week. Approximately 2 months earlier, he presented to a local clinic with dyspnoea on exertion, progressive generalised weakness and fatigue. He was diagnosed with anaemia, haematuria and haemoccult positive stool and was referred to the emergency department. After detecting a haemoglobin 9.3 and haematocrit 27.5, the patient was diagnosed with iron deficiency anaemia and discharged on ferrous sulphate. He followed up for an outpatient GI investigation. Upper endoscopy and colonoscopy revealed mild gastritis, diverticulosis and a colonic polyp but no active bleeding. A polypectomy was performed and later determined to be a benign tubular adenoma. One week after these procedures, the patient returned to the emergency department. At this time, he had progressive dyspnoea when lying down, cough productive of whitish sputum, pedal oedema, one night of sweats, chills, diarrhoea, new onset back pain, fatigue, nasal congestion and occasional palpitations.

Medical history was significant for a systolic murmur diagnosed 2 years earlier and diabetes mellitus type two diagnosed 5 months earlier. Surgical history was non-contributory. Family history was positive for a mother with

Figure 1 Evaluation of endocarditis according to Duke's Criteria. h/o=history of; IVDA, intravenous drug abuse; TTE, transthoracic echo; TEE, transesophageal echo; T, temperature.

mitral valve disease not otherwise specified, and chronic kidney disease secondary to hypertension. Father suffered two myocardial infarcts at ages 63 and 77. Patient's social history included 60 pack-years of smoking and no recent alcohol or drug use. He lived with his mother and cat; and worked as a self-employed financier. Medications included ferrous sulfate and metformin. He denied regular visits to a primary care physician.

On physical examination, he appeared stated age, non-obese, good hygiene, worried and uncomfortable. He was afebrile, tachycardic, tachypneic and hypertensive. Examination showed conjunctival pallor, moderate dentition, inspiratory wheeze, increased work on inspiration, bilateral pitting oedema, 3/6 holosystolic murmur best heard at apex and radiating to axilla, jugular venous distension.

INVESTIGATIONS

Laboratory studies on admission showed blood urea nitrogen of 41, creatinine of 1.8, glomerular filtration rate of 40, white blood cells of 5.6, haemoglobin of 6.9, haematocrit of 20.4, mean corpuscular volume of 74.7, lactate dehydrogenase of 308, brain natriuretic peptide of 943 and troponin within normal limits.

Chest radiograph indicated bilateral pleural effusion and echocardiogram showed low voltage QRS waves. Given the clinical picture, we immediately proceeded with a transthoracic echocardiogram which was suggestive of mitral vegetation. Additionally, diastolic dysfunction was diagnosed with preserved ventricular ejection fraction (55–60%), mildly elevated estimated pulmonary arterial pressure of 55 mm Hg and severely dilated left atrium with moderate to severe mitral insufficiency. Transesophageal

echocardiography confirmed vegetations on both leaflets of mitral valve, sized at 21×6 mm. Two days later blood cultures grew gram positive cocci in chains, later confirmed as *Streptococcus bovis* (*S bovis*).

DIFFERENTIAL DIAGNOSIS

Initial differential diagnosis for such a patient presentation should remain broad, including vasculitis, pulmonary embolism, autoimmune disease, malignancy, CHF, infectious endocarditis, haemorrhage and sepsis. A high clinical suspicion must be maintained for SBE in a person who presents with non-specific symptoms, such as shortness of breath, glomerulonephritis (GN), or anaemia.

TREATMENT

Empiric treatment with intravenous vancomycin was initiated and later changed to intravenous ceftriaxone based on antibiotic sensitivity. Intravenous antibiotics were maintained for 6 weeks.

The patient required 17 days of hospitalisation. Unfortunately, the patient's hospital course early on was complicated by formation of acute pulmonary oedema and immune complex GN requiring aggressive diuresis and supportive care. A week after admission, he underwent preoperative cardiac catheterisation showing no significant coronary artery disease. Worsening renal function warranted temporary haemodialysis less than 24 h postcatheterisation, requiring only 2 days of dialysis. The following day the mitral valve was replaced because of severe mitral insufficiency leading to acute heart failure, persistent bacteremia and septic embolism to the kidneys. The surgeon noted no annular abscess but extensive tissue growth on the valve requiring partial chordate tendon removal.

Regarding the renal findings, 2 weeks into admission outside lab work returned a high titre PR3-ANCA concerning for possible complicating pauci-immune GN. Renal biopsy, post valve replacement, later confirmed the previously assumed immune-complex GN.

OUTCOME AND FOLLOW-UP

The patient's post operative course was relatively uneventful. One week after discharge, he returned to the hospital with shortness of breath due to acute CHF. Pleural fluid removal via thoracentesis and medical management resulted in rapid improvement of the patient's general status and he was discharged home in 1 week.

He has been followed up in the resident clinic for the past 8 months and is clinically improving. Cardiology assessment with repeat echocardiogram showed no signs of worsening diastolic dysfunction, normal physiology with no signs of vegetation or valvular insufficiency. His renal function did not return to baseline. He has stage II chronic kidney disease with a creatinine of 1.3.

DISCUSSION

Anaemia in SBE

Anaemia is present in about 75% of patients with SBE.³ It is most often attributable to anaemia of chronic infection, splenic sequestration and valvular haemolysis. If an SBE patient is presenting with shortness of breath and anaemia, it is probable that the vegetative growth has reached a size significant enough to account for erythrocyte haemolysis and mitral regurgitation. Anaemia in SBE can also be attributed to the haematuria that occurs secondary to the immune-complex mediated glomerulonephritis caused by infectious endocarditis. However, anaemia in SBE is most commonly due to anaemia of chronic infection, evidenced by presence of normocytic normochromic red blood cells on peripheral smear.⁶

Anaemia in *S bovis* SBE

The underlying cause of anaemia in patients with endocarditis can be related to the infectious aetiology. The patient presented in this case suffered from SBE caused by *S bovis*, an agent that is responsible for 5–14% of cases of endocarditis.⁷ The patient had undergone a colonoscopy only 1 week before SBE was diagnosed. However, a polyp was detected and removed during the procedure, a polyp that may have harvested the infectious agent responsible for the patient's mitral valve vegetation. For decades there has been an established association between colon carcinoma and *S bovis* endocarditis.⁷ The very first case was documented in a 1951 case report that miscategorised *S bovis* as an enterococcal pathogen.⁸ On average, 40% of cases of colon carcinoma are associated with *S bovis*.⁹ This percentage of association has been debated since the 1970s. The number reported here reflects the association of *S bovis* with both carcinoma and premalignant adenomas of the colon. The streptococci are thought to achieve bacteremia by adhering to intestinal epithelium and producing vasodilatory cytokines to create capillary permeability.

Colonoscopy in *S bovis* SBE

S bovis can affect the GI track, the blood and the heart. If a patient has SBE due to *S bovis*, each of these systems

must be taken into account, especially when considering probable causes of anaemia. It has already been noted that anaemia of chronic infection is the most common cause of a low haematocrit in SBE patients. However, the patient presented in this case likely had GI blood loss contributing to his anaemia as well. He had haemoccult positive stool weeks before diagnosis of SBE. Studies suggest that this patient should undergo follow-up colonoscopies even years after the initial *S bovis* endocarditis. Ballet *et al* published a report of 53 cases of *S bovis* endocarditis in 1995 documenting that 81% of patients underwent a full colonic examination.¹⁰ Polyps were present in 20 patients and adenocarcinoma in seven. Of those patients which later died, four were due to malignant colonic tumours.¹⁰ The study concludes that the colonic lesions associated with *S bovis* endocarditis can be frequent and severe, warranting colonoscopy for each patient both during and long after the episode of *S bovis* endocarditis. This is important also because, as shown by Hoen *et al* in 1994, the risk of developing infective endocarditis increases as the histopathologic grade of the colonic lesion increases.¹¹

Surgical prevention of complications in SBE

The moment endocarditis is highly suspected, empiric treatment should begin until isolation of organism is achieved. Vancomycin is the drug of choice for empiric treatment of SBE as it covers the most common causative organisms, *Streptococcus viridans*, Enterococcus, and non-Enterococcal Group D Streptococcus.⁴ Gram negative organisms cause an estimated 5% of cases and empiric treatment is not recommended.⁴ Confirmed bacteremia is central to diagnosis, yet positive cultures can take up to 3 days to develop. Once an organism has been isolated, treatment should be specifically tailored.

Vegetations can locally extend or cause septic emboli leading to cor pulmonale, brain abscess and end organ damage commonly in the kidney, spleen and lung. It is difficult to predict who is most susceptible to embolus, but there is evidence to support increased likelihood of embolisation from a mitral vegetation on the anterior valve leaflet. Echocardiography as a predictor of probability of embolus formation has been explored but not yet proven.

The presence of complications increases the likelihood for surgical valve replacement. Surgery is needed in only 15–25% of cases but when complications, such as brain abscess occur, the need for replacement increases to 70%.⁵ New onset CHF is the leading complication of BE with a cumulative mortality as high as 51%.¹² A reduction in the 1-year mortality in cases with CHF is seen with early surgery, usually performed within a week.¹³ However, the decision for surgical therapy should be individualised. The American Heart Association recommends valve replacement in patients with continuous positive blood cultures 1 week after the start of antibiotics, and consideration of surgery in those with valve dehiscence, perforation, rupture, fistula, or perivalvular abscess.¹²

In 1984 Pelletier *et al* showed that major complications of SBE can be prevented with early surgical intervention.¹² Twenty patients underwent surgical intervention for SBE, twelve of which remained in New York Heart Association (NYHA) functional class I and four of which remained in NYHA class II on follow-up 26 months postsurgery.¹² One late death occurred.

Learning points

- ▶ Anaemia is an early sign of SBE present in approximately 75% of all cases.
- ▶ *S bovis* endocarditis is strongly associated with colon polyps and malignancy.
- ▶ Colonoscopy is warranted in patients with *S bovis* endocarditis but it should not delay treatment.
- ▶ Surgical intervention and valve replacement is recommended in all cases with or at risk for septic embolus formation.
- ▶ Early valve replacement surgery improves survival in patients with CHF secondary to infectious endocarditis.

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