Increasing awareness of *Rhodococcus equi* pulmonary infection in the immunocompetent adult: a rare infection with poor prognosis

Samantha Herath, Christopher Lewis, Mitzi Nisbet

**Abstract**

The aim of this case report and review is to increase awareness of this uncommon infection with *Rhodococcus equi* (*R. equi*), in immunocompetent adults. *R. equi* is a soil-dwelling Gram-positive bacillus that frequently causes infection in grazing livestock. Human infection is rare and mostly limited to the immunocompromised hosts.

We present a case of pneumonia caused by *R. equi* infection in a 55-year-old male builder who presented with cough, dyspnoea and night sweats, initially suspected to have pulmonary tuberculosis. Following biopsy of the mediastinal lymph nodes, *R. equi* was cultured, which is usually not a contaminant. Despite extensive investigations a host immune defect was not identified. The patient recovered after three months of combination antibiotic treatment, initially with intravenous vancomycin and meropenem followed by oral clarithromycin and rifampicin.

To further clarify this rare disease we did a literature review that identified 26 adult patients with *R. equi* infection, without an identified host immunosuppressive condition. In this cohort, the median age at presentation was 53 years and infection holds a strong male predominance 19 (73%). An environmental exposure (e.g. farming, horse breeder) was found in 13 (50%). Ten (38%) of these patients had pulmonary infection. All deaths 3 (12%) occurred in the patients had pulmonary infection.

*R. equi* is an infection that is difficult to diagnose and carries a high mortality if prompt treatment is not established. It is important to realise the potential for this disease to be misdiagnosed as pulmonary tuberculosis or community acquired pneumonia. Clinical suspicion is important especially if an environmental exposure is suspected.

*Rhodococcus equi* (*R. equi*), previously known as *Corynebacterium equi*, is an aerobic intracellular Gram-positive rod that is partially acid fast. It is a soil organism that causes infection in grazing animals. It is carried in the gut of many herbivores and widespread in their environment. It was first reported as a cause of human infection in 1967.

Human infection is rare and usually occurs in immunocompromised hosts most commonly reported in patients with human immunodeficiency virus (HIV) infection. It has also been associated with solid organ transplantation, lymphoproliferative malignancies, diabetes mellitus, and the use of long-term steroids.
Infection is usually acquired by the airborne route with pneumonia being the most common manifestation. Infection can also be acquired orally,² or by direct inoculation of the skin.²–⁵

We report a case of R. equi infection in an adult who had no identified immunosuppressive condition. We reviewed the literature to identify all reported cases of adults with R. equi infection who had no identified contributing immunodeficiency and reviewed the clinical characteristics, radiological findings, treatment and clinical outcome to further define this condition and to raise awareness of this disease.

We have focused mainly on pulmonary infection as it is the commonest manifestation and has the worst prognosis.

Case report

In autumn 2010, a 55-year-old builder of New Zealand European ethnicity presented to our emergency department with a 1-week history (day 7) of fevers to 39°C, drenching night sweats and exertional dyspnoea. He reported cough with minimal sputum production. He had lost 5 kg of weight over the preceding 6 weeks. There was no history of haemoptysis or chest pain. He has clear recollection of exposure to dust that was disturbed whilst he was tiling a laundry, the evening prior to the onset of his symptoms (day 1). He also reported that a wedge of a tile had cut his arm resulting in a pustular lesion that had resolved prior to his presentation to hospital.

He had a history of ulcerative colitis diagnosed 15 years prior, which was well controlled on mesalazine. A surveillance colonoscopy 18 months prior to the presentation was normal. He was an ex-smoker with a 10-pack year history having stopped smoking 15 years prior. He denied any history of contact with tuberculosis and his only prior travel was to Australia.

His chest X-ray showed right lower zone opacity (Figure 1).

Figure 1. Right lower zone opacity
At initial presentation he had a white blood cell count of $12.6 \times 10^9/L$ (4–11) and a C-reactive protein of 34 mg/L (<5). Spirometry was normal with a FEV$_1$ of 3.69 L (91% predicted) and a FVC of 5.07 L (96% predicted). He was diagnosed with community acquired pneumonia and due to a previously reported allergy to penicillin; he was discharged home on oral erythromycin (400 mg twice daily).

His symptoms however persisted with drenching night sweats, dyspnoea and cough and a computed tomography (CT) scan of his chest was completed on day 15.

This showed a right lower lobe consolidation (Figure 2) with necrotic enlarged mediastinal lymph nodes (Figure 3). The lung parenchyma was unremarkable. Pulmonary tuberculosis was suspected at the time and a bronchoscopy was performed.

A bronchial wash revealed inflammation of the right lower lobe bronchus, without any evidence of infection. A transbronchial needle aspirate (TBNA) from the subcarinal lymph node (station 7) was completed and on day 32 this cultured a few colonies of *R. equi*.

As *Rhodococcus* is usually not a contaminant and is commonly associated with immunocompromised states, a host immune assessment was completed. He had negative serology for HIV including CD4 and CD8 counts within the normal range. The nitroblue-tetrazolium test for chronic granulomatous disease was negative. Anti-nuclear antibodies and rheumatoid factor were negative. Immunoglobulins, serum protein electrophoresis, lactate dehydrogenase, beta-2-microglobulin, fasting blood sugar and renal function were normal. *Mycobacterium* cultures from left lower lobe bronchial washings were also negative.

The patient was treated initially with 1 week of erythromycin from day 7 to 14. Following this he underwent extensive further investigations and was not given any antibiotic treatment until the positive *R. equi* cultures were noted on day 32.
To exclude the possibility of an additional diagnosis of a malignancy, a further bronchoscopy with endobronchial ultrasound (EBUS) was completed on day 37. Cytology did not identify any malignant cells. However, *R. equi* was again cultured despite previous treatment with a macrolide. The isolate was susceptible to clarithromycin, ciprofloxacin and imipenem.

From day 38 he had 2 weeks of intravenous (IV) imipenem 500 mg q8h and IV vancomycin 2 g q12h (obtaining vancomycin trough levels of 16.6 mg/L and above). After 2 weeks of treatment his fevers had resolved and his CRP had settled to 10 mg/L.

Vancomycin was continued for a further 4 weeks with the addition of oral rifampicin 600 mg daily and oral clarithromycin 500 mg bd. Both oral antibiotics were then subsequently continued to complete a total of 3 months of treatment.

At 3 months, a CT chest scan showed significant improvement with resolution of the right lower lobe pneumonia (Figure 5) and marked reduction of the mediastinal lymphadenopathy (Figure 6). Antibiotics were therefore stopped at this time.

**Figure 5. Resolution of right lower zone pneumonia**

**Figure 6. Resolution of mediastinal adenopathy**

### Literature review

A Medline and Ovid search was completed under the search criteria of *Rhodococcus equi*. The same search was repeated using the previous organism name of *Corynebacterium equi*. The bibliographies of the selected articles were further reviewed to locate articles not listed in Medline or Ovid. See Table 1.

All patients who had an immunocompromising condition including HIV infection, splenectomy, long-term steroid use, malignancy, lymphoproliferative disorders, diabetes mellitus, renal failure or who were a transplant recipient were excluded.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Sex</th>
<th>Exposure</th>
<th>Site</th>
<th>Diagnostic specimen</th>
<th>Antibiotic treatment</th>
<th>Duration (months)</th>
<th>Surgical resection</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones MR 1989</td>
<td>76</td>
<td>M</td>
<td>Gardner</td>
<td>Pulmonary</td>
<td>Sputum</td>
<td>AMO, TIN</td>
<td>0.75</td>
<td>Thoracotomy</td>
<td>Died</td>
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<td>Hillman et al. 1989</td>
<td>29</td>
<td>M</td>
<td>Corneal laceration</td>
<td>Ocular</td>
<td>Vitreous aspirate</td>
<td>CEF, GEN, CLI</td>
<td>NA</td>
<td>Lensectomy</td>
<td>Cured</td>
</tr>
<tr>
<td>Lee-cheiong et al 1995</td>
<td>27</td>
<td>M</td>
<td>Stung by a rock fish (scuba diving)</td>
<td>LN</td>
<td>LN biopsy</td>
<td>EES</td>
<td>1</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Egawa T 1990</td>
<td>28</td>
<td>M</td>
<td>Agricultural student (performing experiments)</td>
<td>Pulmonary</td>
<td>Open lung biopsy</td>
<td>OFX, CFS, LMX 10/7 then OFX/TIC for 1/12</td>
<td>1.3</td>
<td>No</td>
<td>Cured</td>
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<td>Moyer D et al. 1993</td>
<td>76</td>
<td>F</td>
<td>Not known</td>
<td>Pulmonary</td>
<td>Blood culture</td>
<td>EES, RIF, GEN 4/52 then EES/RIF for 2/12</td>
<td>3</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Verville et al. 1995</td>
<td>53</td>
<td>M</td>
<td>Exposure to livestock</td>
<td>Pulmonary</td>
<td>Bronchial washing</td>
<td>CLI, EES, RIF, CTO</td>
<td>7</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Verville et al. 1995</td>
<td>38</td>
<td>M</td>
<td>Not known</td>
<td>Pulmonary</td>
<td>Sputum</td>
<td>EES</td>
<td>0.5</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Walsh et al. 1994</td>
<td>83</td>
<td>F</td>
<td>Not known</td>
<td>Pulmonary</td>
<td>Sputum</td>
<td>AMS</td>
<td>5days</td>
<td>No</td>
<td>Died</td>
</tr>
<tr>
<td>Friedberg F et al. 1995</td>
<td>76</td>
<td>F</td>
<td>Horse breeder</td>
<td>Soft tissue</td>
<td>Biopsy of soft tissue</td>
<td>CIP, RIF</td>
<td>8</td>
<td>No</td>
<td>Relapse (6 weeks)</td>
</tr>
<tr>
<td>DeMarais et al. 1995</td>
<td>24</td>
<td>F</td>
<td>Not known</td>
<td>Meningitis</td>
<td>CSF</td>
<td>PVK/CRO 10/7 then , ACL for 2/52</td>
<td>0.75</td>
<td>No</td>
<td>Lost</td>
</tr>
<tr>
<td>Scott M et al. 1995</td>
<td>55</td>
<td>M</td>
<td>Eye trauma</td>
<td>Ocular</td>
<td>Eye discharge</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Linares M et al. 1997</td>
<td>48</td>
<td>M</td>
<td>Not Known</td>
<td>Pulmonary</td>
<td>Resected RML</td>
<td>NA</td>
<td>NA</td>
<td>RML resection</td>
<td>Cured</td>
</tr>
<tr>
<td>Kedlaya et al. 2001</td>
<td>48</td>
<td>M</td>
<td>Horse stable (following windy day)</td>
<td>Pulmonary</td>
<td>Blood culture</td>
<td>VAN, CRO, RIF, MET 8/52 then RIF, EES for 12 /52</td>
<td>5</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Sigler E 1998</td>
<td>53</td>
<td>F</td>
<td>Not known</td>
<td>Disseminated</td>
<td>Bone marrow aspirate</td>
<td>EES</td>
<td>1</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Tripodi MF et al. 2009</td>
<td>55</td>
<td>M</td>
<td>Not known</td>
<td>Endocarditis</td>
<td>Blood culture</td>
<td>IMP, GEN 2/52 then CLA/SXT for 3/12</td>
<td>3.5</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Nasser et al. 2001</td>
<td>16</td>
<td>M</td>
<td>Scalp laceration on farm</td>
<td>Scalp</td>
<td>Biopsy</td>
<td>EES, RIF</td>
<td>3</td>
<td>Debridement</td>
<td>Cured</td>
</tr>
<tr>
<td>Corne et al. 2001</td>
<td>65</td>
<td>M</td>
<td>Not known</td>
<td>Brain abscess</td>
<td>Brain abscess aspirate</td>
<td>VAN 5/52 then SXT for 9/12</td>
<td>10.25</td>
<td>Debridement</td>
<td>Cured</td>
</tr>
</tbody>
</table>

Table 1. Summary of the 26 reported cases with *R. equi* infection in immunocompetent hosts
<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Sex</th>
<th>Exposure</th>
<th>Site</th>
<th>Diagnostic specimen</th>
<th>Antibiotic treatment</th>
<th>Duration (months)</th>
<th>Surgical resection</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tripodi MF et al. 2009</td>
<td>64</td>
<td>M</td>
<td>Not known</td>
<td>Endocarditis</td>
<td>Blood culture, LN biopsy</td>
<td>VAN, RIF 1/12 then EES, RIF for 1/12</td>
<td>2</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Napoleao F et al. 2005</td>
<td>46</td>
<td>M</td>
<td>Farm/horse exposure</td>
<td>Liver abscess</td>
<td>Aspirate liver abscess</td>
<td>EES, RIF</td>
<td>1</td>
<td>Liver resection</td>
<td>Cured</td>
</tr>
<tr>
<td>Gabrielas P et al. 2006</td>
<td>72</td>
<td>F</td>
<td>Horse stable</td>
<td>Pulmonary, brain abscess</td>
<td>Blood culture</td>
<td>EES, RIF 2/52 then CLA, VAN for 6/52</td>
<td>2</td>
<td>No</td>
<td>Relapse, Died</td>
</tr>
<tr>
<td>Ulivieri S et al. 2006</td>
<td>37</td>
<td>M</td>
<td>Not known</td>
<td>Brain abscess</td>
<td>Brain abscess aspirate</td>
<td>SXT, IMP, LIN</td>
<td>2.5</td>
<td>Debridement</td>
<td>Cured</td>
</tr>
<tr>
<td>Wichmann D 2008</td>
<td>54</td>
<td>M</td>
<td>Not known</td>
<td>Brain abscess</td>
<td>Brain abscess aspirate</td>
<td>RIF, MER, VAN 3/52 then RIF, CLA for 12/12</td>
<td>12.75</td>
<td>Debridement</td>
<td>Cured</td>
</tr>
<tr>
<td>Diapera M et al. 2008</td>
<td>70</td>
<td>M</td>
<td>Farm hand (for horses)</td>
<td>Tongue</td>
<td>Tongue biopsy</td>
<td>CIP, MET</td>
<td>NA</td>
<td>Excision</td>
<td>Cured</td>
</tr>
<tr>
<td>Matsushita et al. 2010</td>
<td>25</td>
<td>M</td>
<td>Not known</td>
<td>Endocarditis</td>
<td>Blood culture</td>
<td>CIP, VAN</td>
<td>1</td>
<td>MV resection</td>
<td>Cured</td>
</tr>
<tr>
<td>Index Case 2010</td>
<td>55</td>
<td>M</td>
<td>Builder working tiling a dusty</td>
<td>Pulmonary</td>
<td>TBNA of sub-carinal LN</td>
<td>VAN 6/52 with CLA, RIF for 3 mon3/12</td>
<td>3</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>Sandkovsky et al 2011</td>
<td>31</td>
<td>F</td>
<td>Breast reduction surgery</td>
<td>Breast tissue</td>
<td>Breast wound discharge</td>
<td>RIF, MOX for 6 weeks</td>
<td>1.5</td>
<td>Debridement</td>
<td>Cured</td>
</tr>
</tbody>
</table>

LN=lymph node, CSF=cerebrospinal fluid, RML=right middle lobe, NA =Not available.
AMO=amoxycillin, ACL=amoxicillin/clavulanic acid, AMS=ampicillin-sulbactum, CEF=cefazolin, CFS=cefsulodin, CRO=ceftriaxone, CIP=ciprofloxacin, CLA=clarithromycin,
CLI=clindamycin, EES=erythromycin, GEN=gentamycine, IMP=imipenem, LMX=latamoxef, LIN=linezolid, MER=merapenam, MET=metronidazole, MOX=moxifloxacin,
OFX=ofloaxcin, PVK=penicillin, RIF=rifampcin, SXT=trimethoprim/sulfamethoxazole, TIC=ticarcillin, TIN=tinadazole, VAN=vancomycin.
Epidemiology

There was a marked male predominance with infection occurring in 19 (73%) males. The median age was 53 (range 16–83) years. A possible environmental exposure source was identified in 13 (50%) cases. Occupations involving animal husbandry like, farmers, horse breeders and gardeners seem most susceptible.

Diagnosis

The primary organ involved was predominantly the lungs. Ten (38%) cases had pulmonary involvement at presentation. Four (15%) patients had brain abscesses, 3 (12%) had endocarditis, 2 (8%) had ocular infection and there was 1 patient each, who had meningitis, lymph node infection, infection of the tongue, infection of the soft tissue over the mandible, liver abscess, infection of the scalp and breast cellulitis.

Of the 10 patients with pulmonary involvement, chest X-rays showed pulmonary infiltrates in 8, cavities in 4, and unilateral pleural effusions in 1 patient. CT chest was performed in 4 out of the 10 patients. Mediastinal adenopathy was not mentioned in the CXR or CT scans in all except the index case. Three patients had no reported respiratory symptoms despite pulmonary infiltrates.

*R. equi* was cultured from all patients who were included in this cohort. Of the 10 patients with pulmonary involvement, *R. equi* was cultured from a spontaneous sputum specimen in 3 patients and blood cultures in 3 patients. In the remaining 4 patients, *R. equi* was cultured from an open lung biopsy, a surgical lobectomy, bronchial washings and a TBNA specimen.

Treatment

Antibiotic treatment was the mainstay of treatment while some patients had surgical treatment in combination or as the sole therapy.

Antibiotic treatment was described in 24 (92%) patients. The median length of treatment for all cases with a successful outcome was 3.8 months (range 2 weeks to 12.8 months).

Six out of the 10 cases of pulmonary infection successfully completed treatment with antibiotics as the sole therapy. The antibiotic treatment in this group was given for a median of 3 months (range 0.5–7 months). One patient had monotherapy with oral erythromycin. The remaining 5 patients received combination therapy including intravenous antibiotic treatment (intravenous antibiotic used were vancomycin in 2, ceftriaxone in 2, gentamicin, ticarcillin and clindamycin in 1 patient each). Oral treatment was most commonly a macrolide (in 4 patients) and was given in combination with rifampicin (4 patients). Other oral agents used were ofloxacin (1 patient) and metranidazole (1 patient).

Surgical resection was completed in 10 patients (42%); 9 (35%) had a resection at a non-pulmonary site. Two (8%) patients with pulmonary involvement had a lobectomy via open thoracotomy. One patient had a surgical resection of the affected lobe (RML resection) as the sole treatment and was cured. One patient who had combination antibiotics (amoxicillin and tinadazole) and a thoracotomy succumbed to the disease.
**Prognosis**

Patients with pulmonary infection had worse outcomes. All deaths 3 (12%) in the whole group occurred in the patients with pulmonary involvement.

One of the patients who died received antibiotic treatment together with a thoracotomy. Of the other 2 patients who died, 1 had treatment with only ampicillin-sulbactum. The other patient had a concomitant brain abscess and was possibly a delayed diagnosis. She was treated with erythromycin and rifampicin for 2 weeks followed by vancomycin and clarithromycin for 6 weeks, but relapsed and later died from this infection.

Overall, 22 patients (85%) in total were initially reported to be successfully treated without no documented relapse and one (4%) patient was lost to follow up. Two (8%) patients relapsed and 1 of these patients subsequently died from infection. The total mortality due to infection was 3 (12%).

**Discussion**

*R. equi* is uncommon pathogen in immunocompetent patients. This infection predominantly occurs in males and is frequently reported in patients with occupations such as horse breeding, gardening and farming that provide potential exposure to this organism. As an environmental exposure can be frequently identified a detailed history is important in assessing patients who may have this infection.

*R. equi* can cause a diverse range of presentations with pulmonary infection being the most common. Clinical symptoms can closely mimic other conditions such as tuberculosis. Given the diagnostic difficulties it is likely it is under diagnosed and when a diagnosis is made, it may be late in the clinical course.

Obtaining an appropriate sample for culture is important prior to commencing treatment. Mediastinal infection may be successfully cultured from a TBNA and this is the first reported case of necrotizing mediastinal adenopathy as a result of *R. equi* infection as well as using EBUS to diagnose *R. equi* pulmonary infection.

Therapy should be individualised depending on the clinical context of disease and response to treatment. It is difficult to conclude the exact duration or the ideal choice of antibiotics from the reported treatment data. However, the successfully treated patients with pulmonary infection required prolonged antibiotic treatment. Successful outcomes have been reported in patients treated with an injectable agent such as vancomycin, ceftriaxone or ticarcillin.

Once clinical symptoms improve antibiotics may be rationalised to an oral treatment regimen. Macrolide have been used effectively to treat this infection. Most patients were treated with rifampicin in addition to a macrolide for at least 3 months. Shorter treatment courses may be adequate; however there is currently insufficient literature to support this.

This disease requires prolonged antibiotic treatment and has a significant mortality even in immunocompetent adults, with all reported deaths occurring in patients with pulmonary infection.
Vigilance and prompt referral for appropriate investigation and treatment is vital to improve morbidity and mortality.

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**Acknowledgement:** We take this opportunity to thank the index patient for his willing participation and informed consent.

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