Actinomyces odontolyticus Bacteremia

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We describe two immunosuppressed female patients with fever and Actinomyces odontolyticus bacteremia, a combination documented once previously in an immunocompetent male patient. The patients were treated with doxycycline and clindamycin; these drugs, with β-lactams, are effective treatment for *A. odontolyticus* infections.

Actinomycosis is a disease of antiquity, having most likely infected the jaw of a fossil rhinoceros (1) and the ribs of a man discovered in southeastern Ontario, Canada, who by radiocarbon dating lived 230 A.D. ± 55 (2). In 1877, Bollinger and Harz (3) named the genus *Actinomyces* when they described the etiologic agent of bovine actinomycosis ("lumpy jaw") and called it *Actinomyces bovis*. However, this organism has never been convincingly proven to cause actinomycosis in humans (4), nor has it been isolated from human mucosa or other human sources.

The major human pathogen for actinomycosis, *A. israelii*, was identified in two patients in 1878 and fully delineated by Israel (5). In 1891, Wolff and Israel (6) described the cultural characteristics and its anaerobic growth. Since then, studies have identified *A. naeslundii*, *A. viscosus*, *A. pyogenes*, *A. denticolens*, *A. howellii*, *A. hordeovulneris*, and *A. meyeri* in humans as well as in dogs and cats. Actinomycosis is the most common infectious disease of kangaroos (7).

In 1958, Batty (8) isolated *A. odontolyticus* from persons with advanced dental caries. During the ensuing 40+ years, 23 patients with invasive infection caused by *A. odontolyticus* have been described in North America, Europe, and Asia (9–25). Thirteen patients had pulmonary, cardiopulmonary or mediastinal disease, 4 had soft tissue infections, 2 had abdominal involvement, 2 had pelvic involvement, 1 had a brain abscess, and 1 other had bimicrobial bacteremia with *Fusobacterium necrophorum*. We describe two cases, in 1998 and 1999, involving immunocompromised patients with fever and bacteremia resulting from *A. odontolyticus* and consider the 23 previously described.

Case Reports

**Patient 1**

In March 1999, a 62-year-old white woman who had worked as a chemotherapy nurse from 1973 to 1979 sought treatment at Eisenhower Medical Center after having pain in her left knee for 2 weeks. Magnetic resonance imaging indicated a left lateral meniscus tear. A routine preoperative complete blood count (CBC) showed a leukocyte count of 6.8 x 10^9/L, hemoglobin (Hb) of 82 g/L, hematocrit (Hct) of 0.26, and a thrombocyte count of 95 x 10^9/L. Examination of the peripheral smear demonstrated frequent blasts with no discernible Auer rods. Flow cytometric analysis of a bone marrow biopsied sample showed involvement with > 30% blasts that were positive for CD13, CD33, CD34, CD117, CD19, and TdT-negative. The markers and morphologic characteristics were consistent with acute myelocytic leukemia, monocytes with aberrant expression of CD19, a B-cell marker. Cytogenetics showed a normal 46,XX female chromosome complement. Fluorescence in situ hybridization (FISH) using polymerase chain reaction (PCR) techniques showed no evidence for monosomy, trisomy 8, or partial deletions of the long arm of chromosome 5 or 7.

Induction chemotherapy consisting of 3 days of idarubicin at 12 mg/m^2 daily and 7 days of cytosine arabinoside by continuous infusion at 100 mg/m^2 was given to the patient. Four days post-treatment, a temperature of 39°C developed in the patient. The CBC showed the leukocyte count was 6.8 x 10^9/L, Hb was 82 g/L, Hct was 0.26, and thrombocyte count was 93 x 10^9/L. Two of four blood cultures (using blood agar, CNA, and Brucella agar) grew *A. odontolyticus* in 24–48 hours. Because of a penicillin allergy, 100 mg of doxycycline was given intravenously to the patient every 12 hours for 2 weeks. Follow-up blood cultures were sterile. The patient’s dental health appeared normal and no source for the bacteremia was identified. The patient entered complete remission. The second cycle of consolidation chemotherapy was also complicated by fever. *Capnocytophaga* spp was isolated from the patient’s blood using blood agar supplemented with CO_2. A fastidious streptococcus that did not grow on agar was also isolated. Oral surgical consultation was obtained and evidence for a dental abscess was uncovered. The abscess was treated with clindamycin. Thirty months after the first consolidation chemotherapy, the patient remained in remission.

**Patient 2**

A 69-year-old white woman had experienced good health until she sought treatment in May 1998 at Eisenhower Medical Center. She reported a 6-month history of worsening generalized abdominal pain, nausea, vomiting, diarrhea, and weight loss. Blood serologic tests indi-

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cated an erythrocyte sedimentation rate (ESR) of 62 mm/h and positive antinuclear antibodies (ANA) at a titer of 640 (homogeneous) but negative cryoglobulins, lupus antico-
agulant, antineutrophil cytoplasmic antibodies (c-ANCA),
and cardiolipin antibodies. Quantitative immunoglobulins
were normal; an upper gastrointestinal series and computer-
ized tomographic scan of the abdomen showed no abnor-
malities. A colonoscopy showed diverticulosis coli with no
other deformities. Magnetic resonance angiography
showed substantial stenosis of the right subclavian, right
brachial, superior mesenteric, bilateral renal, and external
iliac arteries. Giant cell arteritis was diagnosed in the
absence of a confirming biopsy, and the patient received
60 mg prednisone daily. The patient showed no measura-
ble clinical improvement for 7 days. Consequently, aza-
 thioprine therapy at 50 mg daily was initiated. Four days
later, a temperature of 39°C and chills developed in the
patient. Blood cultures using blood agar, CNA, and
Brucella agar grew *A. odontolyticus* in 24–48 hours.
Because of allergies to penicillin, cephalosporin, and teta-
cycline, clindamycin was given to the patient for 14 days.
The recovery was uneventful, and clinical evidence did not
indicate dental disease.

*Actinomyces odontolyticus* is an anaerobic, facultative
capnophilic, gram-positive, nonsporulating, non–acid fast,
non-motile, irregularly staining bacterium. Sometimes
short or medium-sized rods resembling diphtheroids are
seen. Shorter rods resembling propionibacteria are fre-
quently seen with *A. odontolyticus* and may be arranged in
palisades as well as other diphtheroidal arrangements.
On blood agar, the bacteria develop as small, irregular, whitish
colonies that are smooth to slightly granular and show a
dark red pigment when mature (2–14 days). This pigmen-
tation is most obvious when the cultures are left standing in
air at room temperature after primary anaerobic isolation.
The organism also grows well on CNA and Brucella agar.

Definitive identification is made by negative catalase and
oxidase tests, the reduction of nitrate to nitrite, fila-
mentation of microcolonies, and absence of growth at pH
5.5. Generally, the fermentation reactions are variable.

*A. odontolyticus* was speciated in these two case-
patients by using the RapID ANA II System (Remel Inc.,
Lenexa, KS), a qualitative microsystem using convention-
al and chromogenic substrates for the identification by disc
diffusion of anaerobic bacteria of human origin. Both
strains were sensitive to penicillin, ampicillin, cephapirimicins,
tetracycline, clindamycin, chloramphenicol, and erythromycin.

**Discussion**

The previously described and the two present case-
patients are summarized in the Table. Most are men (14 vs.
9 women, with 2 of unknown sex), and the mean age is 50
years. Five patients were immunosuppressed: two had
received prednisone, one had received chemotherapy, and
two had organ transplants. Two of the 25 patients were
known to be alcoholic, and 3 were noted to have periodont-
dental disease.

Clinical disease in patients with *A. odontolyticus* closely
resembles disease caused by *A. israelii* and other actin-
omyces species. Similar to *A. israelii* infections, those
caused by *A. odontolyticus* primarily involve the cervico-
facial regions, the chest, abdomen, and pelvis with rare
involvement of the central nervous system, bones, and
joints. Additional similarities include a more frequent
occurrence in men than women and a peak incidence in the
middle decades of life. Clinical features in 97% of 181
patients with actinomycosis including the following: mass
or swelling, pulmonary disease, draining abscesses,
abdominal disease, dental disease, and intracranial infec-
tion (26).

Only two deaths were recorded: one patient died with a
brain abscess and another with mediastinitis. The patients
responded to various β-lactam therapies including peni-
cillins, cephalosporins, carbapenems as well as macrolides, lincosides, and tetracycline. Responses to imi-
dazole were unpredictable, and the patient with a brain
abscess caused by *A. odontolyticus* was administered
metronidazole and did not recover (11).

**Conclusions**

As with all other actinomycotic diseases, *A. odontolyti-
cus* is an endogenous infection arising from the mucous
membranes. Batty (8), after some experience, was able to
isolate the organism from the dentine of 90% of subjects
studied, while Mitchell and Crow (27) isolated *A.odon-
tolyticus* in female genital tract specimens from 4.8% of
women fitted with intrauterine contraceptive devices, in
4% of women with pelvic inflammatory disease, and in
1.8% of women without pelvic inflammatory disease.

The capacity of actinomycetes to colonize mucosal sur-
faces and dentine appears to depend on two distinct fimбри-
æ, type 1 and type 2, that bind preferentially to salivary
acidic proline-rich proteins and to statherin, or to β-linked
galactose or galactosamine structures on epithelial or bac-
terial surfaces, respectively (28).

We believe that patient 1 (with acute leukemia) had a
dental abscess, probably secondary to *A. odontolyticus*,
that served as a portal for the bacteremia. Of the 23 previ-
ously reported case-patients of *A. odontolyticus* infection,
only one (an otherwise healthy 20-year-old man [9]) had
bacteremia. The two reported case-patients were women:
one had received chemotherapy for acute granulocytic
leukemia and the other had received high dose corticos-
steroids for vasculitis. Immunosuppression probably played
a major role in the etiology of bacteremic *A. odontolyticus*
infection. Further studies to evaluate possible mechanisms would be appropriate.

Dr. Cone is an infectious diseases clinician at the Eisenhower Medical Center, assistant clinical professor of medicine at University of California at Los Angeles, and clinical professor of medicine at University of California, Riverside. His research interests include genetics, immune deficiencies, and sepsis.

References


Table. Reported cases of *Actinomyces odontolyticus* infection

<table>
<thead>
<tr>
<th>Case</th>
<th>Y (Ref)</th>
<th>Disease</th>
<th>Age/Sex</th>
<th>Underlying disease</th>
<th>Presentation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(PR)</td>
<td>Bacteremia</td>
<td>62/F</td>
<td>Acute myelogenous leukemia</td>
<td>Fever</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>2</td>
<td>(PR)</td>
<td>Bacteremia</td>
<td>69/F</td>
<td>Vasculitis, immunosuppression</td>
<td>Fever, chills</td>
<td>Clindamycin</td>
</tr>
<tr>
<td>3</td>
<td>1999 (25)</td>
<td>Pericardial, pleural effusions</td>
<td>68/M</td>
<td>S/P resection malignant gastric polyp</td>
<td>Fever, dyspnea</td>
<td>Ceftriaxone, amoxicillin</td>
</tr>
<tr>
<td>4</td>
<td>1997 (24)</td>
<td>Empyema</td>
<td>50/M</td>
<td>S/P pneumonectomy for tuberculosis and aspergillosis, alcoholism</td>
<td>Fever, dyspnea, chest pain</td>
<td>N/S</td>
</tr>
<tr>
<td>5</td>
<td>1997 (23)</td>
<td>Mediastinitis</td>
<td>43/M</td>
<td>Heart-lung transplant, immunosuppression</td>
<td>Sternal wound drainage</td>
<td>Penicillin</td>
</tr>
<tr>
<td>6</td>
<td>1996 (23)</td>
<td>Pneumonia</td>
<td>61/M</td>
<td>Lung transplant, immunosuppression</td>
<td>Chest pain</td>
<td>Penicillin</td>
</tr>
<tr>
<td>7</td>
<td>1995 (22)</td>
<td>Empyema</td>
<td>40/M</td>
<td>Chronic bronchitis, alcoholism</td>
<td>Fever, chest pain, cough</td>
<td>Penicillin</td>
</tr>
<tr>
<td>8</td>
<td>1994 (21)</td>
<td>Pneumonia, cutaneous abscess</td>
<td>52/M</td>
<td>Periodontal disease, alcoholism</td>
<td>Fever, weight loss, cutaneous drainage</td>
<td>Penicillin</td>
</tr>
<tr>
<td>9</td>
<td>1993 (20)</td>
<td>Thoracic abscess</td>
<td>N/S</td>
<td>N/S</td>
<td>N/S</td>
<td>N/S</td>
</tr>
<tr>
<td>10</td>
<td>1992 (19)</td>
<td>Pneumonia</td>
<td>52/F</td>
<td>Bronchietasis</td>
<td>Fever, weight loss</td>
<td>Imipenem, tetracycline</td>
</tr>
<tr>
<td>11</td>
<td>1992 (18)</td>
<td>Empyema</td>
<td>38/F</td>
<td>Periodontal disease</td>
<td>Fever, chest pain, dyspnea, cough, weight loss</td>
<td>Penicillin</td>
</tr>
<tr>
<td>12</td>
<td>1990 (17)</td>
<td>Pleural lesion, chest wall erosion, spinal and muscle abscesses</td>
<td>58/F</td>
<td>None</td>
<td>Fever, chest pain, weight loss</td>
<td>Penicillin, metronidazole</td>
</tr>
<tr>
<td>13</td>
<td>1985 (16)</td>
<td>Submaxillary gland</td>
<td>65/M</td>
<td>None</td>
<td>Swelling of neck, lymphadenopathy</td>
<td>Tetracycline</td>
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<tr>
<td>14</td>
<td>1985 (16)</td>
<td>Arm abscess</td>
<td>47/M</td>
<td>None</td>
<td>Fever, swelling, erythema of arm</td>
<td>Penicillin, gentamicin, metronidazole</td>
</tr>
<tr>
<td>15</td>
<td>1985 (16)</td>
<td>Pelvic infection</td>
<td>30/F</td>
<td>None</td>
<td>Infected intrauterine device</td>
<td>Device removed, metronidazole</td>
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<tr>
<td>16</td>
<td>1985 (16)</td>
<td>Pelvic abscess</td>
<td>54/F</td>
<td>Alcoholism</td>
<td>Fever, pelvic pain</td>
<td>Tobramycin</td>
</tr>
<tr>
<td>17</td>
<td>1985 (16)</td>
<td>Thumb abscess</td>
<td>40/M</td>
<td>None</td>
<td>Fishbone injury to thumb</td>
<td>Cephalexin</td>
</tr>
<tr>
<td>18</td>
<td>1985 (16)</td>
<td>Bacteremia</td>
<td>19/M</td>
<td>None</td>
<td>Confusion, icterus, fever</td>
<td>Penicillin, metronidazole</td>
</tr>
<tr>
<td>19</td>
<td>1985 (15)</td>
<td>Enterocutaneous fistula</td>
<td>78/M</td>
<td>Diverticulitis, abdominal abscess</td>
<td>Fever, pelvic pain</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>20</td>
<td>1982 (14)</td>
<td>Cholestasis</td>
<td>43/F</td>
<td>None</td>
<td>Abdominal pain</td>
<td>Doxycycline</td>
</tr>
<tr>
<td>21</td>
<td>1979 (13)</td>
<td>Pulmonary abscess</td>
<td>61/F</td>
<td>Rheumatoid arthritis, prednisone</td>
<td>Fever, dyspnea, chest pain</td>
<td>Tetracycline, clindamycin</td>
</tr>
<tr>
<td>22</td>
<td>1979 (12)</td>
<td>Brain abscess</td>
<td>34/M</td>
<td>None</td>
<td>Headache, vomiting, fever</td>
<td>Penicillin, metronidazole</td>
</tr>
<tr>
<td>23</td>
<td>1977 (11)</td>
<td>Empyema</td>
<td>N/S</td>
<td>N/S</td>
<td>N/S</td>
<td>N/S</td>
</tr>
<tr>
<td>24</td>
<td>1977 (10)</td>
<td>Cellulitis</td>
<td>54/M</td>
<td>None</td>
<td>Cheek mass</td>
<td>Penicillin</td>
</tr>
<tr>
<td>25</td>
<td>1974 (9)</td>
<td>Thoracic wall abscess</td>
<td>26/M</td>
<td>None</td>
<td>Subcutaneous chest mass</td>
<td>Clindamycin, penicillin</td>
</tr>
</tbody>
</table>

*PR*, present report; F, woman; M, man; S/P, status post; N/S, not stated.


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