Case Report

Prosthetic valve endocarditis due to *Neisseria elongata* subsp. *elongata* in a patient with Klinefelter's syndrome

Morgan Evans,¹ Farah Yazdani,¹ Henry Malnick,² Jayesh J. Shah² and David P. J. Turner^{1,3}

Correspondence

David P. J. Turner

david.turner@nottingham.ac.uk

¹Department of Clinical Microbiology, Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham NG7 2UH, UK

²Laboratory of HealthCare Associated Infection, Centre for Infections, Health Protection Agency, Colindale, London, UK

³Institute of Infections, Immunity and Inflammation, School of Molecular Medical Sciences, Centre for Biomolecular Sciences, University of Nottingham, Nottingham, UK

A case is reported of prosthetic valve endocarditis due to *Neisseria elongata* subsp. *elongata* in a patient with Klinefelter's syndrome. This is believed to be only the third case of endocarditis reported due to this subspecies. *N. elongata* is difficult to identify, and is morphologically and biochemically similar to *Kingella* spp. Sequencing of the 16S rRNA gene is useful for identification. The patient was successfully treated with amoxicillin and gentamicin, followed by ceftriaxone.

Received 8 January 2007

Accepted 19 February 2007

Case report

A 70-year-old man presented to the emergency department complaining of nausea, vomiting, dyspnoea and rigors for 4 days. He denied any weight loss or fatigue. He had a complicated past history, including Klinefelter's syndrome (karyotype 47 XXY), thyrotoxicosis and rheumatoid arthritis (controlled with hydroxychloroquine), complicated by a mild pancytopenia and rheumatoid lung disease. He had undergone a tissue valve replacement for aortic stenosis 18 months previously. He denied recent dental treatment and no dental problems were identified.

On examination, no murmurs were detected, but chest examination revealed bi-basal crepitations. A fever of 38.8 °C was noted 1 day after admission. A chest radiograph showed a heart at the upper limits of normal size, but no evidence of consolidation. Urinalysis demonstrated 3+ protein and 2+ blood; microscopic haematuria was present, but mid-stream urine culture was sterile. Abnormal blood results included: 127 mmol sodium l⁻¹, 11.6 mmol urea l⁻¹, 103 mmol creatinine l⁻¹, 11.1 g haemoglobin dl⁻¹, 113 × 10⁹ platelets l⁻¹, 170 mg C-reactive protein l⁻¹, and an erythrocyte sedimentation rate of 31 mm h⁻¹. The aerobic bottles (BD BACTEC Plus Aerobic/F) from each of three independently taken sets of blood cultures subsequently grew a Gram-negative bacillus after 1 day of incubation on the BACTEC 9240 instrument

(BD Microbiology Systems), which proved difficult to identify. The anaerobic bottles (BD BACTEC Lytic/10 Anaerobic/F) remained negative after 5 days incubation. Antibiotic sensitivity tests (using the British Society for Antimicrobial Chemotherapy disc diffusion methodology) showed the organism was resistant to trimethoprim, but sensitive to amoxicillin, cefuroxime, ceftriaxone, ceftazidime, gentamicin, ciprofloxacin and meropenem. The patient was treated with 1 g intravenous ceftazidime twice a day and gentamicin. Over the next 5 days, he deteriorated and developed acute renal failure, metabolic acidosis and atrial fibrillation. Transthoracic echocardiography showed that the aortic valve replacement was thickened, which was confirmed by transoesophageal echocardiography.

Based on the Gram stain appearance and the initial biochemical profile, the blood culture isolate was provisionally identified as belonging to the genus *Kingella*, but was formally identified at the Laboratory of HealthCare Associated Infection (LHCAI) as *Neisseria elongata* subsp. *elongata* based on biochemical reactions (oxidase positive, catalase negative, lysine and ornithine negative, indole negative, glucose acid production negative, nitrate reduction negative, nitrite reduction positive) and the sequence of the 16S rRNA gene (GenBank accession no. DQ914524). The 16S rRNA gene was 99.6% identical to both the *N. elongata* subsp. *elongata* and *N. elongata* subsp. *glycolytica* type strain sequences, but the organism was differentiated from the latter by the negative reaction in the catalase test. A negative reaction for nitrate reduction differentiated the organism from *N. elongata* subsp. *nitroreducens*.

Abbreviation: LHCAI, Laboratory of HealthCare Associated Infection.

The GenBank/EMBL/DDBJ accession no. for the 16S rRNA gene sequence of the isolate of *Neisseria elongata* is DQ914524.

A diagnosis of prosthetic aortic valve endocarditis was made, and antibiotic therapy was changed to 2 g intravenous amoxicillin 4 hourly and gentamicin. After 3 weeks, therapy was continued with 2 g intravenous ceftriaxone daily to complete 6 weeks treatment in total. The patient recovered fully.

Discussion

N. elongata was first described in 1970 as a rod-shaped organism within the family *Neisseriaceae*, and is part of the oropharyngeal commensal flora. The species *N. elongata* now includes the three subspecies: *N. elongata* subsp. *elongata*, *N. elongata* subsp. *glycolytica* and *N. elongata* subsp. *nitroreducens* (formerly CDC group M-6). *N. elongata* is closely related to other *Neisseria* and *Kingella* spp., but can be differentiated from these other organisms by biochemical analysis (Lawson *et al.*, 2005). In addition to *N. elongata*, two other rod-shaped species of *Neisseria* are now recognized, *Neisseria weaveri* (formerly CDC group M-5) and *Neisseria* sp. group 105.

Isolates of subspecies *N. elongata* subsp. *nitroreducens* from blood cultures have been described to be frequently in association with endocarditis (Grant *et al.*, 1990). In contrast, there are only two previous reports of endocarditis due to *N. elongata* subsp. *elongata* (Apisarnthanarak *et al.*, 2001; Nawaz *et al.*, 1996) and one due to *N. elongata* subsp. *glycolytica* (Andersen *et al.*, 1995). It is unclear whether the pathogenic potential of the latter two subspecies is lower than that of *N. elongata* subsp. *nitroreducens* or whether *N. elongata* subsp. *nitroreducens* is more readily isolated from blood culture systems. Since 2003, the LHCAI has identified *N. elongata* subsp. *elongata* and *N. elongata* subsp. *glycolytica* from three and two blood cultures, respectively, although the source of infection was unknown. Interestingly, no isolates of *N. elongata* subsp. *nitroreducens* were identified during this period. Overall, *N. elongata* is the most common of the opportunistic *Neisseria* spp. reported as the aetiological cause of endocarditis. The other reported species include: *Neisseria mucosa* (20 cases), *Neisseria sicca* (14 cases), *Neisseria subflava* (12 cases), *Neisseria cinerea* (1 case) and *Neisseria flavescens* (1 case).

The patient described in this report had previously undergone aortic valve replacement surgery for valvular heart disease in association with Klinefelter's syndrome. Patients with Klinefelter's syndrome are recognized to have an increased risk of such disease (principally mitral valve prolapse, but also aortic valve disease), which is associated with increased mortality. Given the relatively high incidence of valvular disease in patients with Klinefelter's syndrome, we were surprised at the apparent absence of reports of endocarditis in association with this syndrome. The importance of good dental care needs to be emphasized in these patients.

The isolate of *N. elongata* subsp. *elongata* in this report proved difficult to formally identify. The isolate grew

rapidly in the aerobic bottles on the BACTEC 9240 instrument, but failed to grow in the three anaerobic bottles. The commercially available identification system, API NH (BioMérieux) was unable to assign the organism to a specific genus. Based on the Gram-stain morphology and initial biochemical tests, the organism was tentatively identified as *Kingella* sp., and referred to the LHCAI for further analysis. At the LHCAI, long-chain cellular fatty acid analysis revealed a profile that was closest to that of *N. weaveri*. However, as the latter is catalase-positive, the sequence of the 16S rRNA gene was determined. The sequence closely matched that of *N. elongata*, and biochemical tests were subsequently able to assign the organism to *N. elongata* subsp. *elongata*. Sequencing of the 16S rRNA gene has previously been reported as useful in the identification of *N. elongata* (Hombrouck-Alet *et al.*, 2003).

We have reviewed the English-language reports of endocarditis due to all the subspecies of *N. elongata*. Eighteen cases of endocarditis due to *N. elongata* (including this case) have been described in detail (Andersen *et al.*, 1995; Apisarnthanarak *et al.*, 2001; Dominguez & Smith, 1998; Grant *et al.*, 1990; Haddow *et al.*, 2003; Hoshino *et al.*, 2005; Imperial *et al.*, 1995; Kaplan & Flaherty, 1991; Kociuba *et al.*, 1993; Meuleman *et al.*, 1996; Nawaz *et al.*, 1996; Perez, 1986; Picu *et al.*, 2003; Rose *et al.*, 1990; Simor & Salit, 1983; Struillou *et al.*, 1993). The reported age range is 7–82 years. Five (28 %) of the cases affected prosthetic valves, and prior dental infection (or treatment) was reported in eight (44 %) cases. All cases were treated with a third generation cephalosporin, benzylpenicillin or ampicillin/amoxicillin, usually combined with gentamicin in the initial phase. The total length of treatment varied between 4 and 7 weeks. Notably, a high proportion of patients (9/18, 50 %) required valvular surgery, but all patients for whom the outcome was stated (17/18) survived.

In conclusion, we describe what is believed to be the third case of endocarditis due to *N. elongata* subsp. *elongata*. Clinical microbiologists and physicians should be alert to the possibility of endocarditis when opportunistic *Neisseria* spp. (particularly *N. elongata*) are isolated from blood cultures. The possibility that rod-shaped isolates, biochemically resembling the genus *Kingella*, may belong to the genus *Neisseria* should also be considered. We suggest that the acronym, 'HACEK', which is widely used to describe a miscellaneous group of Gram-negative coccobacilli that colonize the oropharynx and are rarely associated with endocarditis, should be changed to 'HACNEK' (the 'N' representing *N. elongata*) as an aide-memoire for clinical practice and future studies.

References

- Andersen, B. M., Weyant, R. S., Steigerwalt, A. G., Moss, C. W., Hollis, D. G., Weaver, R. E., Ashford, D. & Brenner, D. J. (1995). Characterization of *Neisseria elongata* subsp. *glycolytica* isolates obtained from human wound specimens and blood cultures. *J Clin Microbiol* **33**, 76–78.

- Apisarnthanarak, A., Dunagan, W. C. & Dunne, W. M. (2001). *Neisseria elongata* subsp. *elongata*, as a cause of human endocarditis. *Diagn Microbiol Infect Dis* **39**, 265–266.
- Dominguez, E. A. & Smith, T. L. (1998). Endocarditis due to *Neisseria elongata* subspecies *nitroreducens*: case report and review. *Clin Infect Dis* **26**, 1471–1473.
- Grant, P. E., Brenner, D. J., Steigerwalt, A. G., Hollis, D. G. & Weaver, R. E. (1990). *Neisseria elongata* subsp. *nitroreducens* subsp. nov., formerly CDC group M-6, a gram-negative bacterium associated with endocarditis. *J Clin Microbiol* **28**, 2591–2596.
- Haddow, L. J., Mulgrew, C., Ansari, A., Miell, J., Jackson, G., Malnick, H. & Rao, G. G. (2003). *Neisseria elongata* endocarditis: case report and literature review. *Clin Microbiol Infect* **9**, 426–430.
- Hombrouck-Alet, C., Poilane, I., Janoir-Jouveshomme, C., Fain, O., Cruaud, P., Thomas, M. & Collignon, A. (2003). Utilization of 16S ribosomal DNA sequencing for diagnosis of septicemia due to *Neisseria elongata* subsp. *glycolytica* in a neutropenic patient. *J Clin Microbiol* **41**, 3436–3437.
- Hoshino, T., Ohkusu, K., Sudo, F., Nakajima, H., Ishiwada, N., Ezaki, T. & Kohno, Y. (2005). *Neisseria elongata* subsp. *nitroreducens* endocarditis in a seven-year-old boy. *Pediatr Infect Dis J* **24**, 391–392.
- Imperial, H. L., Joho, K. L. & Alcid, D. V. (1995). Endocarditis due to *Neisseria elongata* subspecies *nitroreducens*. *Clin Infect Dis* **20**, 1431–1432.
- Kaplan, L. J. & Flaherty, J. (1991). Centers for Disease Control group M-6: a cause of destructive endocarditis. *J Infect Dis* **164**, 822–823.
- Kociuba, K., Munro, R. & Daley, D. (1993). M-6 endocarditis: report of an Australian case. *Pathology* **25**, 310–312.
- Lawson, P. A., Malnick, H., Collins, M. D., Shah, J. J., Chattaway, M. A., Bendall, R. & Hartley, J. W. (2005). Description of *Kingella potus* sp. nov., an organism isolated from a wound caused by an animal bite. *J Clin Microbiol* **43**, 3526–3529.
- Meuleman, P., Erard, K., Herregods, M. C., Peetermans, W. E. & Verhaegen, J. (1996). Bioprosthetic valve endocarditis caused by *Neisseria elongata* subspecies *nitroreducens*. *Infection* **24**, 258–260.
- Nawaz, T., Hardy, D. J. & Bonnez, W. (1996). *Neisseria elongata* subsp. *elongata*, a case of human endocarditis complicated by pseudoaneurysm. *J Clin Microbiol* **34**, 756–758.
- Perez, R. E. (1986). Endocarditis with Moraxella-like M-6 after cardiac catheterization. *J Clin Microbiol* **24**, 501–502.
- Picu, C., Mille, C., Popescu, G. A., Bret, L. & Prazuck, T. (2003). Aortic prosthetic endocarditis with *Neisseria elongata* subspecies *nitroreducens*. *Scand J Infect Dis* **35**, 280–282.
- Rose, R. C., III, Grossman, A. M. & Giles, J. W. (1990). Infective endocarditis due to the CDC group M6 bacillus. *J Tenn Med Assoc* **83**, 603–604.
- Simor, A. E. & Salit, I. E. (1983). Endocarditis caused by M6. *J Clin Microbiol* **17**, 931–933.
- Struillou, L., Raffi, F. & Barrier, J. H. (1993). Endocarditis caused by *Neisseria elongata* subspecies *nitroreducens*: case report and literature review. *Eur J Clin Microbiol Infect Dis* **12**, 625–627.