

Campylobacter fetus bacteraemia in a peritoneal dialysis patient

Bacteriemia a *Campylobacter fetus* num doente em diálise peritoneal

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■ ABSTRACT

Infection is one of the major causes of mortality and morbidity in dialysis patients. Dialysis patients appear to be predisposed to infection due to alterations in primary host defence, advanced age and the presence of comorbid conditions, malnutrition and invasive dialysis procedures. Bacteraemia is seldom a manifestation of infection in peritoneal dialysis patients and is usually secondary to catheter-associated peritonitis. *Campylobacter fetus*, unlike more common isolates of the same genus, is usually grown from blood samples, without accompanying enteritis, in patients with serious underlying conditions. The authors present a case of *Campylobacter fetus* bacteraemia in a peritoneal dialysis patient.

Key-words: Bacteraemia; *Campylobacter fetus*; infection; peritoneal dialysis.

■ RESUMO

A infecção é uma das maiores causas de mortalidade e morbilidade nos doentes em diálise. Os doentes em diálise têm maior susceptibilidade a infecções devido a alterações primárias da imunidade, idade avançada, presença de comorbilidades, desnutrição e procedimentos invasivos. A bacteriemia é raramente uma manifestação de infecção nos doentes em diálise peritoneal e é, na maior parte dos casos, secundária a peritonite relacionada com o catéter. O *Campylobacter fetus*, ao contrário de outras bactérias do mesmo género, é habitualmente isolado em hemoculturas, sem gastroenterite acompanhante, em doentes com múltiplas patologias de base. Os autores apresentam um caso de bacteriemia a *Campylobacter fetus* numa doente em diálise peritoneal.

Palavras-chave: Bacteriemia; *Campylobacter fetus*; diálise peritoneal; infecção.

■ CASE REPORT

A 62-year old woman, with chronic kidney disease stage 5d treated with peritoneal dialysis was admitted to our department with a 1-month history of malaise, anorexia and weight loss. The aetiology of her chronic kidney disease was lupus nephritis, which had been on remission for 15 years on low dose prednisone (5mg/day). She had undergone courses of cyclophosphamide plus prednisolone for 2 years and azathioprine plus prednisolone for 1 year at the time of diagnosis for a class IV/V lupus nephritis.

When she reached chronic kidney disease stage 5, and because peritoneal dialysis was her kidney replacement therapy of choice, a peritoneal dialysis catheter was placed surgically which was later replaced because of a persistent leak. Sixteen days after catheter replacement she presented with abdominal pain and cloudy effluent with a cell count of 800 leucocytes/ μ L. A *Corynebacterium striatum* was later grown from her peritoneal effluent. After 4 days of empiric intraperitoneal therapy with cefazolin and ceftazidime, she was started on intraperitoneal vancomycin. On the 10th day of antibiotic treatment she presented with a pruriginous skin rash, which was assumed to be an adverse allergic reaction to vancomycin. Although intraperitoneal vancomycin administration was stopped, therapeutic serum levels of the drug were maintained for at least 5 additional days and no more antibiotics were administered. On the third day after starting the empiric antibiotic treatment, she denied any abdominal pain and her peritoneal effluent was clear with 300cells/ μ L.

About a month after the completion of the vancomycin course she presented with liquid diarrhoea without blood or mucus. At this time the patient was afebrile. The workup for infectious diarrhoea, including screening for *Clostridium difficile* toxin and stool cultures, was negative. She underwent a colonoscopy that did not show any remarkable findings. During the procedure a colonic biopsy was obtained, which showed a non-specific inflammatory infiltrate. According to our unit protocol, she received prophylactic therapy with intravenous ampicillin, gentamicin and metronidazole prior to the colonoscopy. Her peritoneal effluent was clear and its culture negative. The clinical picture lasted for 2 weeks and was self-limited.

In the following 3 months she developed 2 repeat episodes of *Corynebacterium* spp. peritonitis

presenting the same way as the first one. After the initial 3 days of empiric intraperitoneal antibiotic (cefazolin and ceftazidime), she received 15 days, on the first repeat episode, and 21 days on the second, of oral linezolid, with rapid improvement of the symptoms and clearing of the effluent. The Tenckhoff catheter was not removed because of the rapid response to treatment and because there were no signs of exit-site or tunnel infection.

In the following month she developed progressively worsening malaise, anorexia and weight loss, for which she was admitted in our department. Apart from worsening of chronic low back pain, she did not report any other organ specific symptoms or signs. She denied fever, lower limb motor weakness and sensory changes, abdominal complaints, cloudy effluent, or respiratory symptoms. She lives in a rural area and has contact with poultry.

On physical examination, she was emaciated, afebrile, her blood pressure was 97/65mmHg, pulse rate 98ppm. Cardiopulmonary auscultation was without any remarkable findings. The abdomen was painless, without any palpable masses and her peritoneal effluent was clear, without pleocytosis. She did not report any pain on spinal percussion or palpation. She had no lower limb weakness. She had no palpable lymph nodes.

The patient had a worsening anaemia, without evident blood loss, with increasing need of erythropoiesis-stimulating agent (her haemoglobin was 9g/dL on admission). She also had increasing inflammatory markers (C-reactive protein [CRP] 22mg/dL and procalcitonin [PCT] 2.64ng/dL), as well as *de novo* hypoalbuminemia (2g/dL).

In order to unravel the diagnosis, a set of blood cultures was drawn and a magnetic resonance tomography of the spine was performed. The magnetic resonance tomography of the spine revealed osteoporotic vertebral fractures of the thoracic and lumbar spine without compression of the spinal cord or signs of spondylodiscitis. She also underwent a thoraco-abdominal computed tomography scan, which showed no abnormal findings. Finally, the 3 blood cultures drawn at admission grew *Campylobacter fetus*. The peritoneal effluent culture was negative. Afterwards, a trans-oesophageal echocardiogram showed no focalization of the *Campylobacter fetus* bacteraemia.

Accordingly, she was treated with a 4-week intravenous gentamicin course, with resolution of the symptoms, weight gain, improvement of the anaemia, reduction of the inflammatory markers (CRP 0.8mg/dL) and albumin 3.5g/dL. Otherwise well, she developed a vertiginous syndrome probably secondary to the aminoglycoside therapy. Since the transmission of *Campylobacter* occurs mainly through ingestion of contaminated food and through contact with contaminated animals, the importance of general hygiene measures, such as proper hand washing, was emphasized, as well as the proper handling and cooking of meat.

■ DISCUSSION

Infection is the second leading cause of mortality and morbidity in dialysis patients^{1,2}. Disorders of both innate and adaptive immune systems contribute to an increased susceptibility to infections in the course of chronic kidney disease². Uraemia is associated with alterations in primary host defence mechanisms and increases the risk of bacterial infections. Neutrophils exhibit impaired chemotaxis, oxidative metabolism, phagocytic activity, degranulation, intracellular killing, and dysregulated programmed cell death³. Additional factors contributing to immune dysfunction include malnutrition, trace element deficiencies, iron overload, impaired glucose metabolism, hyperparathyroidism, dialysis, and uraemic retention solutes. These immunologic abnormalities are complicated by the use of immunosuppressive drugs to treat and control underlying diseases, the dialysis procedure, and the disruption of cutaneous and mucosal barriers to infection³.

Bacteraemia is seldom a manifestation of infection in peritoneal dialysis patients. In an analysis of dialysis patients by Wang K. *et al*, bacteraemia in peritoneal dialysis patients was more frequently secondary to peritonitis (37.7%). In 14.5% of cases the bacteraemia had more than one source, in 11.6% it was due to urinary tract infection and 10% of cases had an unknown origin.⁴

Campylobacter is a genus of small gram-negative bacteria, common commensals in the gastrointestinal tract of animals, especially poultry, which is thought to be the principal source of human infection⁵.

The most important species to cause human disease are *Campylobacter jejuni* and *Campylobacter coli*, which usually cause acute enteritis. In contrast to the infection caused by these species, which are seldom complicated by bacteraemia or other extra-intestinal localization, *Campylobacter fetus* is usually isolated from blood samples, without accompanying enteritis or isolation in stools⁶. *Campylobacter fetus* bacteraemia is usually found in patients with serious underlying conditions, such as liver cirrhosis, malignancy, diabetes *mellitus*, HIV infection and therapy-induced immunosuppression^{7,8}. It is a microaerophilic, fastidious to grow microorganism which is thought to colonize the human intestine after oral ingestion⁵. These bacteria are highly serum resistant because of the presence of a surface layer that inhibits C3 binding. As observed with other gram-negative organisms that colonize mucosal surfaces, the property of serum resistance is highly associated with the ability to cause bacteraemia. Thus, colonization of the intestine, which is the ultimate reservoir for the organism in most infected humans, frequently leads to portal bacteraemia. In normal hosts, the reticuloendothelial system phagocytoses *C. fetus* and there is only transient or no systemic bacteraemia. In hosts who are immunocompromised or in whom the presence of a local focalization (for example, atherosclerotic aorta, gravidus uterus), transient bacteraemia can overcome portal circulation and lead to sustained bacteraemia and systemic consequences⁵. Besides its tropism for endovascular tissue it can also cause other forms of focal infection (osteomyelitis, cholecystitis, meningitis, soft tissue and joint infections)^{6,7}. It has also been reported as a rare cause of peritonitis in patients undergoing peritoneal dialysis with or without accompanying bacteraemia^{9,10,11,12}.

Systemic *Campylobacter fetus* infection requires prolonged parenteral antibiotic treatment⁶. In an epidemiologic study, all *Campylobacter* isolates were susceptible to ampicillin, gentamicin, meropenem and imipenem⁶. Although the optimal antimicrobial treatment has not been determined, these are the suggested antibiotics for parenteral treatment of systemic infection⁶. The optimal duration of antibiotic treatment is also not well-established. For sustained bacteraemia associated with acute gastroenteritis, a 10-day to 14-day course of antibiotics is probably sufficient. For bacteraemia without previous acute enteritis, particularly in immunocompromised patients

and in those with relapsing bacteraemia, therapy should probably be more prolonged (at least 3 weeks). Patients with endovascular infections require at least 4 weeks of therapy⁷. Since no gentamicin-resistant *Campylobacter fetus* strains have been reported, some experts advocate the use of a regimen including gentamicin to treat severe bacteraemia and endovascular infection¹³.

The mortality rate associated with *Campylobacter fetus* bacteraemia is difficult to ascertain, as the described series are small. One study described a mortality rate of 15% and the risk factors associated with this outcome were cancer, isolated fever without other clinical manifestations of infection and treatment with fluoroquinolones¹³.

We present the unexpected and rare case of a *Campylobacter fetus* bacteraemia, without evidence of focalization, in a peritoneal dialysis patient, with excellent response to the prescribed antibiotic treatment. Our patient has important baseline risk factors for infection with this particular agent. She has stage 5 chronic kidney disease secondary to an autoimmune disorder, for which she had in the past received immunosuppressive therapy. Moreover, she had recently undergone several prolonged antibiotic courses for 3 repeat episodes of *Corynebacterium* peritonitis. She also had exposure to poultry, which is a known source of *Campylobacter fetus*. Although it is unusual for *Campylobacter fetus* to cause a diarrhoeal disease, some cases have been reported⁶. While we cannot exclude that the diarrhoea episode of our patient was due to an undetected infection with this agent with subsequent bacteraemia, we think this scenario is unlikely since the diarrhoea was self-limited and occurred several weeks before the onset of the complaints. In contrast to the previously described cases of *Campylobacter fetus* infection in peritoneal dialysis patients, in our case there was no peritonitis associated with the bacteraemia. She also did not have any focalization of the infection, which has been reported in several cases^{6,7}.

Although our patient had no focalization of the *Campylobacter fetus* bacteraemia, she had indeed an acute severe wasting disease. Accordingly, she was treated with a 4-week course of gentamicin. She did not have any of the previously described risk factors for a worse outcome and her condition quickly improved. Nevertheless, the successful treatment of

the infection also led to an adverse debilitating effect – ototoxicity.

In summary, we present the case of an immunosuppressed patient under peritoneal dialysis affected by a rare microorganism causing a serious infectious complication.

Conflict of interest statement: None declared

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