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Case Report

Yersinia pseudotuberculosis bacteraemia in a kidney transplant patient

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Introduction

Despite attempts to establish a situation of tolerance to an allograft, at present, kidney transplantation is inevitably associated with the use of immunosuppressive drugs and, consequently, an increased risk of infection [1,2]. Here we present a patient with a kidney transplant who developed a bacteraemia with *Yersinia pseudotuberculosis* 5 years after transplantation, which is a rare complication of *Y.pseudotuberculosis* infection and has been reported only once before in the context of kidney transplantation.

Case

A 54-year-old man was admitted in 1999 because of fever (up to 39.7°C) and chills, which were present for 1 week. Three days prior to admission, erythromycin was added to his medication. Five years earlier, peritoneal dialysis was initiated because of renal failure due to focal segmental glomerulosclerosis, and a few months later he received a cadaveric kidney transplant. His immunosuppressive treatment consisted of cyclosporine and low dose prednisone (10 mg once daily) for 1 year; thereafter cyclosporine was converted to mycophenolate mofetil (MMF). For the next 3 years his immunosuppressive medication was unchanged while his kidney function was stable with a serum creatinine level of 235 mmol/l. On admission, apart from a systolic murmur (2/6), physical examination did not show any abnormalities.

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On laboratory examination, haemoglobin was 6.4 mmol/l, platelet count 253×10^9/l and leukocyte count 5.6×10^9/l. Serum urea was 17.2 mmol/l and creatinine 263 mmol/l. C-reactive protein level (CRP) was elevated (110 mg/l) and ESR was 37 mm/h. Blood glucose level was normal (5.9 mmol/l), serum iron 5 mmol/l, transferrin 1.9 g/l and ferritin 664 mmol/l.

An X-ray of the chest showed no signs of infection. An ultrasonography of the abdomen showed a normal kidney transplant and a normal liver, while the spleen was 11 cm and contained multiple small hypoechogenic lesions, <1 cm in diameter, suggestive of abscesses. A CAT scan of the abdomen confirmed multiple small hypodense lesions in the spleen, suggestive of the presence of abscesses, cysts or lymphomas (Figure 1). Sterile blood cultures, taken repeatedly on consecutive days, in combination with a normal transoesophagal echocardiography ruled out an endocarditis. All cultures of faeces, urine, sputum and bone marrow remained sterile, and no evidence of viral infection was found. An ultrasound-guided sample taken from a lesion in the spleen did not reveal malignancy or granulomas, but showed many

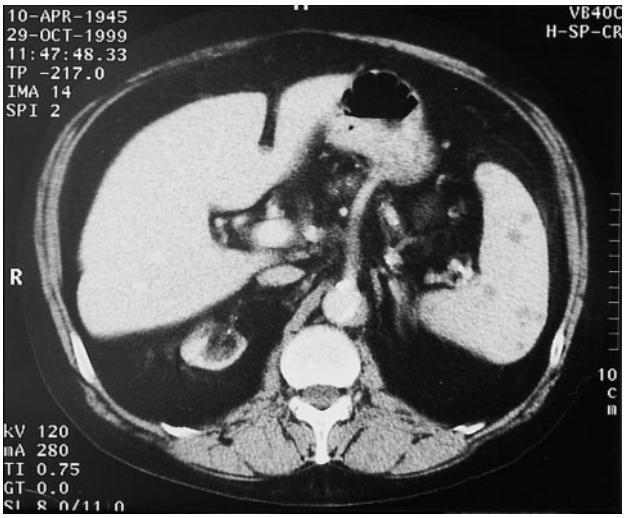

Fig. 1. CAT scan of the abdomen, showing multiple small lesions in the spleen.

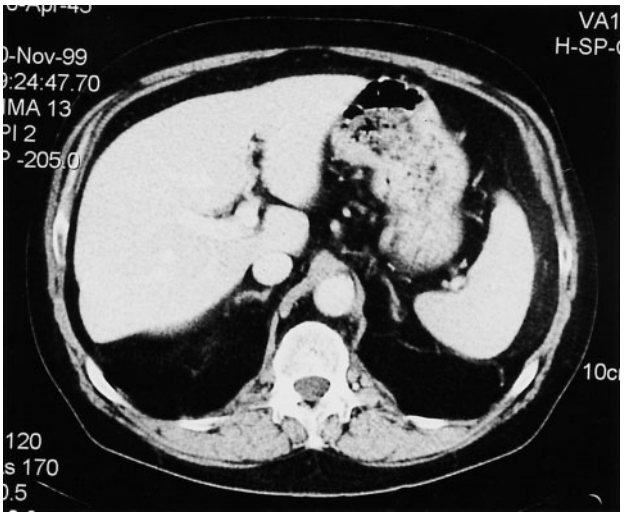

Fig. 2. CAT scan of the abdomen from the same patient, 1 month later. No more lesions are visible in the spleen.

segmented neutrophils, indicating an abscess. Cultures of this specimen for bacteria, mycobacteria and fungi remained sterile.

After a few episodes of spiking fever, with a maximum of 39.5°C, temperature normalized and CRP decreased. No antibiotic treatment was prescribed and immunosuppressive therapy was not reduced. A month later, a CAT scan of the abdomen showed a normal spleen, without focal lesions (Figure 2). The patient was discharged from the hospital, but remained under observation at the outpatients' clinic.

Two months later he was readmitted, presenting with severe lower back pain, chills and fever up to 39°C. He also complained of vomiting and diarrhea and had recently gone through a period of coughing. Physical examination again revealed no abnormalities, his temperature was 37.2°C and laboratory examination was similar to the previous admission. A third CAT scan of the abdomen again showed lesions in the spleen, which were smaller than at the previous admission. In addition, multiple small lesions in both lungs were seen on both an X-ray and a CAT scan of the chest. On a bone scintigraphy, no abnormalities were found; however, magnetic resonance imaging (MRI) of the lumbar spine, performed because of persisting lower back pain, showed an osteolytic lesion in the first lumbar vertebral body, strongly suggestive of malignancy. Because of spiking fever up to 39.5°C and suspicion of a disseminated bacterial infection, treatment with cefuroxime was started. Four blood cultures yielded *Y.pseudotuberculosis*. The minimal inhibitory concentration (MIC) of cefuroxime against the *Yersinia* strain was 0.25 mg/l, while the MIC of erythromycin, doxycycline, gentamicin and ciprofloxacin were 8, 0.50, 0.50 and 0.032 mg/l, respectively. Consequently, antibiotic treatment was changed to ciprofloxacin 500 mg b.d., orally.

During the next 2 weeks, the fever disappeared, CRP decreased (24 mg/l) and the lesions in the lung almost completely disappeared. However, on a second MRI of the lumbar spine, an increase of the osteolytic lesion was seen, complicated by a fracture of the upper substantia compacta. In order to rule out malignancy, a bone biopsy was taken that showed fibrosis and signs of inflammation. No malignant cells were found and cultures of the biopsy specimen (including culture for mycobacteria) remained sterile. Because of the severity of the infection it was decided to continue the ciprofloxacin treatment for a prolonged period. The patient was discharged from the hospital and the antibiotic treatment was continued for 4 months.

Two months after discharge, the osteolytic lesion in L1 remained stable and showed signs of sclerosis. Now, 2 years later, the patient is still well.

Discussion

Infection with *Y.pseudotuberculosis* is uncommon in humans. It is a zoonotic infection with reservoirs in rodents, birds and mammals. Transmission to humans occurs through ingestion of contaminated food or direct contact with an infected animal. Our patient, being a former pigeon fancier, reported to be still in contact with pigeons weekly. He may possibly have contracted *Yersinia* through his hobby. The infection commonly manifests as mesenteric lymphadenitis with fever, abdominal pain, and less often vomiting and diarrhea. This syndrome is most common in children and adolescents, and may be indistinguishable from acute appendicitis. Erythema nodosum and polyarthritis have also been described [3]. The bacteremic form of *Y.pseudotuberculosis* infection is rare. Until now 59 cases have been reported [4,5]. As a complication of bacteraemia, abscesses may occur in various organ systems (e.g. lungs, liver, meninges). In many cases bacteraemia is connected with an underlying disorder such as liver cirrhosis, haemochromatosis, hepatitis or diabetes [4–6]. Iron overload, which is known to be a predisposing factor in *Yersinia enterocolitica* infection, also seems to play a role in the development of *Y.pseudotuberculosis* bacteraemia considering the association with liver cirrhosis and haemochromatosis [7]. Iron overload, liver disease and diabetes were excluded in our patient.

To the best of our knowledge, only one patient with a kidney transplant has been reported to develop *Y.pseudotuberculosis* bacteraemia [4,8]. Apart from the immunosuppressive treatment, which had not been changed recently, no predisposing factors could be defined in our patient. In fact the overall amount of immunosuppressive treatment was on the low side in this patient. Prior to the development of this infection his cyclosporine treatment was changed into MMF. In the literature, the use of MMF has not been reported to be associated with an increased incidence of opportunistic infections as compared with other immunosuppressant drugs. As initially no causative microorganisms were found and the patient recovered

soon, no antibiotic treatment was prescribed. In retrospect, this spontaneous recovery seems to be remarkable. Considering the high MIC of erythromycin, it seems unlikely that the short antibiotic course before admission was effective. There is circumstantial evidence to suggest that the osteolytic lesion in L1 may have also been due to the *Y.pseudotuberculosis* infection, although osteomyelitis due to *Y.pseudotuberculosis* has not been described before. At the second admission our patient reported episodes of fever for at least 4 weeks, which suggest he went through a prolonged period of bacteraemia. Although it has never been described before in *Y.pseudotuberculosis* infection, it seems probable that the prolonged bacteraemia in our patient led to osteomyelitis, as can occur in other bacterial infections. It is true that cultures of the biopsy material remained sterile; however, the biopsy was taken 1 month after the ciprofloxacin treatment was started. In the bone lesion, no evidence was found for other causative microorganisms or malignancy while during follow-up, no signs of metastatic (bone) disease became manifest.

Yersinisa pseudotuberculosis is usually sensitive to ampicillin, tetracycline, chloramphenicol, cephalosporins, fluoroquinolones and aminoglycosides [9]. Although *Y.pseudotuberculosis* is susceptible to cephalosporines *in vitro*, experimental studies have shown that fluoroquinolones, gentamicin and doxycycline result in better killing *in vivo* [10]. In our patient, however, gentamicin was not an option because of the impaired renal function, and doxycycline, being a bacteriostatic drug, was considered a poor choice in this patient under immunosuppressive treatment. Despite antibiotic treatment, deaths still occur from septicaemia with *Y.pseudotuberculosis*. A mortality rate of 75% was reported despite antibiotic treatment [3]; however, in a review of 1995 mortality rate was considerably lower (18%) [4].

In this report we describe a kidney transplant patient who developed the bacteremic form of *Y.pseudotuberculosis* infection, which has been reported previously only once in a transplant recipient. In addition, there is circumstantial evidence that in this case *Y.pseudotuberculosis* bacteraemia was possibly complicated by osteomyelitis, a complication never described before.

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