Endocarditis Due to *Neisseria bacilliformis* in a Patient with a Bicuspid Aortic Valve*$^{\dagger}$

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We report a case of endocarditis due to the rod-shaped *Neisseria* species *Neisseria bacilliformis*. The phenotypic characterization of this recently characterized bacteria is difficult, and the identification requires the sequencing of the 16S rRNA gene. The resolution of the disease was complete after appropriate antibiotic therapy, and surgery was not required.

**CASE REPORT**

A 47-year-old man was admitted to our hospital with a 1-month history of fever, shivering, fatigue, myalgia, headaches, anorexia, and weight loss (6 kg). His medical history included heart murmur diagnosed at the age of 15 years, peripheral facial nerve palsy in 2003, and salmonella diarrhea in 2003. The patient described self-limited headache and flu-like illness 3 months prior to admission. He noted progressive asthenia, fever, and cutaneous lesions suggestive, according to him, of paronychia, self-treated with oral cloxacillin, 500 mg twice daily, for 10 days.

On admission, the patient had fever. Auscultation revealed a grade 3/6 diastolic murmur. Splinter hemorrhages, Janeway's lesion facing the right fifth metacarpus, and a warm, painful left ankle edema were noted. Respiratory, gastrointestinal, and neurological examinations were normal. Laboratory investigations revealed a C-reactive protein concentration of 91 mg/liter (normal [N], 5 mg/liter), an erythrocyte sedimentation rate of 60 mm/h, a fibrinogen concentration of 6.8 g/liter (N, 1.8 to 5.0 g/liter), a leukocyte count of 10.6 $\times$ 10$^3$/liter, and a less significant match (90.2%, 472 of 523 bp) was found. The sequence was compared to the 16S rRNA sequences previously deposited in the GenBank database. Very significant matches were found with strain MDA2833 (accession number AY560519, 99.8% for 498 bp) and strains MDA1552 and CCUG38158 (accession numbers DQ117531 and DQ117530, 98% for 510 bp). When the sequence was compared to the 16S rRNA sequence of strain ATCC 25295$^T$ of *Neisseria elongata* subsp. *elongata*, a less significant match (90.2%, 472 of 523 bp) was found.

Antibiotic susceptibility tests were performed, and the MICs determined by the Etest method (AB Biodisk, Solna, Sweden) on Mueller-Hinton agar supplemented with sheep blood (bioMérieux) were as follows: penicillin G, 0.38 mg/liter; ampicillin, 0.50 mg/liter; cefotaxime, 0.50 mg/liter; ceftriaxone, 0.25 mg/liter; ofloxacin, 0.064 mg/liter; ciprofloxacin, 0.032 mg/liter; moxifloxacin, 0.032 mg/liter; gentamicin, 1.0 mg/liter; and rifampin (rifampicin), 0.75 mg/liter. The strain did not produce a $\beta$-lactamase, based on a negative chromogenic cephalinase test (bioMérieux). Therapy with intravenous cefotaxime (100

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mg/kg of body weight/day) and gentamicin (3 mg/kg/day) led to apyrexia in 24 h and to rapid improvement of the ankle’s inflammation. After 3 days, cefotaxime was changed to ceftiriaxone (2 g/day). After 7 days, gentamicin was changed to oral levofloxacin (500 mg twice a day). The total duration of antibiotic therapy was 1 month. All blood cultures performed after the beginning of antibiotic therapy remained negative. To date, 4 months after the cessation of antibiotics, the patient remains nonfebrile, with normal blood test (C-reactive protein, 8 mg/liter) and negative blood culture. The search for a primary site of infection remained negative. No dental procedure was performed within months before admission, and no dental infection, sinusitis, or pulmonary infection was found despite extensive search by clinical examination, X ray, and thoracic and abdominal computed tomography scan.

The genus Neisseria includes a group of closely related gram-negative bacteria that are primarily commensals of the mucous membranes of humans and animals. Within the 12 species encountered in humans (9), only Neisseria meningitidis and Neisseria gonorrhoeae are considered important pathogens, whereas the others are opportunistic pathogens sporadically involved in infections. Although Neisseria species are usually described as gram-negative diplococci, three rod-shaped species have been described: N. elongata (described in 1970) (4), Neisseria weaveri (described in 1993 as being of dog origin) (1), and Neisseria bacilliformis (described in 2006) (8). According to the first descriptions, N. bacilliformis may cause opportunistic infections in association with other bacteria mainly in the oral cavity and respiratory tract. N. bacilliformis has thus been isolated from a mandibular wound infection, from sputum from patients with bronchitis, and from a lung abscess specimen (8). Six opportunistic Neisseria species have been reported as occasionally responsible for human infective endocarditis (6): Neisseria elongata, Neisseria mucosa, Neisseria cinerea, Neisseria sicca, Neisseria flavescens, and Neisseria subflava.

We report here, to our knowledge, the first confirmed description of subacute endocarditis due to N. bacilliformis, with associated cutaneous lesions, arthritis, and immunological abnormalities. Since N. elongata is morphologically and biochemically close to N. bacilliformis (Table 1), it is possible that some of the cases attributed in the past to N. elongata were in fact due to N. bacilliformis. In the present case, the catalase test was negative, as observed by Han et al. for six out of eight strains (8). This test is not of great help in differentiating N. bacilliformis from N. elongata since it also varies within this latter species: negative for subspecies elongata and nitroreducens and positive for subspecies glycolytica (7). Currently, 16S rRNA gene sequencing is the most reliable tool to differentiate the two species, although a cellular fatty acid analysis has been described (8). The difficulty in identifying these species may lead to a delay in establishing the etiologic diagnosis (5), but when an appropriate antibiotic therapy and/or a valve surgery is implemented, endocarditis due to N. elongata is associated with high survival rates (6, 5). Another case of endocarditis probably caused by N. bacilliformis was reported in 2005 in France (10). The gram-negative bacillus, identified by 16S rRNA gene sequencing analysis (GenBank accession number AY560519), matched at 99% an oral Neisseria species clone, AK105 (GenBank accession number AY005029) (11). Considering the close relationship (99.6% 16S rRNA sequence homology) between this latter clone and variant MDA1552 of N. bacilliformis that was described in 2006 (8), we could presume that this rod-shaped Neisseria isolate was a N. bacilliformis strain. In the present case, the bicuspid aortic valve was a predisposing factor for infective endocarditis and, despite extensive investigations, no primary site of infection was identified. The flu-like illness 3 months before the diagnosis of endocarditis could be a putative primary infection, but clinical examination and computed tomography scanning did not reveal any abnormality. Although no synovial fluid tests have been performed, the left ankle edema was considered nonspecific arthritis and the positive rheumatoid factors and rapid improvement with systemic antibiotherapy are strong arguments for this hypothesis. In addition to ceftriaxone, the treatment recommended for HACEK (“H” for Haemophilus, “A” for Actinobacillus, “C” for Cardiobacterium, “E” for Eikenella, and “K” for Kingella) endocarditis (3), the patient received gentamicin, which was changed to levofloxacin because of the lack of experience for this unusual type of endocarditis.

In conclusion, we describe the first reported case of endocarditis due to N. bacilliformis, isolated from blood culture and identified by sequencing the 16S rDNA gene. Although opportunistic Neisseria spp. are infrequently encountered in infection, physicians should be aware of the possibility of endocarditis due to rod-shaped Neisseria species. Some authors (6) have suggested that the acronym “HACEK,” which represents a miscellaneous group of gram-negative cocobacilli that colonize the oropharynx and can be associated with endocarditis, should be changed to “HACNEK,” with the “N” representing the Neisseria genus.
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REFERENCES


