

# Pulmonary Infection Caused by *Rhodococcus equi* in Patients with Human Immunodeficiency Virus Infection : Report of 23 Cases from Chiang Mai

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## Abstract

Between June 1993 and November 1995, 26 cases of *R. equi* infection were diagnosed at Chiang Mai University Hospital. Of the 26 patients, 24 cases (92%) were also infected with HIV. The primary site of infection was the lung in 23 cases. The common presenting symptoms were fever, cough, sputum production, chest pain and hemoptysis. Chest roentgenograms showed dense pulmonary infiltration and/or cavitory lesion in 19 cases. Diagnosis of the etiologic microorganism in ten cases was accurately made based on clinical features, chest roentgenograms and sputum examination showing acid-fast coccobacilli before culture results were available. Nineteen patients had concurrent HIV-related infections namely oral candidiasis, *Penicillium marneffei* infection, salmonella septicemia, and *Pneumocystis carinii* pneumonia in 14, 2, 2 and 1 cases respectively. It was concluded that pulmonary infection due to *R. equi* is not uncommon in HIV-infected individuals in northern Thailand. (*J Infect Dis Antimicrob Agents* 1996;13:95-9.)

## INTRODUCTION

Patients in the late stage of human immunodeficiency virus (HIV) infection are susceptible to many kinds of opportunistic organisms. The relative incidence of these opportunistic infections varies according to different geographic location. Common opportunistic infections in Thailand are tuberculosis, cryptococcosis, *Pneumocystis carinii* pneumonia and penicilliosis marneffei (1).

*Rhodococcus equi*, a Gram-positive acid-fast coccobacilli, was originally isolated in 1923 as *Corynebacterium equi* (2). *R. equi* is a well established pathogen in foals and other domestic livestock (3,4). It has been a rare cause of disease in humans. The first human case was reported in 1967 (5). The disease was uncommon because only 12 cases were reported within 16 years after the first case report (6). Most human infections

have been associated with compromised immune function. A marked increase of the infection has been reported since the HIV epidemic in 1981 (7-11). Infection caused by *R. equi* has never been reported in Thailand. We reported the clinical features of the first 23 HIV-infected patients with pulmonary infection caused by this organism from Chiang Mai University Hospital.

## MATERIALS AND METHODS

We reviewed microbiology records at Chiang Mai University Hospital from June 1993 through November 1995. *R. equi* was isolated from clinical specimens in 29 patients. Of the 29 patients, 26 medical records were available for review. Information sought included demographic data, place of residence and employment, presenting signs and symptoms, subsequent clinical

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course, findings from chest roentgenogram, laboratory data including anti-HIV antibody, treatment regimen and outcome. Routine nonselective media was used to isolate *R. equi* from clinical specimens and it was identified with method described by Prescott (4). Antibiotic susceptibility was determined by standard disk susceptibility test (12). The isolate from the first patient was sent to the microbiology laboratory at the School of Hygiene and Public Health, Johns Hopkins University, USA for confirmation of the identification. Isolates from the other two patients were sent to the Department of Medical Sciences of the Ministry of Public Health. All three isolates were identified and confirmed as *R. equi*.

## RESULTS

Of the 26 patients, two were not infected with HIV. One patient was a 69-year-old man with late stage of Hodgkin's disease. The other was a 25-year-old woman with end-stage chronic renal failure. Both had *R. equi* pulmonary infection. The remaining 24 patients were infected with HIV as evidenced by the presence of anti-HIV antibody in their serum specimens on repeated testings. Their demographic data, risk factors for HIV infection, place of residence and employment were shown in Table 1. The sources of clinical specimens which yielded positive culture for *R. equi* were shown in Table 2. One of these 24 HIV-infected patients, a 24-year-old hilltribe man from Mae Hong Son province, had *R. equi* pyopericardium. The remaining 23 patients had *R. equi* pulmonary infection diagnosed by clinical features, chest roentgenograms, and the source from which the organism was cultured. The presenting symptoms of these 23 patients were shown in Table 3. The interval from their first symptom to the time they sought medical attention ranged from 5 days to 3 months, with the mean of 32.8 days. The results of complete blood count and chest roentgenogram obtained on admission were shown in Table 4 and 5 respectively. Table 6 showed the number of patients with HIV-related infection diagnosed within 1 month of the diagnosis of *R. equi* infection. In addition one patient had pulmonary tuberculosis 9 months before the diagnosis of *R. equi* infection and two patients had *Pneumocystis carinii* pneumonia two and three months before the diagnosis of *R. equi* infection respectively.

Antibiotic susceptibility to penicillin, ampicillin, cephalothin, and erythromycin was determined in 15 isolates. All were susceptible to erythromycin. Only 4,

**Table 1. Demographic data of the 24 HIV-infected patients with *Rhodococcus equi* infection.**

Sex :	all male	
Age :	range 22-42 yrs, mean 30.2 yrs	
Marital status :	single	16
	married	4
	unknown	4
Risk factor :	heterosexual	23
	IVDU	1
Residence :	urban	3
	rural	21
Employment :	laborer/farmer	21
	others	3

**Table 2. Sources of clinical specimens that yielded positive culture in 24 HIV-infected patients with *Rhodococcus equi* infection.**

Sputum (only)	13
Broncho-alveolar lavage, BAL (only)	1
Pleural fluid (only)	1
Sputum + BAL	1
Sputum + blood	4
Sputum + blood + pleural fluid	1
Blood (only)	2
Pus from pericardiocentesis	1

**Table 3. Presenting symptoms of 23 HIV-infected patients with pulmonary infection caused by *Rhodococcus equi*.**

Fever (range 38.1 - 40° C, mean 39° C)	20
Cough	18
Sputum production	16
Chest pain	12
Hemoptysis	8
Weight loss	14

**Table 4. The results of complete blood count obtained on admission.**

Hemoglobin	
≥ 10 g/dl	5
< 10 g/dl	13
not available	5
White blood cell count	
> 10,000 /mm <sup>3</sup>	7
5,000 - 10,000 /mm <sup>3</sup>	6
< 5,000 /mm <sup>3</sup>	5
not available	5

**Table 5. The results of chest roentgenography obtained on admission.**

A) Pulmonary infiltration (including nodule and "mass-like" infiltration)	10
B) A + cavity (or cavities)	5
C) A + pleural effusion	1
D) A + cavity + pleural effusion	1
E) Lung abscess (cavitary lesion $\pm$ air fluid level)	4
F) Pleural effusion	2

**Table 6. HIV-related infection diagnosed within one month of the diagnosis of *R. equi* infection.**

Salmonella septicemia	2
<i>Pneumocystis carinii</i> pneumonia	1
<i>Penicillium marneffei</i> infection	1
<i>Penicillium marneffei</i> infection and <i>S. aureus</i> septicemia	1
<i>Shigella sonnei</i> colitis	1
Oral candidiasis	14

6, and 2 isolates were susceptible to penicillin, ampicillin, and cephalothin respectively. Fourteen patients were treated for *R. equi* infection. Eleven were given erythromycin 2 g per day together with rifampin 600 mg per day, three cases were given erythromycin 2 g per day alone. In 10 of these 14 patients, a presumptive diagnosis based on clinical findings was made before the result of the culture was available. Four patients were treated after the result of the culture was known. The remaining 9 patients were not treated for *R. equi* infection, because the result of the culture was available after the patients died or lost to follow-up. Six patients had been treated with anti-tuberculous drugs at some time during the course of the illness caused by *R. equi*. The patients' response to treatment could not be adequately evaluated. Eight of the 14 patients who received treatment for *R. equi* infection lost to follow-up. One patient died within the first few days of treatment, and two patients left the hospital against medical advice in moribund stage. The remaining three patients responded well initially, but two of these three patients died 3 and 5 months respectively after the start of treatment. The remaining patients remained well 6 months after the start of treatment.

## DISCUSSION

*Rhodococcus equi* is an aerobic, non-motile, non-spore forming, pleomorphic Gram-positive coccobacillus

which may also be weakly acid-fast (4). It has been a rare cause of disease in man. A total of 84 cases were published in the English literature (13-15). Of these 84 patients, 38 cases (45%) had been infected with HIV and 34 cases (40%) were immunocompromised from other causes. Pulmonary infection was the most common form of infection by *R. equi* (13-15). Disease caused by *R. equi* has never been reported in Thailand. During a 30-month period from June 1993 to November 1995, 26 cases of *R. equi* infection had been diagnosed at Chiang Mai University Hospital. The sudden appearance of patients with *R. equi* infection was due to the HIV epidemic that started in Thailand in late 1987 (1). HIV infection has been found to be the most common underlying condition of *Rhodococcus equi* infection (14,15). However, another factor that led to the increased number of diagnosed cases of *R. equi* infection at our hospital was the awareness by the laboratory technicians and physicians that this microorganism exists and can cause disease in man. In fact, the sputum culture from our first patient was originally identified as *Micrococcus* spp., suggestive of oropharyngeal normal flora. It was after an astute laboratory technician noticed that the organisms were acid-fast on the Ziehl-Neelson-stained smear that the isolate was reexamined and found to be *R. equi*. Likewise, after a few cases were diagnosed, physicians at our hospital were able to make presumptive diagnosis based on clinical features, chest roentgenogram, and sputum examination and prescribed appropriate antibiotics before the result of the culture became available. When more laboratory technicians, clinical microbiologists and physicians are aware of this infection, *R. equi* may turn out to be another important opportunistic organism in HIV-infected patients in Thailand.

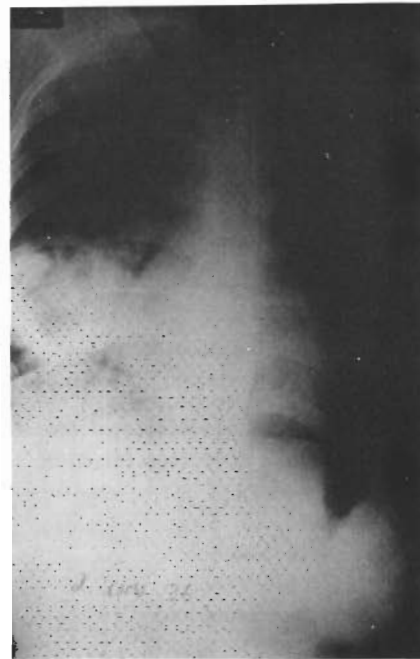
The demographic data including the risk factor for HIV infection reflected the characteristics of HIV-infected persons in Thailand (1). That the majority of our patients were laborers/farmers who lived in the rural area may be related to the fact that *R. equi* is a soil organism carried in the gut of many herbivores. But since this is a retrospective study and no specific questions were asked about exposure to horse or other herbivores, this correlation should be made only with extreme caution.

All 24 cases of HIV-infected patients with *R. equi* infection were proven by culture as shown in Table 2. The 2 patients, whose positive culture could be obtained from the blood specimens only, had clinical findings

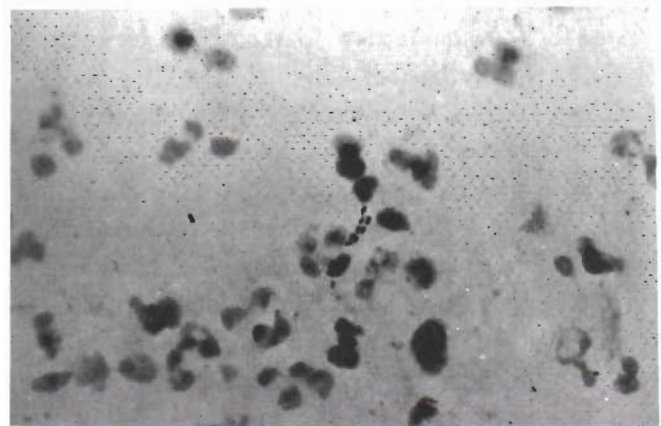
and chest roentgenogram diagnostic of *R. equi* pulmonary infection. The presenting symptoms and results of chest roentgenogram shown in Tables 3 and 5 were similar to those reported in the literature (13-15). Typical presentation included a subacute onset, high fever, cough, sputum production, chest pain, and hemoptysis. The chest roentgenogram usually showed dense pulmonary infiltration, which in some instances had been described as nodule or "mass-like" infiltration. The lung lesions may cavitate and form a lung abscess (Fig.1). Pleural effusion may also be present. The results of the complete blood count were not helpful in arriving at the diagnosis. Examination of the sputum, broncho-alveolar lavage, or pleural fluid may show Gram-positive coccobacilli which were also acid-fast (see Fig.2). Pulmonary infection with *R. equi* in HIV-infected individuals may be difficult to differentiate from mycobacterium or nocardia infection. In fact six of our patients had been treated with anti-tuberculous drugs at some time during the course of *R. equi* infection. It should be noted that the genus *Rhodococcus* belongs to the order Actinomycetales and is closely related to the genera *Corynebacterium*, *Mycobacterium*, and *Nocardia* (16).

Determination of T cell subsets was not routinely available at Chiang Mai University Hospital. The majority of our patients had HIV-related infection within 1 month of the diagnosis of *R. equi* infection (Table 6). Three patients had pulmonary tuberculosis or *Pneumocystis carinii* pneumonia 2 to 9 months before the diagnosis of *R. equi* infection. Thus, *R. equi* infection occurred in the later stage of HIV infection.

In our study, *R. equi* is sensitive to erythromycin and resistant to beta-lactam antibiotics. This is consistent with reports in the literature. *R. equi* is resistant to penicillin and penicillinase-resistant penicillins, and resistant or moderately susceptible to first and second-generation cephalosporins (6). Among beta-lactam drugs, third-generation cephalosporins and imipenem are effective against *R. equi*, but resistance to beta-lactam antibiotics has been shown to develop during therapy (7,17). The organism is particularly susceptible to erythromycin, clindamycin, rifampin, fluoroquinolones vancomycin and aminoglycosides. However, since *R. equi* is an intracellular organism (18), antibiotics that penetrate and concentrate within infected cells are recommended. These include erythromycin, rifampin, ciprofloxacin, and vancomycin. The most commonly used antibiotic regimen was the combination of erythromycin and



**Fig.1** Chest roentgenogram of a patient with *Rhodococcus equi* pulmonary infection showing dense infiltration and cavity.



**Fig.2** Gram-stained smear of the sputum from a patient with *Rhodococcus equi* pulmonary infection showing Gram-positive coccobacilli.

rifampin (19). Despite treatment with appropriate antibiotics, the mortality rate of patients with *R. equi* pulmonary infection was relatively high at 25 percent (19).

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