

RHODOCOCCUS EQUI INFECTION IN 3 AIDS PATIENTS

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SUMMARY

Three cases of AIDS complicated by *Rhodococcus equi* infection are reported. At least one of the patients acquired his *Rhodococcus* infection in Africa. Despite the fact that the *R. equi* strains were susceptible to tetracycline, erythromycin, amikacin, co-trimoxazole, rifampicin and vancomycin, these antibiotics were clinically not successful. A clinical improvement was observed in only one patient during teicoplanin and imipenem-cilastatin treatment. Multicentre clinical trials are needed to determine the optimal treatment of *R. equi* infections in AIDS patients.

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INTRODUCTION

Rhodococcus equi is mainly a veterinary pathogen causing pneumonia in various animals including horses, pigs and cows (1). The organism, an aerobic intracellular, pleomorphic, coryneform gram positive bacillus, is ubiquitous in nature. The natural reservoir is the soil, this probably explains the higher prevalence of the infection in herbivores (1). Recently *R. equi* infections have also been observed in humans immunocompromised as a result of malignancies, organ transplantation, immunosuppressive treatment, HIV infection (1-13) and occasionally in nonimmunocompromised humans (14). Human infections probably occur worldwide but so far only one case of *R. equi* infection in

an HIV infected individual who had been living in Africa has been reported in Belgium (3). Between August 1993 and October 1994, three cases of *R. equi* infection in AIDS patients were diagnosed at the University Hospital of Antwerp, Belgium.

CASE REPORTS

The patient characteristics and clinical findings for the 3 patients with *R. equi* infection are summarized in Table 1.

Case 1

This patient had a concomitant *Histoplasma capsulatum* infection and has previously been described elsewhere (15).

Case 2

In February 1994, a 41-year-old Belgian HIV seropositive schizophrenic man was transferred from a psychiatric clinic to the Antwerp University Hospital because of nausea, high fever and a dry cough. Before admission he had been treated with zidovudine, fluconazole and neuroleptics. Physical examination on admission revealed oral candidiasis, involuntary movements of the tongue, and a brown pigmentation of the lower limbs. His CD4 lymphocyte count was 10/mm³. A chest X-ray showed an irregular mass in the left lower lobe. *R. equi* was cultured on 5% horse blood agar from the fluid aspirated from this mass, as well as from blood cultures (Bactec plus/HR7A aerobic and anaerobic medium respectively). A CT of the brain showed a

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TABLE 1: THREE AIDS PATIENTS WITH A *RHODOCOCCUS EQUI* INFECTION

	CASE 1	CASE 2	CASE 3
Sex	Male	Male	Male
Age (years)	41	41	42
Nationality	Polish	Belgian	Belgian
Stay Overseas	Africa (Zaire)	All continents (sailor)	Africa (Burundi)
Contact with farm animals	?	?	Horses > 20 years ago
CD4 lymphocyte count (/mm ³)	40	10	0
Chest X-ray	Cavity upper left lobe	Irregular mass left lower lobe	Cavity upper left lobe
<i>Rhodococcus equi</i> isolated from	Blood, BAL*	Blood, BAL*	Sputum, BAL*, stools
Treatment	Cotrimoxazole Minocycline Amikacin	Erythromycin, Rifampicin	Erythromycin, Rifampicin Cotrimoxazole, Vancomycin Teicoplanin, Imipenem-clastatin Meropenem
Response to treatment	No cure	No cure	Improvement since Teicoplanin Imipenem-Cilastatin treatment
Survival time after <i>Rhodococcus</i> diagnosis	4 months	6 months †	9 months

* Broncho-alveolar lavage fluid

single, non-enhancing lesion in the thalamocapsulolenticular region. The patient was treated with oral erythromycin 4 g daily for the *R. equi* infection and with oral pyrimethamine, 50 mg daily, and oral sulfadiazine, 4 g daily, for the clinically suspected cerebral toxoplasmosis. His fever decreased but after one week his general condition worsened again. Oral rifampicin 600 mg daily was added. A chest X-ray one month later did not show any decrease of the pulmonary mass. The general condition of the patient deteriorated progressively. He became comatose and died 6 weeks after the diagnosis of the *Rhodococcus* infection. A postmortem examination revealed pulmonary oedema and a necrotic area in the left lower lobe with presence of many gram positive cocci. *Rhodococcus equi* was cultured from the lung tissue. Other post-mortem findings were a cytomegalovirus adrenalitis and a cerebral toxoplasmosis abscess.

Case 3

In November 1994 a 42-year-old Belgian scientist, known to be HIV seropositive since 1988, was admitted to the Antwerp University Hospital because of a productive cough for 2 weeks, fever, and left thoracic pain. He had lived in Burundi from 1981 to 1984. In July 1994 he

developed a cerebral toxoplasmosis abscess and was treated with pyrimethamine 75 mg weekly and dapsone 100 mg twice weekly. Since January 1990 he had been treated with zidovudine and since September 1994 with didanosine. In October 1994 an inhomogeneous infiltration in the upper segment of the left lower lobe was observed on a chest X-ray.

Physical examination on admission revealed oral candidiasis. A chest X-ray showed a large infiltration with a central cavity in the upper segment of the left lower lobe. CD4 count was 0/mm³. A sputum culture from a broncho-alveolar lavage grew *R. equi* on 5 % blood agar. Mycobacterium cultures remained negative. The patient was treated with rifampicin 600 mg daily, erythromycin 2 g daily and co-trimoxazole 1920 mg twice daily. After a few days his fever and thoracic pain disappeared, but the pulmonary infiltration and cavity did not decrease in size.

In March 1995 he was again hospitalized because of persistent cough and high fever (> 39°C). *R. equi* was again isolated from a bronchoalveolar lavage and also from stools. Initially he was treated with vancomycin 2 g IV daily and erythromycin 4 g IV daily and later with ciprofloxacin and clarithromycin without success.

Clinical and radiological improvement was finally observed with teicoplanin 400 mg IV daily and imipenem-cilastatin 2 g IV daily. In April 1995 he developed a cytomegalovirus retinitis which was treated with foscarnet. During the teicoplanin, imipenem-cilastatin and foscarnet treatment his general condition improved but he became confused and euphoric. After stopping all treatment his mental status returned to normal but he refused to restart antibiotic treatment. In June 1995, he was again hospitalized because of a reactivated cytomegalovirus retinitis but had no fever and only a slight cough. On a chest X-ray and a chest CT scan the pulmonary infiltration and cavity were still present but had decreased in size. He was treated with ganciclovir, teicoplanin and meropenem. His general condition however deteriorated progressively and he finally died in July 1995. No post-mortem examination was done.

RHODOCOCCLUS EQUI STRAINS

The organisms produced large mucoid pink colonies of gram positive partially acid fast coccoid organisms, developing into small rods with rudimentary branching.

By the disc diffusion method the *R. equi* strains isolated from the 3 patients were found to be resistant to penicillin, and susceptible to tetracycline, erythromycin, gentamicin, amikacin, ciprofloxacin, cotrimoxazole, rifampicin, vancomycin and imipenem.

DISCUSSION

The clinical presentations of the *R. equi* infections in these three patients were similar to those reported in most patients in the literature (2-13). In HIV infected individuals a *R. equi* infection generally occurs when the patient is in an advanced stage of the disease, often in the presence of other opportunistic infections. One patient reported in the literature also had a concomitant disseminated histoplasmosis as in

case 1 (4). *R. equi* is most frequently isolated from blood, sputum and bronchial washings.

Clinically, pulmonary *R. equi* infection strongly mimics a *Mycobacterium tuberculosis* infection. For this reason two of the patients initially received anti-tuberculous treatment. In recent years in Africa, increasing numbers of HIV seropositive, smear negative, tuberculosis cases have been observed (16). Some of these could be pulmonary infections with *R. equi* that remain undiagnosed because of the lack of diagnostic facilities.

How the three patients presented here acquired their *R. equi* infection is unclear. In a study comparing *R. equi* infection in HIV infected and non-HIV infected patients, it was found that 9 (60%) of 15 non-HIV infected patients reported a history of exposure to farm animals compared with only 2 (18%) of 11 HIV infected individuals (8). Only the 3rd patient had frequently been exposed to horses (but more than 20 years before he developed his *R. equi* infection).

All isolates of *R. equi* from animals and soil are sensitive to penicillin but most isolates of human origin are resistant to this antibiotic (8). Because *R. equi* is resistant to phagocytosis and intracellular killing by macrophages, antibiotics which penetrate intracellularly such as erythromycin, rifampicin or perhaps chloramphenicol, should be administered. Although *R. equi* is susceptible to several antibiotics in vitro, therapeutic failures are common (6) as are relapses after stopping treatment (7). Therefore mortality due to *R. equi* infection in HIV infected individuals is high: 20-50 % (8). It is possible that the *Rhodococcus* infection of the first patient was cured by the combination of co-trimoxazole, minocycline and amikacin. A combination therapy of rifampicin and erythromycin, which was reported to have cured at least one patient (11), was not successful in our second and third patients. In the latter patient a clinical improvement was only observed during teicoplanin and imipenem-cilastatin treatment. These antibio-

tics (17) as well as the imipenem/vancomycin combination (18), which have a high bactericidal activity in vitro but a poor intracellular penetration, were previously shown to be clinically successful. After treatment with these bactericidal antibiotics consolidation treatment with intracellularly active drugs is probably needed (18).

In the future *R. equi* infection in AIDS patients may be recognized more frequently. Studies to determine the optimal treatment regimen for this infection are needed.

SAMENVATTING

Drie patiënten met AIDS en een *Rhodococcus equi* infectie worden beschreven. Minstens één van de patiënten ontwikkelde zijn *Rhodococcus* infectie in Afrika. Ondanks het feit dat de *R. equi* stammen gevoelig waren voor tetracycline, erytromycine, amikacine, co-trimoxazole, rifampicine en vancomycine, bleken deze geen gunstig klinisch effect te hebben. Klinische verbetering werd enkel vastgesteld bij één patiënt tijdens teicoplanine en imipenem-cilastatine behandeling. Multicentrische klinische studies zijn nodig om de beste behandelingswijze te bepalen voor *R. equi* infecties bij AIDS patiënten.

RESUME

Trois patients atteints de SIDA avec une infection à *Rhodococcus equi* sont décrits. Au moins un des patients a développé son infection à *R. equi* en Afrique. Quoique les souches de *R. equi* aient été sensibles à la tétracycline, l'érythromycine, l'amikacine, le co-trimoxazole, la rifampicine et la vancomycine, ces antibiotiques n'ont pas été cliniquement efficaces. Une amélioration clinique n'a été observée que chez un patient durant un traitement par teicoplanine et imipénème-cilastatine. Des essais cliniques multicentriques sont nécessaires pour déterminer le traitement optimal de l'infection à *R. equi* chez les patients atteints de SIDA.

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