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NOTES

Endocarditis Due to a New Rod-Shaped *Neisseria* sp.

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We report the first case of pacemaker endocarditis due to a new rod-shaped *Neisseria* sp. isolated from blood culture. On the basis of *rrs* sequencing, the isolate was found to be most closely related to an uncultured organism from human subgingival plaque and was identified as *Neisseria* sp. group AK105. A cure was achieved after a combination of surgical and antibiotic treatment. Oral flora-induced pacemaker endocarditis is a rare condition that reinforces the need for good oral hygiene as an important preventive measure.

Apart from *Neisseria meningitidis* and *N. gonorrhoeae*, which are primary pathogens, all other *Neisseria* species are considered commensal inhabitants of the oro- or nasopharynx of humans or animals. These *Neisseria* spp. have only sporadically been associated with human illness, such as meningitis, bacteremia, endocarditis, pericarditis, empyema, or pneumonia, as opportunistic pathogens (19). Among these, only seven opportunistic *Neisseria* species have been occasionally involved in infective endocarditis: *Neisseria elongata* subsp. *nitroreducens* (9, 13, 22), *Neisseria elongata* subsp. *elongata* (4, 20), *N. mucosa* (7, 17, 26), *N. cinerea* (5), *N. sicca* (12, 14, 24), *N. flavescens* (25), and *N. subflava* (2, 23). While *Neisseria* species are typically gram-negative diplococci, there are some rod-shaped species such as *N. elongata* (6) and *N. weaveri* (3). We report the first case of pacemaker endocarditis with secondary arthritis localization due to a new rod-shaped *Neisseria* sp. It was identified by sequencing the *rrs* gene coding for the 16S rRNA gene.

A 38-year-old man presented with acute pain in the left shoulder associated with local inflammatory signs. During the preceding 3 weeks, he had developed dizziness, myalgia, and intense shivers. The patient had had a grade I atrioventricular block detected in 1993 and had then been equipped with a permanent pacemaker system. On admission, physical examination revealed left sternoclavicular stiffness and pain with localized heat and erythema around the affected joint. The patient presented neither fever nor respiratory, cardiovascular, gastrointestinal, or neurological signs. He complained also about dental pain which had started a few weeks before, although teeth and gums seemed healthy. Laboratory investigations revealed an erythrocyte sedimentation rate (ESR) of 92 mm/h, a C-reactive protein (CRP) concentration of 149 mg/liter, and a leukocyte count of 9.8×10^9/liter with 75% polymorphonuclear (PMN) cells. Urine culture was negative. Plain dental and maxillary sinus X rays were normal. Plain X rays and a computed tomography scan of the sternoclavicular joints showed left joint space widening due to a localized edema, joint effusion, soft tissue swelling, and left clavicle erosion.

Forty-eight hours after admission, the patient developed an acute-onset fever up to 39°C, chills, and shivers. Initial transesophageal echocardiography visualized a small heterogeneous mass suggesting vegetation on the intracardiac portion of the pacing wire on the atrial septum. Three sets of blood cultures (10 to 20 ml per set) were obtained within 48 h. The three aerobic cultures were found to be positive in less than 48 h in a BACTEC 9240 automated system (Becton Dickinson Microbiology Systems, Le Pont de Claix, France) and grew gram-negative aerobic rods. Colonies appeared on 5% sheep blood agar and on chocolate agar (bioMérieux, Marcy l'Etoile, France) 48 h after inoculation. Colonies were about 1 or 2 mm in diameter, circular, convex with a flat border, smooth, nonpigmented, and nonhemolytic (Fig. 1A). Very little growth was obtained on Trypticase soy agar or Mueller-Hinton agar (bioMérieux). The organism did not grow on MacConkey or Drigalski agar (bioMérieux). There was no anaerobic growth. Gram staining of the culture demonstrated thin, short to long gram-negative non-spore-forming rods (Fig. 1B). Oxidase and catalase tests were positive. The isolate was nonreactive in routinely used API 20E, API 20NE, and API NH identification strips (bioMérieux). Antibiotic susceptibility tests were performed on Mueller-Hinton agar supplemented with 5% sheep blood (bioMérieux). Determination of MICs by the Etest method (AB Biodisk, Solna, Sweden) gave the following results (in milligrams per liter): amoxicillin, 0.023; piperacillin, 0.25; piperacillin-tazobactam, 0.016; cefotaxime, 0.125; imipenem, 0.016; ciprofloxacin, 0.016; amikacin, 0.25; rifampin, 0.5. A diagnosis of infective endocarditis from the ventricular wire with secondary arthritis localization due to an unidentified

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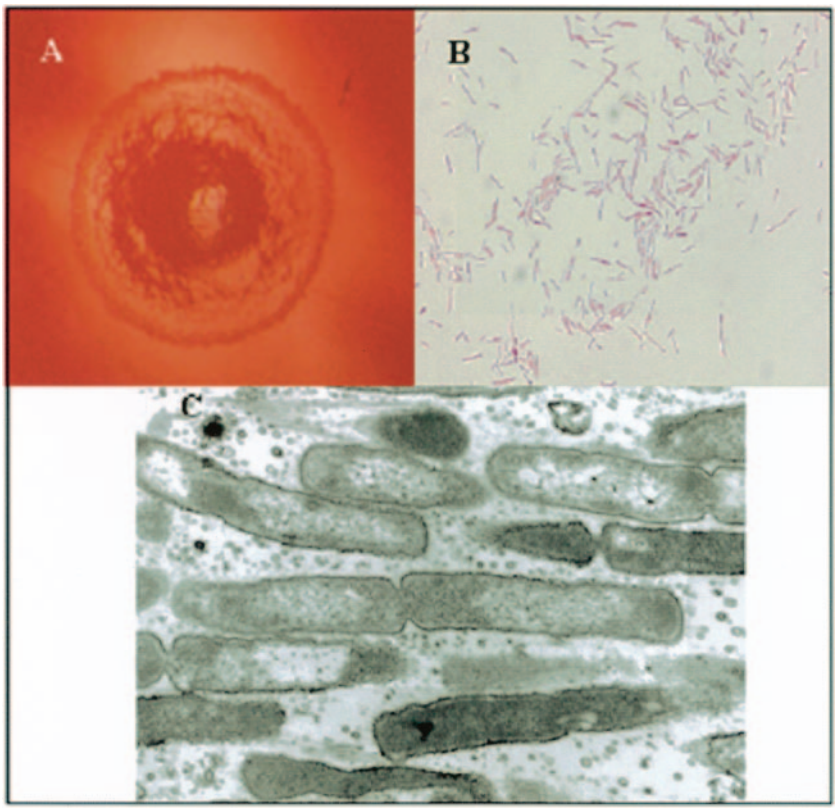

FIG. 1. Morphology of the isolate. (A) Morphology of a colony after growth on blood agar. (B) Gram staining of the isolate demonstrating thin, short to long gram-negative rods. (C) Electron micrograph.

gram-negative rod was made, and subsequently therapy with oral ofloxacin (200 mg twice daily) and intravenous tobramycin (250 mg once daily) was started.

After 48 h of treatment, results of a physical examination were unremarkable except for a low-grade fever (37.9°C). Ten days after his admission, the patient presented fever again. Laboratory investigations revealed a CRP concentration of 51 mg/liter, an ESR of 96 mm/h, and a leukocyte count of 18.2×10^9/liter with 90% PMN cells. A second transesophageal echocardiography showed an increase in the amount of vegetation on the ventricular portion of the pacing wire with an oscillating and polylobar aspect. Although three repeated sets of blood cultures obtained within 24 h remained negative after 5 days of incubation, antimicrobial treatment was empirically changed to intravenous cefotaxime (2,000 mg five times daily), intravenous amikacin (1,200 mg once daily), and a continuous infusion of vancomycin (2,500 mg daily). The patient was then transferred to the surgical department for ablation of the infected material and excision of vegetation. Cultures of the different bacterial swabs collected aseptically on the tips of the wire on the initial pacing box site and on the vegetation remained negative. The patient's status then rapidly improved. After 1 week, biological parameters returned to normal levels. The patient was discharged with an oral therapy of pristinamycin (3,000 mg daily) for 4 weeks. After 2 months in a rehabilitation unit, the patient was discharged. The resolution of the disease was complete.

Bacterial identification of our isolate was carried out. On an API 50CH identification strip (bioMérieux), acid was produced from 5-ketogluconate only. No growth occurred after 6 days in a Biotype-100 identification test (bioMérieux). An electron micrograph confirmed that the cells were rods (Fig. 1C), mostly in pairs. Identification of this gram-negative, oxidase-positive, aerobic, nonmotile, rod-shaped bacterium was finally performed by sequencing of the 16S RNA gene. A nearly complete *rrs* sequence (1,434 bp) was obtained by following a published procedure (10). Closely related sequences were searched in GenBank by using the BLAST (basic local alignment search tool) server (http://www.ncbi.nlm.nih.gov/BLAST/) (1). These homologous sequences belonged to the genus *Neisseria*. The *rrs* sequence of the isolate was aligned with other *Neisseria rrs* sequences by using CLUSTAL V (15). The phylogenetic tree built by using the neighbor-joining algorithm is shown in Fig. 2. The most closely related sequence was that of an uncultured organism referred to as oral clone AK105 (99% homology) (21). The closest named species was *N. canis* (95.2% homology). Therefore, the isolate was identified as *Neisseria* sp. group AK105.

Neisseria sp. group AK105 has a rod-shaped morphology that led to a delay in diagnosis. Cellular shape has long been relied on as a bacterial identification factor. However, since the descriptions of two rod-shaped *Neisseria* species, *N. elongata* in 1970 (6) and *N. weaveri* in 1993 (3), investigators should keep in mind that cellular shape is in fact not an absolute criterion in *Neisseria* identification.

Recently, Paster et al. investigated the bacterial diversity of human subgingival plaque by *rrs* gene cloning and sequencing

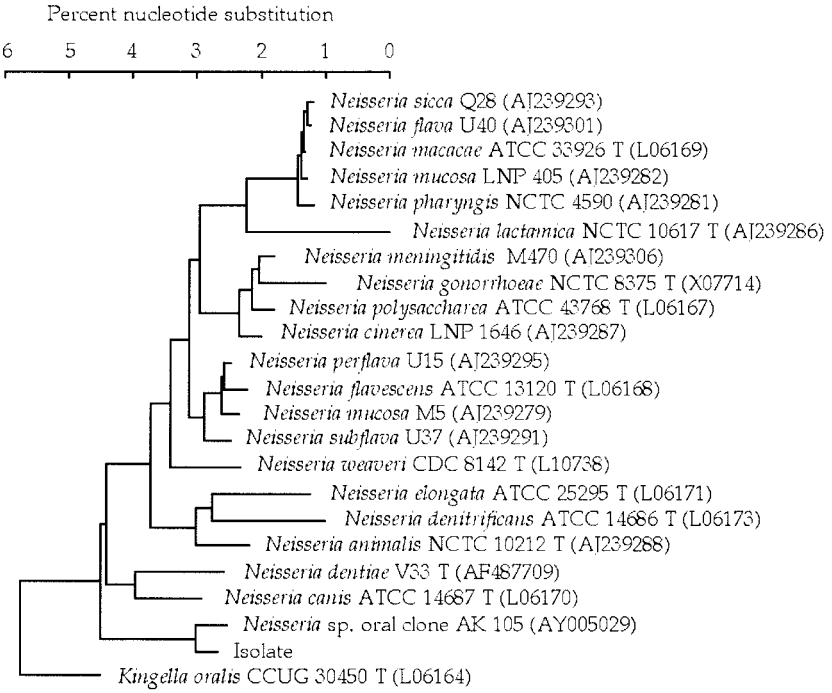

FIG. 2. Neighbor-joining dendrogram of the *rrs* sequences of the isolate, *Neisseria* sp. oral clone AK105, and other *Neisseria* species. The sequence of *Kingella oralis* was used as an outgroup. Reference sequences were obtained from the GenBank/EMBL databases; accession numbers are given in parentheses.

(21). According to the authors, as many as 40% of the clones represented novel bacterial species. Among these, oral clone AK105 appeared to belong to a novel cluster in the genus *Neisseria*. This clone originated from a case of refractory periodontitis. We noted that the patient in our case report had complained about dental pain prior to developing endocarditis. Therefore, *Neisseria* sp. group AK105 could have originated from the oral flora of the patient. Dental problems are indeed known risk factors for *Neisseria*-induced endocarditis. Preexisting conditions that predispose to infection include prosthetic valves (80% of patients) and previous dental procedures (20% of patients) (8). Moreover, the development of *Neisseria*-induced endocarditis is usually associated with other common predisposing factors including an age under 40, preexisting valve or congenital heart disease, drug addiction or immunodeficiency (such as AIDS), chronic alcoholism, asplenia, and diabetes mellitus (8). Our patient was 38 years old and had a permanent pacemaker system.

Though life-threatening, pacemaker infection is rare, and the most frequent pathogens implicated are *Staphylococcus aureus* and *Staphylococcus epidermidis* (18, 27). We present the first case of *Neisseria*-induced pacemaker endocarditis. To date, seven opportunistic *Neisseria* species or subspecies have occasionally been involved in endocarditis. Those most frequently encountered are *N. elongata* subsp. *nitroreducens* (at least 27 cases) (9, 13, 22), *N. mucosa* (20 cases) (7, 17, 26), *N. sicca* (14 cases) (12, 14, 24), and *N. subflava* (12 cases) (2, 23). Other species, such as *N. elongata* subsp. *elongata* (4, 20), *N. cinerea* (5), and *N. flavescens* (25), have also been reported at least once. *Neisseria*-induced endocarditis usually results in acute febrile endocarditis with large vegetation and a destructive process that often causes severe cardiac and systemic complications (8). The present case of endocarditis with secondary arthritis localization is the first reported case of a systemic infection due to *Neisseria* sp. group AK105. This case of pacemaker endocarditis was resolved after a combination of antibiotic and surgical treatment. In the case of *Neisseria*-induced endocarditis, surgical valve replacement is required in half of the patients (8). Moreover, to date, most studies investigating pacemaker infections have demonstrated the importance of device removal in the treatment of these infections (11).

In terms of prevention, the presence of a cardiac pacemaker is not a patient condition that poses a high risk of infection and hence does not require antimicrobial prophylaxis according to the guidelines of the Task Force on Infective Endocarditis of the European Society of Cardiology (16). Nevertheless, this case of *Neisseria* oral clone-induced pacemaker endocarditis demonstrates that patient education in general hygiene practices, with particular attention to oral and dental care, is a critical issue.

In conclusion, the striking features of our isolate are as follows: (i) it is a new rod-shaped member of the genus *Neisseria*, presently identified; (ii) it was isolated from a patient with a case of pacemaker infective endocarditis; (iii) its *rrs* sequence matches that of an uncultured organism from human subgingival plaque. It would be interesting to search for similar isolates in dental plaque before formally describing a new species. But the rod-shaped morphology of the cultivable isolate and its strongly nonreactive phenotype are indeed elements which at least raise the possibility of describing a new *Neisseria* species. Furthermore, if this strain proves to be as-

sociated with disease again in the future, its characterization would be a useful contribution for clinical microbiologists.

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