Neisseria elongata endocarditis complicated by brain embolism and abscess

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We report a case of Neisseria elongata endocarditis with thalamic septic embolization and subsequent brain abscess formation, which to the best of our knowledge has never been reported in the literature. The brain abscess completely resolved after a surgical repair of the infected mitral valve and an additional 4 weeks of antimicrobial therapy. Based on a review of all previous reports of N. elongata endocarditis, including ours, this will remind physicians that invasive N. elongata infections should be managed and followed up cautiously, as surgical intervention is often required.

Introduction

Neisseria elongata, formally known as Centers for Disease Control and Prevention (CDC) group M-6, is a commensal organism of the human oropharyngeal flora (Grant et al., 1990). It used to be considered as non-pathogenic, but it has recently been recognized as an important pathogen responsible for significant infections in humans, such as infective endocarditis, septicemia and osteomyelitis (Garner & Briant, 1986; Grant et al., 1990; Wong & Janda, 1992). N. elongata endocarditis is very rare but is important, since it causes a variety of serious complications, such as systemic embolization, congestive heart failure, renal failure, cerebrovascular embolism and myocardial abscess (Table 1). We describe a case of N. elongata endocarditis complicated with thalamic septic embolization and brain abscess, and review all previous reports of this micro-organism.

Case report

A 42-year-old man with thalassaemia was admitted to a district general hospital with left-sided numbness, malaise, myalgia and arthralgia for 2 weeks. He also had fever up to 38.5 °C and mild dyspnoea on exertion 1 day prior to admission. He denied intravenous drug abuse or recent hospitalization with any invasive procedure, although he had received dental cleaning 6 months earlier. On admission, his temperature was 38.6 °C, his heart rate was 108 beats min⁻¹ and his blood pressure was 115/68 mmHg, and a grade IV/VI systolic murmur was detected at the apex and left lower sternal border. He had hepatosplenomegaly but had no splinter haemorrhage, Janeway’s lesions or Osler’s nodes. The neurological examination was unremarkable, except decreased pinprick sensation at the left side. The haemogram revealed leukocytosis (leukocyte count 14.8 × 10⁹ l⁻¹, with 82 % segment and 1 % band neutrophils), anaemia (haemoglobin 75 g l⁻¹), elevated C-reactive protein (CRP) (38.7 mg l⁻¹; normal <5 mg l⁻¹), and abnormal liver function tests (aspartate aminotransferase 39 U l⁻¹ and alanine aminotransferase 54 U l⁻¹). Chest X-ray and urinalysis were unremarkable. Transthoracic echocardiography revealed elongation of the mitral valve with moderate regurgitation and mitral valve vegetation. Brain computed tomography (CT) indicated right thalamic infarction (Fig. 1a). Four sets of blood cultures were drawn at half-hour intervals before therapy. Empiric antimicrobial therapy was started with intravenous aqueous penicillin-G and gentamicin. Two days later, he was transferred to the emergency room (ER) of our Medical Centre, a 3000-bed tertiary teaching hospital in North Taiwan.

Three additional sets of blood cultures were drawn half an hour apart on admission to our ER. Ultrasound of the abdomen revealed hepatosplenomegaly and splenic infarct

Abbreviations: CRP, C-reactive protein; CT, computed tomography; ER, emergency room; MRI, magnetic resonance imaging.
Table 1. Characteristics of cases of *N. elongata* endocarditis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)</th>
<th>Risk factor</th>
<th>No. of positive blood cultures</th>
<th>Echo criteria</th>
<th>Duke’s criteria</th>
<th>Medication and duration</th>
<th>Complications</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perez (1986)*</td>
<td>57</td>
<td>RHD, AR, history of IE catheterization</td>
<td>11 of 11</td>
<td>None</td>
<td>1 major, 2 minor</td>
<td>Ampicillin, 43d</td>
<td>CHF</td>
<td>AVR</td>
</tr>
<tr>
<td>Simor &amp; Salit (1983)</td>
<td>31</td>
<td>Dental procedure, MVP</td>
<td>6 of 6</td>
<td>Veg on MV</td>
<td>2 major</td>
<td>Tobramycin, 26d</td>
<td>Myocardial abscess, renal failure, CHF</td>
<td>MVR</td>
</tr>
<tr>
<td>Rose et al. (1990)*</td>
<td>65</td>
<td>None</td>
<td>6 of 6</td>
<td>Veg on MV</td>
<td>2 major</td>
<td>Penicillin, 2d</td>
<td>none</td>
<td>None</td>
</tr>
<tr>
<td>Garner &amp; Briant (1986)</td>
<td>31</td>
<td>MVP</td>
<td>6 of 6</td>
<td>MR</td>
<td>1 major, 3 minor</td>
<td>Gentamicin, 2d, Ampicillin, 4w</td>
<td>Myocardial abscess, systemic embolism</td>
<td>AVR</td>
</tr>
<tr>
<td>Kaplan &amp; Flaherty (1991)</td>
<td>82</td>
<td>Dental procedure, myxomatous MV</td>
<td>4 of 5</td>
<td>Veg on MV, MR</td>
<td>2 major</td>
<td>Ceftriaxone, 4w</td>
<td>stroke, SAH, subvalvular abscess</td>
<td>AVR</td>
</tr>
<tr>
<td>Kociuba et al. (1993)</td>
<td>33</td>
<td>Dental procedure, bicuspid AV</td>
<td>3 of 3</td>
<td>Veg on AV, AR, abscess</td>
<td>2 major</td>
<td>Penicillin, gentamicin, penicillin, 65d</td>
<td>none</td>
<td>None</td>
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<td>Struillou et al. (1993)</td>
<td>27</td>
<td>MVP, dental infection</td>
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<td>MVP</td>
<td>1 major, 3 minor</td>
<td>Ceftriaxone, 6w, Gentamicin, 4w</td>
<td>brachial pseudoaneurysm</td>
<td>None</td>
</tr>
<tr>
<td>Andersen et al. (1995)†</td>
<td>57</td>
<td>None</td>
<td>6 of 6</td>
<td>Veg on AV</td>
<td>2 major</td>
<td>Penicillin, gentamicin, 5w</td>
<td>none</td>
<td>None</td>
</tr>
<tr>
<td>Imperial et al. (1995)*</td>
<td>31</td>
<td>None</td>
<td>2 of 2</td>
<td>Veg on AV</td>
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<td>Ampicillin, gentamicin, ceftriaxone, 4w</td>
<td>none</td>
<td>None</td>
</tr>
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<td>Meuleman et al. (1996)*</td>
<td>74</td>
<td>Dental infection, bioprosthetic AV</td>
<td>19 of 24</td>
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<td>Ampicillin, Gentamicin, 2w</td>
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</tr>
<tr>
<td>Nawaz et al. (1996)‡</td>
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<td>None</td>
<td>3 of 5</td>
<td>Veg on MV, MR</td>
<td>2 major</td>
<td>Ampicillin, Vancomycin, 3d</td>
<td>Brachial pseudoaneurysm</td>
<td>None</td>
</tr>
<tr>
<td>Dominguez &amp; Smith (1998)</td>
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<td>Prosthetic valve</td>
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<td>Veg on AV, subvalvular abscess</td>
<td>1 major, 4 minor</td>
<td>Vancomycin, gentamicin, ampicillin, 4w</td>
<td>Stroke, SAH, subvalvular abscess</td>
<td>AVR</td>
</tr>
<tr>
<td>Hofstad et al. (1998)*</td>
<td>30</td>
<td>HoCM</td>
<td>3 of 3</td>
<td>None</td>
<td>1 major, 2 minor</td>
<td>Benzylpenicillin, 2w, Netilmicin, 2w</td>
<td>none</td>
<td>None</td>
</tr>
<tr>
<td>Haddow et al. (2003)</td>
<td>54</td>
<td>Bicuspid AV, dental procedure</td>
<td>3 of 3</td>
<td>Veg on AV, AR, abscess</td>
<td>2 major</td>
<td>Ceftrazidime, 7w, Gentamicin, 4w</td>
<td>CHF aortic root, myocardial abscess</td>
<td>AVR</td>
</tr>
</tbody>
</table>
with a 4 cm wedge-shaped lesion, but no abscess was discovered. A $^{67}$Gallium-citrate scan was negative. He still had intermittent low-grade fever around 37.8 °C even after using a combination regimen of penicillin and gentamicin for 1 week. The regimen was then changed to ceftriaxone 1 g 12-hourly intravenously from the eighth hospital day. He became afebrile 3 days later. The three additional sets of blood cultures obtained at our ER had no growth of bacteria. Two weeks after admission, his serum CRP level declined to 29.6 mg l$^{-1}$, but his haemoglobin level was 65 g l$^{-1}$ without any clinical sign of active bleeding or blood loss. The follow-up echocardiogram showed severe mitral regurgitation and multiple oscillating large vegetations on the atrial side of the anterior mitral leaflet (A3 scallop) (Fig. 2). For the persistent left-sided numbness, brain CT was followed up and showed a cystic lesion at the right thalamus. Magnetic resonance imaging (MRI) with angiogram proved the presence of a brain abscess without micro-aneurysm (Fig. 1b). The dosage of ceftriaxone was then adjusted to 2 g 12-hourly.

Two of the first four sets of blood cultures in the first hospital grew Gram-negative bacilli from aerobic bottles, which were initially identified as *Moraxella* species based on Gram staining and biochemical tests. Gram staining of the colonies grown on the agar plate showed Gram-negative coccobacilli, and identification was performed using the semiautomated ATB ID 32 GN system (bioMérieux). The antimicrobial susceptibility was determined by the disc diffusion method according to guideline M2-A9 of the Clinical and Laboratory Standards Institute. This isolate was susceptible to amoxicillin/clavulanate, ceftriaxone and cefuroxime.

Since the identity of the isolate by phenotypic methods was equivocal, further identification was performed using 16S rRNA sequencing. Briefly, nucleic acid was extracted from 200 µl bacterial suspension using the QIAamp DNA Mini Kit (Qiagen). PCR assays targeting a 1.5 kb fragment of the 16S rRNA gene of the isolate using the primers 8FPL (5'–AGAGTTTGATCCTGGCTCAG-3') and 1492 (5'–GGTTACCTTGTTACGACTT-3') were performed (Relman et al., 1990). PCR products were purified and subjected to partial sequencing (500 bp) in both directions using the primers 8FPL and 531R (5'–TACCGCGGCTGCTGGCA-3'). After a search for homologous sequences in the GenBank database using BLAST (http://www.ncbi.nlm.nih.gov/blast/Blast.cgi), the sequencing demonstrated that this isolate was identical to *N. elongata* subsp. *glycolytica* (GenBank accession no. AY167422). As only a comparison of the first 500 bp of the 16S rRNA gene was done, the partial sequence was not informative enough to conclusively identify the isolate to the subspecies level.

This patient received surgery at the fourth week of hospitalization. The surgical findings were rupture of the posterior commissure and the chordae tendenae that attach to the mitral anterior leaflet, and floating vegetations on the chordae. Resection of the vegetation and the chordae transferring from the secondary chordae to the primary
site of the anterior leaflet, and repair of the posterior commissure and mitral valve were performed. Ceftriaxone was continued for a further 4-week course after surgery. The follow-up brain CT indicated resolution of the brain abscess. He recovered fully from the illness and was followed up at the cardiovascular medicine outpatient clinic without any sign of recurrence.

**Discussion**

*N. elongata* was first described by Bovre & Holten (1970). It contains three subspecies that are separated on the basis of biochemical differences, namely *N. elongata* subsp. *elongata*, *N. elongata* subsp. *glycolytica* and *N. elongata* subsp. *nitroreducens*. These organisms are difficult to identify. They have been reported to cause a variety of systemic infections, such as septicaemia, endocarditis and osteomyelitis (Table 1). Among these infections, endocarditis due to *N. elongata* subsp. *nitroreducens* is most frequently reported.

A review of the literature from 1966 to 2007 revealed that only 18 cases of endocarditis due to *N. elongata* met the modified Duke criteria (Lamas & Eykyn, 1997) for definite or possible infective endocarditis (Table 1). Of the 18 cases,
15 were caused by N. elongata subsp. nitroreducens, two by N. elongata subsp. elongata, and one by N. elongata subsp. glycolytica. After inclusion of this index case, a total of 12 cases of definite infective endocarditis and seven cases of possible infective endocarditis were included in this review. Preexisting heart diseases, previous dental procedures and odontogenic infections were considered as the risk factors. Of the 18 cases in previous reports, five had dental procedures without the use of prophylactic antibiotics, and three had infected teeth. Preexisting heart diseases were present in 12 of the 18 cases. This index case had severe mitral regurgitation and had received dental cleaning 6 months earlier without prophylactic antibiotics.

N. elongata endocarditis often causes an invasive infection with a destructive progress. Table 1 shows the reported complications, including systemic embolization (three cases), brachial pseudoaneurysm (one case), azotaemia (four cases), thrombotic thrombocytopenic purpura (one case), subarachnoid haemorrhage (one case), heart failure (six cases) and myocardial abscess (four cases). There was no death in this review. Surgical intervention was required in eight cases. Development of vegetation and destructive progression were also noted even after optimal antibiotic therapy (Kaplan & Flaherty, 1991). The index case had a similar clinical course to that of the previous reports. His fever subsided and serum CRP level declined mainly after therapy (Kaplan & Flaherty, 1991). The index case had severe mitral regurgitation and had received dental cleaning 6 months earlier without prophylactic antibiotics.

To the best of our knowledge, a brain abscess as a complication of N. elongata endocarditis has not been reported before. A brain abscess is relatively rare, accounting for a very small percentage of neurological complications in patients with infective endocarditis. Viridans streptococci and Staphylococcus aureus are most frequently associated. The index case emphasises that a brain abscess is crucial if any neurological deficit deteriorates or does not improve after optimal antibiotic therapy. This rare but important complication can be overlooked if physicians do not pay attention to slight deteriorations, such as the persistent left-sided numbness in this index case, which occurred despite appropriate treatment. Treatment of brain abscesses with antimicrobial agents alone after eradication of the primary infected foci has been proposed to be both feasible and effective (Lu et al., 2006), and indeed the index case recovered fully after removal and replacement of the infected valve.

In conclusion, infective endocarditis caused by N. elongata is rare but important, since it often requires surgical intervention. Although this pathogen is susceptible to a wide range of antimicrobial agents, an infection in which it is implicated should be managed with great caution and with close follow-up of any major complications that arise, such as systemic embolization or brain abscess. The application of such a cautious approach will lead to a more comprehensive patient evaluation.

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References


