Case Report

Sepsis from *Rhodococcus equi* successfully treated in a kidney transplant recipient

M. Barsotti, A. Cupisti, E. Morelli, M. Meola and G. Barsotti

Clinica Medica 1 Institute, University of Pisa, Italy

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**Introduction**

AIDS or organ transplant immunodepressed patients are susceptible to infectious diseases from weakly pathogenic bacteria. This is the case of infection from *Rhodococcus equi*, a Gram-positive aerobic bacterium with intracellular tropism that is usually present in stools of horses and in soil [1]. In veterinary medicine it is well known as a pathogen for several mammalians, including horses, cows, and others. Humans are rarely affected with the infection limited to immunodepressed patients [1].

*Rhodococcus equi* was first described in 1923 as *Corynebacterium equi* by Magnusson, who isolated it from the lungs of 10 foals with pneumonia. The first case of human disease from *R. equi* was reported in 1967 by Golub et al. who described cavitary pneumonia in a steroid-treated patient affected by plasma cell hepatitis [1].

Until 1983, only 12 cases of *R. equi* infection had been described in humans, eight of them receiving immunosuppressive therapy for haematological diseases and four for renal transplantation [2]. In 1986, Samies et al. described a case of *R. equi* infection in a patient with AIDS [3]. During the following years, these cases have been reported more frequently due to the increasing number of cases of AIDS and transplant patients. In the last review of the literature, Verville et al. reports 72 cases of infectious diseases from *R. equi* in humans [4]. More recently, Tang et al. described a *R. equi* peritonitis in two patients on continuous ambulatory peritoneal dialysis [5].

We report a successfully treated sepsis from *Rhodococcus equi* in an adult male patient on maintenance immunosuppression for renal transplantation. **Case report**

A 48-year-old male renal transplant recipient was admitted because of chest pain, dyspnea, cough and fever lasting 4 weeks.

Since 1969 he suffered from chronic renal failure due to congenital vesico-ureteral reflux. In 1990 haemodialysis treatment was started and in 1993 he received a cadaveric renal transplant. Six months later he presented with a rejection episode treated by prednisone pulse therapy. Subsequently, renal function was stable and serum creatinine ranged from 2.2 to 2.5 mg/dl. Chronic immunosuppression was achieved with prednisone (10 mg/day), cyclosporine A (175 mg/day) and azathioprine (75 mg/day).

One month before admission he presented with fever reaching 39.5°C in the late afternoon and decreasing during the night, with weakness, pain on the left side of the chest with submammary irradiation, and fasciculations. Broad spectrum antibiotic and analgesic drug therapy were unsuccessful, as well as paravertebral (D8–D9) injections of steroids and anaesthetic drugs. A thoracic radiograph revealed an opacity in the mid portion of the left lung.

At admission, we observed a seriously sick patient, complaining of dyspnea, weakness, chest pain on the left side, and unproductive cough. Physical examination revealed a 3 cm diameter subcutaneous nodule with warm, erythematous skin in the left interscapular-rachidean region. Breath sound reduction and rales were detected in the lower area of the left lung. Axillary temperature was 39°C.

Biochemistry showed serum creatinine 2.7 mg/dl, creatinine clearance 17.3 ml/min, cyclosporinemia 168 ng/ml, WBC count 4900 (neutrophils 90%), RBC 3.49 × 10⁶, haemoglobin 10.9 g/dl, HCT 33%, and platelets 246.000; sGOT 47 U/l, sGPT 29/U/l, and γ-GT 75 U/l. Serum glucose, bilirubin, total cholesterol, triglycerides, electrolytes, total protein, electrophoresis, and urine analysis were normal. HIV-Ab, HBV-Ag and HCV-Ab were negative.

Thoracic radiograph confirmed the opacity in the middle-lower portion of the left lung (Figure 1). A thin-needle biopsy of the nodule revealed that the...
We immediately started therapy with some broad-spectrum antibiotics (cefotaxime, clysatatine) and one against Gram-positive, penicillase producing bacteria (teicoplanine), as well as antimycotic and antitubercular agents which were without any effect. We then modified the immunosuppressive schedule by reducing cyclosporine A to 125 mg/day and increasing prednisone to 25 mg/day, while azathioprine was withdrawn.

Sepsis from \textit{R. equi} was diagnosed after repeated haemocultures. The identified micro-organism showed \textit{in vitro} sensitivity to ceftriaxone, imipenem, gentamicin, netilmicin, and penicillin. Since resistance to penicillin has been frequently described and ceftriaxone and imipenem were already used without effect, netilmicin 150 mg/day i.m. was started. The subcutaneous abscess was surgically drained.

During the following days, the fever disappeared and a remarkable improvement of the general condition occurred. After 2 weeks thoracic radiography and CT showed reduction of the dorsal swelling and of empyema and disappearance of the micronodular spreading. However, a pathological fracture of the back portion of the left VIII rib was seen. After 4 weeks netilmicin was replaced with ceftriaxone (1 g/day i.m.) and the patient was discharged without significant changes in renal graft function (serum creatinine 2.5 mg/dl).

Two months later the patient was again hospitalized for a relapse. At admission, fever, asthenia, and chest pain were present and the dorsal abscess had grown in size. Surgical draining was performed together with netilmicin treatment, followed by disappearance of the fever and other symptoms. The haemoculture confirmed a \textit{R. equi} sepsis. One month later, the CT showed a significant reduction of the empyema and complete ossification of the rib fracture (Figures 4 and 5). The patient was discharged, but the antibiotic therapy (ceftriaxone and imipenem) was continued for 5 months at home. Up to now, more than 1 year later, the patient is well and the graft function is stable on cyclosporine A (150 mg/day) and prednisone (10 mg/day) treatment. Follow-up thoracic radio-

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\textbf{Fig. 1.} Thoracic radiograph showing the opacity in the middle-lower portion of the left lung (arrow).

\textbf{Fig. 2.} Thoracic CT scan showing the localized empyema (1) and the subcutaneous abscess (2).

\textbf{Fig. 3.} Thoracic CT scan showing the micronodular, pseudo-miliariform spreading.

\textbf{Fig. 4.} Thoracic CT scan showing the marked reduction of empyema and subcutaneous swelling after adequate treatment.
Fig. 5. Thoracic CT scan showing the disappearance of the micronodular spreading.

graphy confirmed the absence of pneumonia or empyema.

Discussion

Rhodococcus equi is a facultative, intracellular pathogen that is transmitted to humans mainly by inhalation. Subcutaneous infection through skin lesions has also been described [6]. Despite a negative anamnesis for direct contact with animals, the patient is a physician in a country hospital where he often examines farmers and shepherds. It is unlikely that the paravertebral injections were responsible for R. equi inoculation because they were administered after the onset of fever, cough, and chest pain, i.e. when infection was already present. It is quite likely that a primary pulmonary infection from R. equi occurred in our patient, causing these symptoms as well as the empyema and subcutaneous abscess. The rib fracture was probably pathological because of its contiguity with the subcutaneous abscess and no history of previous trauma. Moreover cases of osteomyelitis from R. equi have been reported [7].

The uncertain taxonomy of R. equi [1,8] makes its rapid identification in biological fluids very difficult, causing delays in diagnosis which may favour its haematogenous diffusion [8]. In addition, its intracellular replication makes it strongly resistant to several antibiotics [8].

Infection from R. equi in immunosuppressed patients is difficult to diagnose and to successfully treat because of its very insidious onset, the bacterial resistance to antibiotics and the frequency of relapses. For these reasons the infection may have a lethal outcome, 50% in AIDS and 25% in remaining cases [9].

Although subcutaneous or cerebral abscesses by R. equi have been described [2,6] pneumonia is the most common clinical manifestation. The onset is insidious and characterized by fever, cough, dyspnea, chest pleural pain, and sometimes haemoptysis. Micronodular necrotizing pneumonia with abscesses and cavities are the prevalent pathological features [8]. For these reasons it can be easily mistaken for other pulmonary infections from opportunists, mycobacteria, and mycetes. Also the microscopic identification of cultured micro-organism from biological specimens is difficult because R. equi can be easily mistaken for other pathogens.

The therapy of R. equi infection is not yet well codified. In vitro it shows sensitivity to vancomycin, gentamicin, teicoplanin, ciprofloxacin, and trimethoprim–cotrimoxazol and resistance to penicillin, clindamycin, and cephalosporins [10]. As an initial approach the use of two antibiotics is recommended [2]. The treatment should not be withdrawn until the patient is clinically recovered, and haemocultures become negative [2,8]. Cultures should also be performed during antibiotic therapy.

As a rule, R. equi infection requires 2–6 months to completely recover in successfully treated cases. In addition to the use of antimicrobial drugs, the treatment tools involve the drainage of supplicative lesions, the surgical removal of granulomatous tissue, and treatment of immunodeficiency when possible [1,2].

The favourable outcome of our case suggests the possibility to obtain good results by monotherapy with a potentially nephrotoxic drug, although the more common therapeutic approach is the use of two antibiotics [1,2]. The withdrawal of azathioprine may have played a key role in the recovery from the infectious disease without negative effects on the graft function.

Our experience suggests that in immunosuppressed patients with a feature of pulmonary disease or abscess, R. equi infection must be taken into account.

References


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