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CASE REPORTS

Laryngeal Scleroma Associated with *Klebsiella pneumoniae* subsp. *ozaenae*

C. De Champs,[1,2]* J. F. Vellin,[3] L. Diancourt,[5] S. Brisse,[5] J. L. Kemeny,[4] L. Gilain,[3] and T. Mom[3]

Service de Bactériologie, Faculté de Médecine, 28 Place Henri-Dunant, 63001 Clermont-Ferrand, France[1]; Service de Bactériologie-Virologie-Hygiène, CHU Robert Debré, Rue du Général Koenig, 51092 Reims Cedex, France[2]; Service d'ORL, Hôpital Gabriel-Montpied, 63000 Clermont-Ferrand, France[3]; Service d'Anatomopathologie, Hôpital Gabriel-Montpied, 63000 Clermont-Ferrand, France[4]; and Unité Biodiversité des Bactéries Pathogènes Emergentes (INSERM U389), Institut Pasteur, 25-28 rue du Dr Roux, 75724 Paris Cedex, France[5]

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***Klebsiella pneumoniae* subsp. *ozaenae* was isolated from the pharynx of a woman with laryngeal scleroma. *K. pneumoniae* subsp. *ozaenae* is rarely isolated from clinical infections and has never been reported in laryngeal scleroma, which is usually caused by *K. pneumoniae* subsp. *rhinoscleromatis*.**

CASE REPORT

In 1999, a 33-year-old woman who was a native of Algeria was admitted to the otolaryngology ward for a 3-year evolutive chronic dysphonia. Her history showed that she had had idiopathic thrombopenic purpura and chronic maxillary sinusitis. Fibroscopic laryngeal examination revealed an irregularity of the right vocal cord. The larynx was mobile, and there was a purulent posterior discharge descending from her inflammatory nasal fossae. Computed tomography showed a mucosal hyperplasia of the maxillary sinus. Endoscopy of the upper respiratory tract under general anesthesia showed an indurate whitish lesion located at the front third of the right vocal cord, the anterior commissure, and the front subglottis and a second similar lesion at the front subglottis 1 cm below the vocal folds. Biopsy specimens were taken under a microscope. The lesions were then vaporized with a carbon dioxide laser device.

Histopathologic features revealed lymphoplasmocytic inflammation of the vocal cord and a subglottic lymphoplasmocytic hyperplasia with fibrosis of the underlying cord. The patient was treated with aerosol and speech therapy.

One year later, after a 3-week stay in Algeria, the patient again consulted for an increase in the dysphonia without dyspnea. Explorations were prescribed, including biologic examinations and laryngeal computed tomography. Blood samples were normal; and two lesions of calcic density were seen on the computed tomography scan, one at the right subglottis and the other at the anterior subglottal region. The diagnosis of laryngeal scleroma was evoked. A microlaryngoscopic exploration was performed and showed a glottal and a subglottal cartilaginous-like lesions. The second histopathological examination showed an inflammatory reorganization, including plasmocytes and giant histiocytes with piles of bacteria at the glottic level, tracheal parakeratosis, and bony metaplasia.

Bacteriological cultures of the glottal biopsy specimens were sterile. Nasal and pharyngeal swabs showed a combination of gram-negative bacilli and gram-positive cocci. *Klebsiella pneumoniae* subsp. *ozaenae* (isolate CH137), *Morganella morganii*, *Pseudomonas aeruginosa*, and alpha-hemolytic streptococci were isolated in cultures. The patient was treated with cefixime at 400 mg/day per os for 3 weeks and was seen 1 and 2 years later. Her voice had improved, but the scar of the front subglottal scleroma and the spreading inflammation of the nasal mucosa were persistent. Because scleroma can be caused by *Klebsiella pneumoniae* subsp. *rhinoscleromatis* but has not been described to be caused by *Klebsiella pneumoniae* subsp. *ozaenae*, classical biochemical tests that are known to distinguish the three subspecies of *K. pneumoniae* were performed for identification of the CH137 isolate (Table 1) (8). From these data it was clear that our isolate conformed totally to *K. pneumoniae* subsp. *ozaenae* and not to *K. pneumoniae* subsp. *rhinoscleromatis* or *K. pneumoniae* subsp. *pneumoniae*. *K. pneumoniae* subsp. *ozaenae* CH137 identification was confirmed by sequencing internal portions of the four housekeeping genes *rpoB*, *gapA*, *mdh*, and *phoE* (5). The alleles of strain CH137 were identical to those of strain ATCC 11269, the type strain of *K. pneumoniae* subsp. *ozaenae* strain tested. No strain of *K. pneumoniae* subsp. *pneumoniae* (more than 120 strains tested) and no strains of *K. pneumoniae* subsp. *rhinoscleromatis* ($n = 6$) were identical to *K. pneumoniae* subsp. *ozaenae* by consideration of the sequences of the four genes. The nucleotide se-

* Corresponding author. Mailing address: Service de Bactériologie-Virologie-Hygiène, CHU Robert Debré Rue du Général Koenig, 51092 Reims Cedex, France. Phone: 33 3 26 78 92 51. Fax: 33 3 26 78 41 34. E-mail: cdechamps@chu-reims.fr.

TABLE 1. Biochemical characteristics of the three subspecies of *K. pneumoniae* and the CH137 isolate

Test	Result[a] for:			
	K. pneumoniae subsp. *pneumoniae*	*K. pneumoniae* subsp. *rhinoscleromatis*	*K. pneumoniae* subsp. *ozaenae*	CH137
Urease	+	−	d	−
Malonate	+	+	−	−
Voges-Proskauer	+	−	−	−
ONPG[b]	+	−	+	+
Lysine decarboxylase	+	−	d	−
Utilization of:				
D-Alanine	+	−	+	+
D-Galacturonate	+	−	+	+
D-Glucuronate	+	−	+	+
Maltitol	+	−	+	+
1-*O*-Methyl-β-galactoside	+	−	+	+
1-O-Methyl-α-D-glucoside	d	−	+	+
Palatinose	+	−	+	+

[a] +, positive; −, negative; d, variable.
[b] ONPG, *o*-nitrophenyl-β-D-galactopyranoside.

quences of type strain *K. pneumoniae* subsp. *pneumoniae* ATCC 13883 showed seven nucleotide differences with the sequences of the *K. pneumoniae* subsp. *ozaenae* alleles (one in *rpoB*, three in *gapA*, and three in *phoE*), and the sequences of type strain *K. pneumoniae* subsp. *rhinoscleromatis* CIP52-210 showed 10 differences with the sequences of the *K. pneumoniae* subsp. *ozaenae* alleles (two in *rpoB*, one in *gapA*, two in *mdh*, and five in *phoE*). All nucleotide positions were supported by at least two chromatogram traces.

Rhinoscleroma is a granulomatous chronic infection of the upper respiratory tract caused by *Klebsiella pneumoniae* subsp. *rhinoscleromatis* (11). The disease first affects the nasal mucosa and progresses through three overlapping stages: catarrhal, with a nonspecific inflammation; proliferative, typified by a granulomatous reaction and the appearance of Mikulicz cells; and cicatricial, characterized by scar formation (4). Scleroma may affect any portion of the respiratory tract from the nose to the tracheobronchial tree. The diagnosis is confirmed by biopsies with staging and by evidencing *Klebsiella pneumoniae* subsp. *rhinoscleromatis* in nasal secretions or sometimes in the biopsy specimens.

The major deleterious effect of rhinoscleroma is the airway obstruction, which requires endoscopic treatment (1). Affected patients are usually between 15 and 35 years of age. Both sexes are affected, but women slightly more so (12). The regions of endemicity are tropical Africa, India, Southeast Asia, Central and South America, and also Central Europe. Ninety-five percent of scleromas are located in the nasal fossae. Laryngeal scleromas are found in 15 to 80% of cases. The usual laryngeal location is the subglottal region.

Klebsiella pneumoniae subsp. *ozaenae* is known to be related to the so-called ozena, or primary atrophic rhinitis. This disease is characterized by mucosal atrophy together with bone resorption and a thick endonasal crust that caries a fetid odor (10). Beside the bony destruction usually seen in the nasal cavities, osseous wall thickening of the maxillary and ethmoid sinuses has also been evidenced (13). It is currently thought that ozena has a multifactorial origin comprising a combination of a genetic predisposition and environmental factors (10). *K. pneumoniae* subsp. *ozaenae* is frequently isolated, which supports the hypothesis of its pathogenicity, even if it is difficult to determine whether it is a pathogen or a colonizer and if in some cases *Pseudomonas aeruginosa* or *Proteus* is simultaneously isolated (9, 10). Cure is obtained with antibiotics, but the therapeutic scheme is controversial (6). Good results are obtained with sulfamethoxazole-trimethoprim. A combination of ciprofloxacin with rifampin is interesting because of the drug concentration in nasal secretions and macrophages. Until now, there has been no report of resistance to extended-spectrum cephalosporins in *K. pneumoniae* subsp. *ozaenae*, which explains why we chose this antibiotic for the present case.

The case described in this case report is remarkable because of the isolation of *K. pneumoniae* subsp. *ozaenae* in nasal secretions instead of the expected organism *Klebsiella pneumoniae* subsp. *rhinoscleromatis*. The most likely cause of the scleroma was the *Klebsiella* isolate, because isolation of such an organism in our laboratory is uncommon: 1 isolate in the last 5 years, compared to 20,000 isolates of the family *Enterobacteriaceae* and about 2,500 *K. pneumoniae* subsp. *pneumoniae* isolates. In other laboratories, 64 isolates of *K. pneumoniae* subsp. *ozaenae* but 7,500 *K. pneumoniae* subsp. *pneumoniae* isolates were isolated in the Anaerobic Bacteriology Laboratory of the Veterans Affairs Wadsworth Hospital Center and the Bacteriology Laboratory of the University of California at Los Angeles Medical Center between January 1974 and May 1977 (7). *K. pneumoniae* subsp. *ozaenae* was reported to cause chronic inflammatory lesions of the upper respiratory tract. *K. pneumoniae* subsp. *ozaenae* has also been isolated from acute infections, such as the wounds of patients with underlying diseases (3, 7). The pathogenicity of *K. pneumoniae* subsp. *rhinoscleromatis* was attributed to the composition of the capsular polysaccharides of *Klebsiella* serotype K3, which enables the organism to resist phagocytosis (4). Because of the rarity of this bacterium in human infections, there have been very few recent studies published about its pathogenicity. A comparative study of *K. pneumoniae* subsp. *pneumoniae*, *K. pneumoniae* subsp. *ozaenae*, and *K. pneumoniae* subsp. *rhinoscleromatis* would be interesting, especially to explore whether pathogenicity factors have been transferred between *K. pneumoniae* subsp. *ozaenae* and *K. pneumoniae* subsp. *rhinoscleromatis* (2).

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REFERENCES

1. **Amoils, C. P., and M. L. Shindo.** 1996. Laryngotracheal manifestations of rhinoscleroma. Ann. Otol. Rhinol. Laryngol. **105:**336–340.
2. **Bach, S., A. de Almeida, and E. Carniel.** 2000. The *Yersinia* high-pathogenicity island is present in different members of the family *Enterobacteriaceae*. FEMS Microbiol. Lett. **183:**289–294.
3. **Berger, S. A., A. A. Pollock, and A. S. Richmond.** 1977. Isolation of *Klebsiella ozaenae* and *Klebsiella rhinoscleromatis* in a general hospital. Am. J. Clin. Pathol. **67:**499–502.
4. **Canalis, R. F., and L. Zamboni.** 2001. An interpretation of the structural changes responsible for the chronicity of rhinoscleroma. Laryngoscope **111:** 1020–1026.
5. **Diancourt, L., V. Passet, J. Verhoef, P. A. D. Grimont, and S. Brisse.** 2005. Multilocus sequence typing of *Klebsiella pneumoniae* nosocomial isolates. J. Clin. Microbiol. **43:**4178–4182.
6. **Evrard, I., X. Gruyer, P. Desse, A. François, J. P. Marie, D. Dehesdin, and**

J. Andrieu-Guitrancourt. 1998. Rhinosclérome ou sclérome du sinus sphénoïdal. Ann. Otolaryngol. Chir. Cervicofac. **115:**85–88.
7. **Golstein, E. J. C., R. P. Lewis, W. J. Martin, and P. H. Edelstein.** 1978. Infections caused by *Klebsiella ozaenae*: a changing disease spectrum. J. Clin. Microbiol. **8:**413–418.
8. **Grimont, F., P. A. D. Grimont, and C. Richard.** 1992. The genus *Klebsiella*, p. 2775–2796. *In* A. Balows, H. G. Trüper, M. Dworkin, W. Harder, and K.-H Schleifer (ed.), The prokaryotes. Springer-Verlag, New York, N.Y.
9. **Krylov, I. A.** 1988. Interrelations between *Klebsiella ozaenae* and other members of a microbial association in a pathological ozenous focus. Microbiol. Epidemiol. Immunobiol. **2:**17–20.
10. **Medina, L., M. Benazzo, G. Bertino, C. M. Montecucco, C. Danesino, M. Martinetti, and E. Mira.** 2003. Clinical, genetic and immunologic analysis of a family affected by ozena. Eur. Arch. Otorhinolaryngol. **7:**390–394.
11. **Miller, R. H., J. B. Schulman, R. F. Canalis, and P. H. Ward.** 1979. *Klebsiella rhinoscleromatis*: a clinical and pathogenic enigma. Otolaryngol. Head Neck Surg. **87:**212–221.
12. **Sedano, H. O., R. Carlos, and I. G. Koutlas.** 1996. Respiratory scleroma. A clinicopathologic and ultrastructural study. Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod. **81:**665–671.
13. **Talmi, Y. P., J. Bar-Ziv, D. Cohen, Y. Finkelstein, and J. Kronenberg.** 1995. Computed tomography study involvement in ozena. Am. J. Rhinol. **9:**281–284.