**Klebsiella ozaenae** Septicemia Associated with Hansen’s Disease

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Two cases of *Klebsiella ozaenae* septicemia from the National Hansen’s Disease Center, Carville, La., are discussed: one fatal and one nonfatal. Although both patients had nasal complications of Hansen’s disease (leprosy), the organism was grown initially from spinal fluid, blood, and wound cultures. This report confirms the potential pathogenicity of the *K. ozaenae* species and its widening disease spectrum.

Klebsiella infections usually result from *K. pneumoniae* species (3), but recent reports have documented the importance of infections with other *Klebsiella* species (1, 5, 6, 8). *K. ozaenae* and *K. rhinoscleromatis* infections are relatively rare and usually confined to patients with chronic rhinitis, sinusitis, or nasal atrophy (8). At the National Hansen’s Disease Center in Carville, La., chronic rhinitis is seen frequently with lepromatous Hansen’s disease (HD; leprosy). Colonization of the nasopharynx with *K. ozaenae* is not rare; nearly 20% of all positive nasal and sputum cultures include *K. ozaenae* in mixed cultures. However, bacteremia with *K. ozaenae* is rare, reported in only five cases to date, and all but one of these were fatal (1, 5, 6).

We wish to report two additional cases of *K. ozaenae* septicemia, both of which emphasize the widening spectrum of disease caused by this organism.

**Case reports.** (i) **Case 1.** A 74-year-old white male with emphysema, antrhacilicosis, chronic obstructive pulmonary disease, hypertension, obesity, alcoholic liver disease, and inactive lepromatous HD had chronic atrophic rhinitis with nasoseptal perforation. He was treated for acute *Haemophilus influenzae* otitis in mid-December of 1976, but 10 days later he was brought to the hospital unresponsive and hyperventilating at 52/min with a stiff neck and a right-sided Babinski sign. The temperature was 39.0°C; pulse was 110/min. Lumbar puncture revealed an opening pressure of 420 mm, cloudy spinal fluid, 919 neutrophils and 186 lymphocytes per mm³ of spinal fluid, and gram-negative rods on smear. The leukocyte count was 7,200/mm³ with 42% bands. The blood urea nitrogen was 33 mg/dl, and creatinine was 1.4 mg/dl; he was given 5 days of dexamethasone and intravenous gentamicin (80 mg every 9 h) and intravenous carbenicillin (7 g every 6 h) for 8 days. When the patient awoke and became agitated, he was sedated with chloridiazepoxide and given vitamin supplements. Two of four blood cultures and the spinal fluid culture grew *K. ozaenae* (as classified by Edwards and Ewing [2]) in the API 20E system (Analytab Products, Inc., Plainview, N.Y.). The strain was sensitive to ampicillin, chloramphenicol, carbenicillin, and the aminoglycosides as measured with standardized disk agar diffusion techniques (C. Thornsberry, Centers for Disease Control Laboratory Update no. 80-22, Bacteriology Division, Atlanta, Ga., January 1980). Cultures of thick sputum yielded *Citrobacter diversus*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, and urine cultures also grew *S. aureus* and *C. diversus*. After the first week, treatment was changed to oral ampicillin and intramuscular gentamicin until the patient relapsed with fever, dehydration, and recurrent obtundation in spite of normal renal function. Intravenous gentamicin was restarted and continued until day 12 of hospitalization, by which time there was resolution of his neurological signs. A repeat spinal tap on day 14 of hospitalization was normal. The patient felt better, was afebrile, had a leukocyte count of 5,300/mm³ with only 4% bands, and had normal chemistries. On day 22 of hospitalization, shortly after voiding, the patient suddenly became tremulous and died, possibly from acute myocardial infarction. An autopsy was not performed.

(ii) **Case 2.** A 16-year-old Philippino-born white male was referred to Carville in March 1980 with active lepromatous HD, fevers, chills, myalgias, arthralgias, and a systemic rash. For 4 weeks he had been taking 60 mg of prednisone daily; 3 weeks before admission he burned his hand without feeling it, and his dermatologist
diagnosed HD with a skin biopsy highly positive for acid-fast organisms. The patient had subacute rhinitis with frequent epistaxis on arrival at Carville. He was initially afebrile and normotensive. Physical examination revealed a weak, tremulous boy with erythematous, warm, and indurated lesions covering the face and body. The nose was crusty with dried blood, a purulent exudate, and mucosal inflammation, but the septum was not perforated. The extremities were swollen and cyanotic with multiple nontender lepomas and several tender nodules over the arms and legs. Skin scrapings were highly positive for bacilli all over the body. A skin biopsy from the left lower leg revealed active lepromatous HD and erythema nodosum leprosum with high bacteriological and morphological indices (11). Prednisone was continued for severe reaction (60 to 100 mg daily), and the hands and wrists were splinted. The patient’s glucose 6-phosphate dehydrogenase enzyme activity was normal, and dapsone (100 mg daily) and rifampin (600 mg daily) treatment was begun. The patient deteriorated clinically, however, with high fevers, lymphadenopathy, and weakening of the bands bilaterally. He suffered a transient right-sided facial nerve paresis, reversed only with high doses of prednisone (100 to 200 mg daily). The hemoglobin dropped from 15 to 6 g/dl, and the hematocrit fell from 45 to 29%. The leukocyte count remained at 11,000/mm³ throughout his hospitalization, and platelets were normal.

The patient now had a temperature of 39°C and large, hemorrhagic skin ulcers. Dapsone and rifampin were discontinued, and clofazimine (B663, Lamprene) was started. K. ozaenae was grown from one leg ulcer and all four blood culture bottles. Although there was neither clinical nor radiographic evidence of pneumonia, induced sputum cultures grew K. pneumoniae. The patient was begun on intravenous ampicillin and gentamicin, but ampicillin was discontinued 3 days later and doxycycline was begun because the strain of K. ozaenae was seen to be resistant to ampicillin with less than an 11-mm zone of inhibition on disk agar diffusion plates. The patient responded well to 2 weeks of gentamicin and oral doxycycline, decreasing amounts of steroids, and iron supplements. After 3 months, he returned home on clofazimine (100 mg daily) and prednisone (50 mg on alternate days) therapy. Six and 12 months later, on follow-up examinations, the patient was asymptomatic. Nasal cultures grew S. aureus and K. ozaenae, but the strain of K. ozaenae isolated at 6 months was fully sensitive to ampicillin whereas that isolated at 12 months was again resistant to ampicillin.

Discussion. K. ozaenae is usually a pathogen of the nose in patients with chronic mucopurulent or atrophic rhinitis (8, 12). Recent reports suggest that, although K. ozaenae isolates are much rarer than K. pneumoniae, K. ozaenae infections may involve not only the head and neck but also the colon, urine, blood, soft tissues, and even the meninges and blood (1, 5, 6). Clinical features of seven patients with K. ozaenae septicemia described in the literature are shown in Table 1. Factors associated with K. ozaenae bacteremia include rhinitis and malignancy, alcoholism, immunosuppression, previous antibiotic usage, and old age, many of which predispose the host to gram-negative colonization in general (4, 7, 9, 10). Our first case of K. ozaenae septicemia was an elderly male with chronic pulmonary disease and alcoholism, and the second case, although young, was acutely ill with active lepromatous HD and erythema nodosum leprosum for which he was receiving high doses of prednisone. Besides this second case, only one other nonfatal case of K. ozaenae septicemia has been reported (case no. 3 of Table 1) (5).

Some strains of K. ozaenae appear to be sensitive to ampicillin and carbenicillin (1), unlike the antibiotic susceptibility of K. pneumoniae (3, 10). Both ampicillin-sensitive and ampicillin-resistant strains of K. ozaenae have been reported to cause septicemia, possibly depending upon previous antibiotic usage (1, 5). Resistant strains are appearing more frequently at the National Hansen’s Disease Center; in the second case reported, both sensitive and resistant types appeared at different times within the same patient. He probably had K. ozaenae colonization of the nares as well as the leg ulcer, but nasal cultures were not obtained on the first admission. Of the two K. ozaenae septicemia patients seen at Carville, the first patient’s organism was ampicillin sensitive, whereas the second patient’s blood isolate was ampicillin resistant. Of 16 strains of K. ozaenae isolated at Carville in 1980, all were sensitive to amikacin, cephalothin, chloramphenicol, gentamicin, kanamycin, streptomycin, and tetracycline. However, 81.2% were resistant to ampicillin, and 87.5% were resistant to carbenicillin.

Throughout 1980, about 200 Carville patients suffered from bacterial infections of the lower extremities, urine, upper extremities, respiratory tract, eye, soft tissues, and blood (given in descending order of frequency). From 24 patients, 40 isolates of Klebsiella species were obtained; 16 of the 40 isolates were due to K. ozaenae (40%), and they occurred in 12 of the 24 patients (50%) with Klebsiella isolates in 1980. Seventy-
Table 1. Characteristics of patients with K. ozaenae bacteremia

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Sex</th>
<th>Ethnic group</th>
<th>Sources</th>
<th>Diseases</th>
<th>Immunosuppression</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>M</td>
<td>W</td>
<td>Sputum, blood (not nose)</td>
<td>SLE, lung cancer, renal failure</td>
<td>Prednisone</td>
<td>Death</td>
<td>(1)</td>
</tr>
<tr>
<td>2</td>
<td>79</td>
<td>M</td>
<td>B</td>
<td>Blood (not spinal fluid)</td>
<td>Dementia, 2 CVAs, aortic stenosis, MI, pacemaker wire</td>
<td>No</td>
<td>Death</td>
<td>(1)</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>M</td>
<td>W</td>
<td>External ear, mastoid, blood</td>
<td>Alcoholic liver disease, diabetes, hypertension, otitis</td>
<td>No</td>
<td>Recovered</td>
<td>(5)</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>M</td>
<td>H</td>
<td>Stool, rectal fissure, blood</td>
<td>Acute myelomonocytic leukemia</td>
<td>6-Thioguanine, Ara-C, daunomycin</td>
<td>Death</td>
<td>(5)</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>M</td>
<td>B</td>
<td>Sputum, spinal fluid, blood</td>
<td>Seizures, meningitis</td>
<td>No</td>
<td>Death</td>
<td>(6)</td>
</tr>
<tr>
<td>6</td>
<td>74</td>
<td>M</td>
<td>W</td>
<td>Blood, spinal fluid (not nose)</td>
<td>Alcoholic liver disease, emphysema and COPD, atrophic rhinitis, otitis, meningitis, inactive HD</td>
<td>No</td>
<td>Death</td>
<td>This paper</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>M</td>
<td>W</td>
<td>Blood, nares, leg ulcer</td>
<td>Rhinitis, active lepromatous HD and ENL</td>
<td>Prednisone</td>
<td>Recovered</td>
<td>This paper</td>
</tr>
</tbody>
</table>

*W. White; B. black; H. hispanic.

SLE, Systemic lupus erythematosus; CVA, cerebrovascular accident; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; ENL, erythema nodosum leprosum.

Ara-C, Cytosine arabinoside.

Five percent (12/16) of the isolates appeared from sputum or ear, nose, and throat cultures, and the organisms grew usually as a colonizer among mixed flora. Exceptions were one woman on prednisone with exposure keratopathy, who grew K. ozaenae from eye cultures; an elderly man with chronic bronchitis, who grew K. ozaenae from a leg ulcer as well as sputum cultures, and the young boy described as case no. 2, who grew K. ozaenae from wound as well as blood cultures.

The two cases of K. ozaenae septicemia presented above show how K. ozaenae may become a serious pathogen in some immunocompromised or elderly, debilitated patients. Although relatively rare, K. ozaenae should be mentioned in future reports on Klebsiella bacteremias (10), recognizing that a widening spectrum of disease with this organism may be appearing in the future.

Literature Cited