Vertebral Osteomyelitis Due to \textit{Rhodococcus equi} in a Liver Transplant Recipient

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\textit{Rhodococcus equi} is a rare but well-documented cause of cavitary pneumonia in immunocompromised patients. In this report the first case of \textit{R. equi} infection manifesting as vertebral osteomyelitis is described. A 39-year-old liver transplant recipient presented with recurrent pneumonia and a pleura-based lung abscess and subsequently developed osteomyelitis of the lower thoracic spine. Surgical debridement and prolonged treatment with rifabutin and clarithromycin resulted in clinical cure. In the literature, 12 other cases of \textit{R. equi} infection in solid-organ transplant recipients have been reported. Ten of these patients had documented pulmonary disease and seven had extrapulmonary manifestations. Prolonged antibiotic therapy and surgical drainage resulted in clinical improvement in >90% of the reported cases.

\textit{Rhodococcus equi} is a well-documented veterinary pathogen causing granulomatous pneumonia in foals. Since 1980, the organism has increasingly been recognized as a cause of human disease. Impairment of cell-mediated immunity is the most important risk factor for infection with \textit{R. equi} in humans [1]. The majority of cases have involved patients with advanced HIV infection. Patients with no or other immunocompromising conditions, however, may also be affected [2]. To our knowledge, we report the first case of vertebral osteomyelitis due to \textit{R. equi} in a liver transplant recipient. We also review other cases of \textit{R. equi} infection in patients undergoing solid-organ transplantation.

Case Report and Review of the Literature

A 39-year-old male farmer with decompensated cryptic liver cirrhosis underwent liver transplantation in March 1994. Immunosuppressive treatment was administered with antilymphocyte globulin, cyclosporin A, corticosteroids, and azathioprine. Apart from poor control of preexisting diabetes mellitus, the postoperative course was uneventful.

In October 1994 the patient was readmitted for left-sided pleuritic chest pain. He was afebrile and otherwise generally well. Physical examination findings were unremarkable apart from crepitations at the base of the left lung. Laboratory tests revealed a normal WBC count and a slightly elevated C-reactive protein (CRP) level (28 mg/L; normal, <10 mg/L). A chest radiograph showed an infiltrate in the left lower lobe.

Treatment with cefotaxime resulted in resolution of the infiltrate. Two months later the patient again presented with left-sided pleuritic chest pain. At this time he was dyspneic and tachycardic but afebrile. The CRP level was markedly elevated (123 mg/L), whereas the WBC count was normal. On clinical examination the thoracic spine and the left paravertebral region were tender to palpation. Chest radiography again revealed a left-lower-lobe infiltrate. A CT scan showed a small pleura-based lesion of 1.5 cm in diameter with central necrosis. Bronchoscopy with bronchoalveolar lavage (BAL) and repeated CT-guided biopsies were nondiagnostic. Eight days of cefotaxime treatment again resulted in normalization of the CRP level and clinical improvement.

During the ensuing 9 months, the patient continued to complain of chronic back and left-sided chest pain. An unexplained febrile episode resolved with empirical antibiotic therapy with cefaclor. In September 1995 the patient was readmitted with incapacitating back pain. An admission radiograph of the spine showed sclerosis and wedge-shaped deformities of TH 11 and TH 12. A radionuclide bone scan showed markedly increased uptake in this area, which was believed to be due to consolidation of a steroid-induced osteoporotic fracture.

Within 5 days the patient developed fevers and progressive respiratory distress requiring intubation and mechanical ventilation. Chest radiography showed generalized interstitial infiltrates with consolidation of the right lower lobe. Sputum, BAL fluid, and blood cultures yielded \textit{R. equi}. The patient was treated with erythromycin and imipenem for 2 weeks, followed by erythromycin monotherapy.
Postoperatively, the patient received intravenous imipenem, vancomycin, and erythromycin for 14 days and then oral clarithromycin and rifabutin. This antibiotic regimen resulted in a slight increase of transaminase levels but was otherwise tolerated well. The patient was discharged while receiving maintenance antibiotic therapy in February 1996 and has remained asymptomatic since.

A literature search with use of MEDLINE and a subsequent review of reports referenced in identified articles revealed 12 other patients with \textit{R. equi} infection following solid-organ transplantation [2–13] (table 1). All affected patients were receiving immunosuppressive medication, with the exception of one kidney transplant recipient, who had not had immunosuppressive therapy for 3 years (following an unsuccessful kidney grafting) [9]. In all patients rhodococcal infection presented late after transplantation (median, 4 years; range, 19 months [4] to 15 years [7]). Exposure to farm animals was reported in only two cases [4, 10]; in four cases contact with contaminated soil or manure was considered a likely infectious source [5, 11–13].

Ten patients had pulmonary and/or pleural involvement. One patient had no clinical symptoms of pulmonary disease [13], despite significant chest radiographic and CT changes. Pulmonary cavitation or abscess formation was reported in seven patients. Associated extrapulmonary disease, including femoral osteomyelitis [6], paraspinal [7] and subcutaneous [2, 13] abscess formation, and pericarditis [9], was documented in five patients. In two patients, extrapulmonary disease manifested as late as 5 months [7] and 2 years [6] after the initial pulmonary infection. Two patients developed exclusively extrapulmonary infections after skin injuries [5, 11].

In 11 cases \textit{R. equi} infection was confirmed by culture of abscess material. Blood cultures were positive for four patients and negative for two patients [4, 13]. One patient had positive sputum cultures [4], whereas sputum was nondiagnostic in four cases [3, 7, 10, 13]. The average time lag between the first occurrence of symptoms attributable to rhodococcal infection and identification of the organism was 2–5 months. In one patient \textit{R. equi} was initially misidentified as a commensal diphtheroid [6].

Two renal transplant recipients died. One patient [8] had relapsing pneumonia unresponsive to erythromycin, cefuroxime, and subsequent triple-drug tuberculostatic therapy. The second patient’s condition [4] improved radiologically with erythromycin and gentamicin therapy before she succumbed to noninfectious complications. All patients received antimicrobial therapy, and six patients were also treated surgically. Most patients received erythromycin and/or ciprofloxacin in combination therapy, which was generally associated with successful outcome. Recurrent disease was observed after initial treatment with imipenem and tobramycin in the fatal case mentioned above [8] and in all three patients receiving monotherapy [3, 4, 12].

\textbf{Discussion}

Solid-organ transplant recipients are rarely affected by \textit{R. equi}. As in patients with HIV infection or other underlying

\textbf{Figure 1.} Sagittal T$_2$-weighted MRI of the thoracic spine in October 1995 showed \textit{Rhodococcus equi} spondylodiscitis at TH 11/12 and destruction of the adjacent upper and lower vertebral body plate. There is marked perifocal edema (\textit{A} = anterior; \textit{P} = posterior).

In November 1995 MRI showed massive spondylodiscitis of TH 11/12 (figure 1), with paraspinal and intraspinous abscess formation. Neurological symptoms were absent. A posterior costotransversectomy at TH 11, with drainage of the paraspinal abscess and removal of the infected bone, was performed. Culture of the drained pus yielded \textit{R. equi}. The isolate’s growth patterns and antibiotic susceptibilities were identical to those of the isolate recovered 2 months previously.
Table 1. Characteristics of 13 solid-organ transplant recipients with *Rhodococcus equi* infection and data pertaining to diagnosis, treatment, and outcome.

<table>
<thead>
<tr>
<th>Case no. [reference]</th>
<th>Patient’s age (y)/ sex</th>
<th>Graft</th>
<th>Immuno-suppressive agents given</th>
<th>Clinical presentation</th>
<th>Pulmonary involvement</th>
<th>Source of isolate and/or means of recovery</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [3]</td>
<td>35/F</td>
<td>Kidney</td>
<td>Pred, Aza</td>
<td>Pleuritic chest pain, fever, nonproductive cough</td>
<td>Infiltrate LUL, cavitating next 2 mo</td>
<td>Abscess</td>
<td>Tet (10 d); lobectomy</td>
<td>Resolution</td>
</tr>
<tr>
<td>2 [4]</td>
<td>45/F</td>
<td>Kidney</td>
<td>Pred, Aza</td>
<td>Cough, fever, chest pain, later hemoptysis</td>
<td>Abscess LUL</td>
<td>Bronchial brush biopsy; sputum</td>
<td>AmB + 5-FC + Amp (10 d); Em, Gm (maintenance)</td>
<td>Radiological improvement; death due to ischemic heart disease, pancytopenia</td>
</tr>
<tr>
<td>3 [5]</td>
<td>35/M</td>
<td>Kidney</td>
<td>Pred, Aza</td>
<td>Infected wound (burn)</td>
<td>NR</td>
<td>Biopsy; pus</td>
<td>Amp (repeated courses)</td>
<td>Multiple recurrences</td>
</tr>
<tr>
<td>4 [6]</td>
<td>57/M</td>
<td>Kidney</td>
<td>Pred, Aza</td>
<td>Femur osteomyelitis and abscess</td>
<td>Abscess RUL, surgically resected 2 y earlier</td>
<td>Tissue culture; “diphtheroids” noted in lung biopsy and urine specimens 2 y previously</td>
<td>Surgical drainage; Em, Vm, Em, TMP-SMZ (maintenance)</td>
<td>Resolution</td>
</tr>
<tr>
<td>5 [7]</td>
<td>52/F</td>
<td>Kidney</td>
<td>Pred, Aza</td>
<td>Backache, fever, paraspinal abscess</td>
<td>Thickening of adjacent pleura</td>
<td>Abscess</td>
<td>Surgical drainage; Em, Rif (2 w); Em (10 w)</td>
<td>Resolution</td>
</tr>
<tr>
<td>6 [8]</td>
<td>62/M</td>
<td>Kidney</td>
<td>Cysp, Pred, Aza</td>
<td>Pneumonia, fever</td>
<td>Bilateral pneumonia, pleural effusion; recurrence with consolidation (RUL + RML) and pleural effusion</td>
<td>Right lung; all other samples negative (autopsy)</td>
<td>Surgical drainage; Em, Rif (10 d); Em, Cfr (20 d); Rif, Eih, INH (10 d)</td>
<td>Death due to recurrent pneumonia</td>
</tr>
<tr>
<td>7 [9]</td>
<td>29/F</td>
<td>Kidney (failed)</td>
<td>None</td>
<td>Cough, weight loss, chest pain, fever, pericarditis</td>
<td>Pleural effusion</td>
<td>Pericardial effusion</td>
<td>Surgical drainage; INH, Rif, Amk; Vm (1 mo); Em, Rif (maintenance)</td>
<td>Resolution</td>
</tr>
<tr>
<td>9 [10]</td>
<td>38/F</td>
<td>Heart</td>
<td>Cysp, Pred, Aza</td>
<td>Cough, fever, weight loss</td>
<td>Cavitary lesion RUL, pleural thickening</td>
<td>BAL fluid, fine-needle aspirate, blood</td>
<td>Vm, Cpx (15 d); Cpx, AmC (4 mo)</td>
<td>Resolution</td>
</tr>
<tr>
<td>10 [11]</td>
<td>65/M</td>
<td>Heart</td>
<td>Pred, Aza</td>
<td>Subcutaneous abscess Cough, dyspnea, fever</td>
<td>NR Initially no pneumonia; relapse with pneumonia (RLL) and mediastinal lymph node abscess</td>
<td>Abscess</td>
<td>Surgical drainage</td>
<td>Mino (4 mo); Tei, Gm (maintenance)</td>
</tr>
<tr>
<td>11 [12]</td>
<td>57/M</td>
<td>Lung</td>
<td>Cysp, Pred, Aza</td>
<td>Subcutaneous abscess, fever, no pulmonary symptoms</td>
<td>Necrotizing bilateral pneumonia, abscess LLL</td>
<td>Abscess</td>
<td>Surgical drainage; Em, Cpx, Rif (2 mo); Em, Cpx (maintenance)</td>
<td>Resolution</td>
</tr>
<tr>
<td>12 [13]</td>
<td>58/M</td>
<td>Liver</td>
<td>Cysp, Pred, Aza</td>
<td>Recurrent pneumonia, fever, chest pain, back pain, vertebral osteomyelitis, and paraspinal abscess</td>
<td>Recurrent pneumonia, abscess LLL</td>
<td>Sputum, BAL fluid, blood (during severe recurrent pneumonia); abscess, bone</td>
<td>Ctx (repeated courses); Em, Lmi (3 w); Em (3 w); Lmi, Vm, Em (2 w); Clm, Rib (maintenance)</td>
<td>Multiple recurrences, resolution after surgery and maintained antibiotic therapy</td>
</tr>
<tr>
<td>13 [PR]</td>
<td>39/M</td>
<td>Liver</td>
<td>Cysp, Pred, Aza</td>
<td>Recurrent pneumonia, abscess LLL</td>
<td>Bronchial abscess</td>
<td>Sputum, BAL fluid, blood</td>
<td>Ctx (repeated courses); Em, Lmi (3 w); Em (3 w); Lmi, Vm, Em (2 w); Clm, Rib (maintenance)</td>
<td>Multiple recurrences, resolution after surgery and maintained antibiotic therapy</td>
</tr>
</tbody>
</table>

**NOTE.** AmB = amphotericin B; AmC = amoxicillin/clavulanate; Amik = amikacin; Amp = ampicillin; AzA = azathioprine; BAL = bronchoalveolar lavage; 5-FC = 5-fluorocytosine; Cfr = cefotaxime; Clm = clarithromycin; Cpx = ciprofloxacin; Ctx = cefotaxime; Cysp = cyclosporin A; Em = erythromycin; Eth = ethambutol; Gm = gentamicin; Imi = imipenem; INH = isoniazid; LLL = left lower lobe; LUL = left upper lobe; Mino = minocycline; NR = not reported; PR = present report; Pred = prednisolone; Rif = rifabutin; Rif = rifampin; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; Tei = teicoplanin; Tet = tetracycline; Tm = tobramycin; TMP-SMZ = trimethoprim-sulfamethoxazole; Vm = vancomycin.
immunocompromising conditions, the lungs are the most commonly affected organs. Extrapulmonary manifestations were observed in 6 of 11 transplant recipients (54%) with pulmonary rhodococcal infection but in only 10 of 72 cases (7%) reported in a recent literature review [14]. Soft-tissue infection was quite common in transplant recipients. Two other patients had involvement of bony structures, which otherwise is rarely seen in human rhodococcal infection [15, 16].

Vertebral osteomyelitis due to \textit{R. equi} is a well-documented complication of rhodococcal infection in foals; however, to our knowledge, its occurrence in humans has not previously been described. The reported mortality associated with rhodococcal infection in transplantation patients (two of 13 died) was comparable to the mortality rate of 20% observed among patients with immunocompromising conditions other than HIV infection [14].

The diagnosis of human \textit{R. equi} infection is often delayed [14]. For the patient reported, the diagnosis of pyogenic vertebral osteomyelitis was not entertained earlier because osteoporosis is very common and by far the most likely cause of back pain in transplant recipients [17]. Furthermore, initial treatment with cefotaxime resulted in clinical improvement. This was unexpected but is in agreement with recent reports of the inhibitory activity [18] of cefotaxime, which may also explain the inability to culture the organism early in the disease course. Monotherapy must be considered insufficient for transplant recipients with \textit{R. equi} infection. Long-term maintenance therapy might be warranted, considering the necessity of continuous immunosuppressive medication in these patients.

In summary, \textit{R. equi} must be included in the differential diagnosis of recurrent pneumonia or lung abscess in transplant recipients. Metastatic spread of the infection is common in these patients, and diagnosis of pulmonary rhodococcal infection should prompt a search for additional involvement of extrapulmonary sites.

References