CASE REPORT

Enterobacter cloacae pericardial effusion in a frail elderly patient

H J Blundell, C A Mason

Department of Medicine for the Elderly, Addenbrooke's Hospital, Cambridge, UK

Correspondence to

Dr H J Blundell,
harriet.blundell@nhs.net

Accepted 29 January 2015

SUMMARY

We report a case of a frail 82-year-old man with seronegative rheumatoid arthritis and a recent pacemaker insertion, admitted with pulmonary oedema and a symptomatic pericardial effusion. He was treated with diuretics and an urgent pericardiocentesis, a sample from which cultured *Enterobacter cloacae*. A subsequent abdominal CT scan revealed faecal loading, an abnormal anorectal canal and sigmoid colon and a bowel perforation. Endoscopy, biopsies and histopathology confirmed a diagnosis of cytomegalovirus (CMV) colitis with coexistent fungal infection. The *E. cloacae* infection was successfully treated with 6 weeks of intravenous meropenem, while the CMV and fungal infections were treated with a combination of valganciclovir and fluconazole. We postulate that the bowel perforation resulted from a combination of CMV colitis, faecal loading and steroid therapy and led to bacterial translocation of *E. cloacae* and the development of the pericardial effusion. This case represents an unusual pathophysiology for the development of an *E. cloacae* pericardial effusion.

BACKGROUND

Enterobacter cloacae is an opportunistic, facultatively anaerobic Gram-negative bacterium¹ of increasing clinical significance^{2 3} accounting for up to 5% of hospital-acquired sepsis.³ Its genus *Enterobacter* spp, is recognised by Public Health England (PHE) and Centers for Disease Control and Prevention (CDC) as an emerging global health concern,^{4 5} with evolving resistance to carbapenems over the last decade.⁶

E. cloacae is widely distributed in the environment. It exists on human skin and gastrointestinal flora and also in water, soil, sewage, meat and hospital environments.²

Although outbreaks have been associated with a single exogenous source for example, contaminated intravenous fluids, stethoscopes and intra-arterial monitoring devices, studies suggest that most infections arise from hospitalised patients' endogenous gastrointestinal flora.^{2 7}

As was the case for our patient, the 'sine qua non' for the development of bacteraemia secondary to *Enterobacter* spp is severe underlying disease.² Patients who have recently received broad-spectrum antibiotics, cephalosporins in particular, may be particularly susceptible as is any patient with a condition compromising systemic immunity or with a breach of a natural barrier, for example, the gastrointestinal tract. Recent invasive procedures and/or the placement of devices have been implicated as they disrupt the integument favouring the organism's access to the vasculature.² *E. cloacae*'s ability to adhere to and invade eukaryotic cells and to

chelate iron in the host blood stream is key to its ability to manifest a wide variety of extraintestinal clinical manifestations.⁷

E. cloacae have been identified as a causative organism in lower respiratory tract infections, urinary tract infections, intra-abdominal infections, endocarditis, septic arthritis, osteomyelitis, skin and soft tissue infections.²

With evolving *Enterobacter* spp resistance to the World Health Organisation (WHO) defined 'essential antimicrobial' class of carbapenems,⁴⁻⁶ it is increasingly important that clinicians are aware of possible *Enterobacter* spp presentations to enable appropriate management.

CASE PRESENTATION

An 82-year-old Caucasian man presented with a 1-week history of increasing dyspnoea and bipedal oedema on a background of several months of general malaise. He had a past medical history of seronegative rheumatoid arthritis, severe aortic stenosis and sinus nodal disease for which a permanent pacemaker was inserted 4 months previously. He had a low anterior resection for Duke's B adenocarcinoma over 30 years ago. He also had a history of recurrent urinary tract infections for which he was on prophylactic antibiotics for over 20 years.

His admission medications included dabigatran, simvastatin, co-amlofruse, folic acid and ferrous sulfate. He had been receiving low-dose prednisolone for his arthritis but this had been stopped 1 week prior to admission having been on these with good effect for the previous 4 years. He was a retired mechanical engineer who lived with his wife. He had no significant family, travel or sexual history. Prior to admission he was mobilising independently, with no carers.

On clinical examination, he was haemodynamically stable and afebrile. He had marked pallor but was comfortable at rest with no signs of respiratory distress. He had no stigmata of infective endocarditis. On palpation, he had a slow rising regular pulse and his jugular venous pressure was raised at 6 cm. On auscultation he had an ejection systolic murmur and bilateral basal crepitations in his lung fields. His abdomen was soft and non-tender, with no masses or organomegaly and normal bowel sounds. He had bilateral pitting pedal oedema. A digital rectal examination revealed a 3 cm ulcer at the anterior anal verge with dark impacted faeces.

INVESTIGATIONS

His admission blood results demonstrated microcytic anaemia (haemoglobin 100 g/L, mean cell

CrossMark

To cite: Blundell HJ, Mason CA. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-207025

Figure 1 CT pulmonary angiogram demonstrating a 3 cm pericardial effusion, bilateral pleural effusions and artefact from a ventricular dual chamber pacemaker lead.

volume 70.5 fL), mild thrombocytopenia (platelets $132 \times 10^9/L$) and lymphopenia (lymphocytes $0.56 \times 10^9/L$). C reactive protein was slightly raised at 34 mg/L. Overall white cell count, neutrophil count, renal and hepatic function tests were all within normal limits.

His chest X-ray revealed bilateral airspace shadowing consistent with pulmonary oedema or infection. An admission diagnosis of community-acquired pneumonia and congestive cardiac failure was made.

Despite initial treatment with co-amoxiclav, the patient's condition deteriorated with increasing dyspnoea and hypotensive episodes. An urgent transthoracic echocardiogram revealed a large pericardial effusion with Doppler evidence of haemodynamic compromise. An urgent CT pulmonary angiogram showed bilateral pleural effusions and confirmed a 3 cm pericardial effusion (figure 1).

Urgent pericardiocentesis was performed and provided good symptomatic relief. Cloudy blood stained fluid was aspirated and subsequently cultured a heavy growth of *E. cloacae* (table 1). The patient was placed on intravenous meropenem and gentamicin.

Blood cultures were taken prior to the pericardiocentesis and showed no growth after 5 days of incubation, they were

however taken at a time when our patient was already receiving antibiotics for suspected community acquired pneumonia. Blood cultures were unfortunately not taken prior to the initiation of antibiotic therapy and no further blood cultures were taken during our patient's admission.

To investigate the iron deficiency anaemia and the gastrointestinal tract, the patient then underwent a CT abdomen and pelvis. This demonstrated a significant pneumoperitoneum, dilation of small bowel loops and significant faecal loading of the large bowel loops. Radiologically, this suggested a stercoral perforation. Owing to frailty, it was felt he would not tolerate surgery and so he was managed conservatively with the advice of the colorectal surgical team. He remained frail and unwell but seemed to respond to antibiotics and supportive care.

An interval CT scan, 2 weeks later, showed improvement in the pericardial effusion (17 mm) and pneumoperitoneum, but now demonstrated rectal and sigmoid thickening, a left ischioanal fossa collection and splenomegaly. A flexible sigmoidoscopy was performed that demonstrated an ulcerated lesion in the rectum and also, sigmoid colitis, both of which were biopsied (figure 2). CT positron emission tomography (PET) scan showed high tracer uptake in the anus, extending to the rectum (figure 3).

The endoscopic and radiological evidence at this stage was highly suspicious for malignancy.

Histology from both areas, however, revealed active chronic ulceration with deep-seated granulomatous inflammation and fungi, together with features suggesting an on-going cytomegalovirus (CMV) colitis (figure 4).

Serum CMV IgG was >180 iu/mL (antibody detected) and IgM 137 au/mL (0–18 au/mL) consistent with CMV infection. CMV serology from a different hospital admission 8 months previously revealed CMV IgG of 70 iu/mL (antibody detected) and CMV IgM <18.0 au/mL suggesting that the current infection was a reactivation of latent CMV infection. CMV PCR was conducted twice on blood and was negative, however an immunohistochemical stain for CMV on the biopsy samples was positive. To our knowledge, CMV PCR was not conducted on the biopsy samples. Consent for HIV testing was obtained and was negative.

Collections of fungi were seen microscopically in the deep aspect of the biopsy, some were also present within the lymphovascular spaces. A periodic acid-Schiff stain confirmed fungal elements and our infectious disease service recommended treatment with fluconazole.

Table 1 Biochemistry, microbiology and cytology results from aspirated pericardial fluid

Pericardial fluid sample	Results
Biochemistry	Protein 39 g/L
Cytology	This sample consists of a few lymphocytes and macrophages, in a background of red blood cells. No malignant cells identified
Microbiology	Epithelial cells—none seen Gram film—Gram-negative bacilli seen Macroscopic appearance—blood stained Pus cells + Red cells ++ Enriched aerobic culture— <i>Enterobacter cloacae</i> , heavy growth Enriched anaerobic culture—No growth after two days of incubation

Figure 2 Flexible sigmoidoscopy of the upper rectum which is oedematous with linear ulcerations.

Figure 3 CT positron emission tomography demonstrating increased tracer uptake in anus, extending to the rectum. An attenuation corrected fluorodeoxyglucose study from midbrain to upper thigh.

We postulate that our frail elderly patient suffered a bowel perforation from a combination of CMV colitis and faecal loading that allowed *E. cloacae* to enter the bloodstream and spread haematogenously to the pericardium where it led to the patient's presentation with a pericardial effusion and cardiac compromise.

DIFFERENTIAL DIAGNOSIS

The patient presented with atypical pulmonary oedema in the setting of a haemodynamically significant pericardial effusion and a recent development of iron deficiency anaemia.

The initial differential diagnosis included decompensated aortic valve disease; ischaemic left ventricular failure and superimposed community-acquired pneumonia. The pericardial aspiration led to the primary diagnosis of an *Enterobacter* pericardial effusion.

Figure 4 A biopsy taken from the ulcer at the anterior anal verge, demonstrating a cytomegalovirus inclusion beside a vessel, with background inflammatory changes. H&E staining, $\times 40$ microscopy.

The nature of the organism and the iron deficiency anaemia led to a focus on the gastrointestinal tract and colon that subsequently demonstrated the bowel perforation and faecal loading. When the faecal loading was treated and the sigmoidoscopy and CT PET were performed, the initial differential diagnosis was a recurrence or a new primary colorectal tumour. The subsequent biopsies provided the unexpected finding of CMV colitis.

The patient had long-standing leucopenia and had had frequent urinary tract infections throughout his life but had no specifically defined immunodeficiency state. He had inflammatory arthritis but was seronegative for rheumatoid arthritis. His only disease modifying treatment was low-dose oral prednisolone, stopped 1 week prior to admission. He had splenomegaly but the opinion from the Haematology and Infectious Disease services was that he was most likely immunocompromised as a consequence of being frail and elderly rather than due to a primary immunodeficiency disorder. The patient declined bone marrow examination.

The recent pacemaker insertion was considered as another potential source of invasive *Enterobacter* infection but in this case, it was felt to be more likely that the source of his infection was his own gastrointestinal tract.

TREATMENT

The patient was treated with 6 weeks of intravenous meropenem, 10 days of intravenous gentamicin, 6 weeks of valganciclovir and 10 days of oral fluconazole.

The surgical team deemed that he was too frail to tolerate any major surgical intervention. A minimally invasive defunctioning colostomy was offered but our patient declined.

OUTCOME AND FOLLOW-UP

After a protracted hospital stay complicated by severe deconditioning, reactive depression, hypoactive delirium, severe weight loss and marked physical and cognitive decline, the patient declined further invasive investigations and treatments. He was discharged home with an extensive care package with the expectation that further decline was likely and that end-of-life care may become appropriate at some stage.

Despite this, he is currently still alive and at home 3 months later. He has become somewhat more mobile and independent. He and his wife now manage without any care package. He continues to have faecal incontinence managed with pads and antidiarrhoeal agents. His cognitive impairment remains but has improved. He has returned to some light gardening. His appetite has improved and he has gained weight. He has not had any further hospital admissions to date. An outpatient biopsy in the colorectal clinic continued to show inflamed granulation tissue in the perianal region but now with negative immunohistochemical staining for CMV suggesting successful treatment of the CMV colitis.

DISCUSSION

This is an unusual case of an *E. cloacae* pericardial effusion as we postulate that it spread via haematogenous seeding from the gastrointestinal tract, as opposed to a previous case report of an *E. cloacae* and fungal pericardial effusion and empyema, which described local contiguous spread for example, spread from a retropharyngeal abscess via descending necrotising mediastinitis.⁸

For a pericardial effusion of suspected bacterial origin, the European Society of Cardiology (ESC) recommends a pericardiocentesis and aetiological search.⁹ If pericardiocentesis fails to relieve the effusion, the formation of a pericardial window is recommended.⁹ This was not necessary in our patient's case. The ESC provides no specific advice on duration of antibiotic therapy for pericardial effusions of bacterial origin.⁹

On the advice of our infectious diseases' service, he was treated initially with gentamicin and meropenem and then stepped down to meropenem alone after 10 days.

There is currently little consensus regarding the use of combination versus single agent antimicrobial therapy in the context of non-pseudomonas gram negative bacteraemia.¹⁰ Meta-analysis has shown that dual therapy does not reduce mortality,¹⁰ but research suggests that it may prevent the emergence

of antibiotic resistance.¹¹ This meta-analysis was inconclusive regarding the effect on antibiotic resistance.¹⁰

In the case of *Enterobacter* endocarditis, a close anatomical comparator to our patient's pericardial effusion, combination therapy has been traditionally used.¹² Emerging evidence in this relatively uncommon condition suggests that combination antimicrobial therapy is not synergistically beneficial.¹² It does not draw conclusions regarding the effects on antibiotic resistance.¹²

In terms of antibiotic stewardship, it is also important to highlight that our patient was on prophylactic antibiotics for urinary tract infections for over 20 years. It is plausible that this may have contributed to the selection of more resistant gut flora—such as *E. cloacae*, in our patient's case.

We hope therefore, that by reporting this case, we can raise awareness of this emerging nosocomial infection, the diagnosis and treatment of which highlights the challenges of antibiotic resistance currently faced by health organisations worldwide.

Acknowledgements The authors acknowledge Miss NS Fearnhead (Consultant Colorectal Surgeon—specialist consultation and acquisition of biopsies), Dr HK Cheow (Consultant Radiologist—provision of radiology images), Dr M O'Donovan (Consultant Histopathologist—provision of histopathology image and clinical reports), Dr Lim (Gastroenterology Registrar—provision of flexible sigmoidoscopy image and clinical reports).

Contributors Written patient consent was obtained by CAM.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Mims C, Dockrell H, Goering RV, et al. *Medical Microbiology*. 3rd edn. Edinburgh: Elsevier Mosby, 2004.
- 2 Sanders WE, Sanders CC. *Enterobacter* spp.: pathogens poised to flourish at the turn of the century. *Clin Microbiol Rev* 1997;10:220–41.
- 3 Hoffmann H, Roggenkamp A. Population genetics of the nomenclature *Enterobacter cloacae*. *Appl Environ Microbiol* 2003;69:5306–18.
- 4 NHS England. *Patient safety alert on addressing trends and outbreaks in carbapenemase producing Enterobacteriaceae*. <http://www.england.nhs.uk/wp-content/uploads/2014/03/psa-carbapenemase.pdf> (accessed 2 Jul 2014).
- 5 Centers for Disease Control and Prevention. *Technical information—Multi-Site Gram-Negative Bacilli Surveillance Initiative (MuGSI)*. http://www.cdc.gov/hai/eip/mugsi_techinfo.html#publications (accessed 2 Jul 2014).
- 6 Centers for Disease Control and Prevention. *Vital Signs: Carbapenem resistant Enterobacteriaceae, Morbidity and Mortality Weekly Report*. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6209a3.htm> (accessed 2 Jul 2014).
- 7 Keller R, Pedrosa MZ, Ritchmann R, et al. Occurrence of virulence-associated properties in *Enterobacter cloacae*. *Infect Immun* 1998;66:645–64.
- 8 Takao M, Ido K, Hamaguchi H, et al. Descending necrotizing mediastinitis secondary to retropharyngeal abscess. *Eur Respir J* 1994;7:1716–18.
- 9 Massimo I, Yehuda A. Management of pericardial effusion. *Eur Heart J* 2013;34:1186–97.
- 10 Safdar H, Hendelsman J, Maki DG. Does combination antimicrobial therapy reduce mortality in Gram-negative bacteraemia? A meta-analysis. *Lancet Infect Dis* 2004;4:519–27.
- 11 Milatovic D, Braveny I. Development of resistance during antibiotic therapy. *Eur J Clin Microbiol* 1987;6:234–44.
- 12 Moon J, Smith T, Sahud A, et al. An unusual etiology of infective endocarditis: *Enterobacter cloacae*. *J Infect Chemother* 2012;18:925–30.

Learning points

- *Enterobacter cloacae* has been implicated in the pathogenesis of a pericardial effusion, via haematogenous seeding from the gastrointestinal tract.
- *E. cloacae* and other species of *Enterobacter* have a wide variety of clinical presentations and should be considered as a potential causative organism in any patient with immunocompromise, recent cephalosporin use and prolonged hospitalisation.
- The increasing issue of antibiotic resistance in *E. cloacae* and many other pathogens highlights the increased need for proactive antibiotic stewardship in local, national and international policies and guidelines.

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