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 ever 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.

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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/m² daily and 7 days of cytosine arabinoside by continuous infusion at 100 mg/m² 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-

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 anticoagulant, antineutrophil cytoplasmic antibodies (c-ANCA), and cardiolipin antibodies. Quantitative immunoglobulins were normal; an upper gastrointestinal series and computerized tomographic scan of the abdomen showed no abnormalities. 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 measurable clinical improvement for 7 days. Consequently, azathioprine 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 tetracycline, 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 frequently 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 pigmentation 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, filamentation 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 conventional and chromogenic substrates for the identification by disc diffusion of anaerobic bacteria of human origin. Both strains were sensitive to penicillin, ampicillin, cephalosporins, 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 periodontal disease.

Clinical disease in patients with *A. odontolyticus* closely resembles disease caused by *A. israelii* and other actinomyces species. Similar to *A. israelii* infections, those caused by *A. odontolyticus* primarily involve the cervicofacial 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 infection (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 penicillins, cephalosporins, carbapenems as well as macrolides, lincosides, and tetracycline. Responses to imidazoles 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. odontolyticus* 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. odontolyticus* 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 surfaces and dentine appears to depend on two distinct fimbriae, 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 bacterial 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 previously 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 corticosteroids for vasculitis. Immunosuppression probably played a major role in the etiology of bacteremic *A. odontolyticus*

Table. Reported cases of *Actinomyces odontolyticus* infection

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

[a](PR), present report; F, woman; M, man; S/P, status post; N/S, not stated.

infection. Further studies to evaluate possible mechanisms would be appropriate.

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