Meningitis and Bacteremia Due to *Neisseria cinerea* following a Percutaneous Rhizotomy of the Trigeminal Ganglion

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*Neisseria cinerea* is a human commensal. The first known case of meningitis and bacteremia due to *Neisseria cinerea* following percutaneous glycerol instillation of the trigeminal ganglion is reported. Conventional phenotypic methods and complete 16S RNA gene sequencing accurately identified the pathogen. Difficulties in differentiation from pathogenic neisseriae are discussed.

CASE REPORT

A 58-year-old male patient presented the day after a percutaneous glycerol rhizotomy of the trigeminal ganglion with fever (38.2°C), clinical signs of meningitis without new focal neurologic deficits, and a normal neurocognitive status.

His personal history was remarkable for severe trigeminal neuralgia refractory to medical treatment and for diagnosis of primary progressive multiple sclerosis for 13 years without immunosuppressive treatment.

His white blood cell count (18.9 G/liter; 90% neutrophils, no left shift) and his C-reactive protein level (189 mg/dl) were elevated. Two sets of blood cultures and a lumbar puncture were immediately performed, and empirical antibiotic treatment with intravenous (i.v.) ceftriaxone administered in two doses at 2 g per dose (2x2g) was started. The cerebrospinal fluid (CSF) sample showed 4,115 nuclear cells/μl, with 89% polymorphonuclear neutrophils. Protein and glucose (GLU) levels were abnormal, with 1.32 g (normal, 0.15 to 0.45) of protein/liter and 0.29 mmol (normal, 2.2 to 3.9) of glucose/liter in the CSF. Gram staining of the CSF revealed Gram-labile cocci.

A computed tomography (CT) scan showed a small amount of intracerebral air near the trigeminal ganglion, confirming accidental involvement of intracerebral structures during rhizotomy (Fig. 1A). Flucloxacillin (6x2g) was added to the regimen. Droplet isolation precautions were not considered necessary because the clinical picture was suggestive for iatrogenic complication and not for meningococcal meningitis (1, 2).

The following day, *Neisseria* species, susceptible to penicillin, ampicillin, ceftriaxone, and ciprofloxacin, grew in one of two sets of blood cultures and the CSF cultures (Table 1). Flucloxacillin treatment was stopped, and ceftriaxone treatment was continued for 7 days in total, according to the recommended treatment duration for meningitis due to *N. meningitidis* (3). The patient recovered rapidly. After 1 week, he was asymptomatic, with normal blood values.

The CSF isolate was identified by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) analysis (MALDI BioTyper; Bruker Daltonik, Bremen, Germany) as *Neisseria meningitidis*, with a score of 1.82 (sufficient only for genus assignment). *Neisseria cinerea* was the third species proposed by MALDI-TOF MS, with a minimal difference in the score (1.81). The colony morphology turned out to show no pigmentation. API NH V3.0 (bioMérieux Suisse SA, Geneva, Switzerland) testing was performed, with a positive reaction only for ProA, consistent with *N. cinerea*, and negative test results for glucose (GLU), maltose (MAL), and γ-glutamyl aminopeptidase (GGT), which almost certainly excluded *N. meningitidis*. The AB MicroSeq 500 16S rDNA PCR kit (Applied BioSystems/Life Technologies, Zug, Switzerland) could not discriminate between *N. meningitidis* and *N. cinerea*. *N. meningitidis* was definitely excluded by negative results of *ctrA* and *sodC* PCR performed on extracted DNA of the strain (4, 5). Serogroup determination by PCR and culture-based agglutination (DiFC Neisseria meningitidis antisera; Becton Dickinson, Allschwil, Switzerland) were both negative.

*Neisseria cinerea* was confirmed by complete 16S rRNA gene sequencing (Fig. 2).

Percutaneous treatment of the trigeminal ganglion is one op-
tation in cases of severe trigeminal neuralgia and can be executed either by instillation of glycerol or by applying radiofrequency. The ganglion lies close to the foramen ovale and is reached by passing a thin needle under fluoroscopic control via the skin of the cheek and the facial muscles through the foramen ovale, where glycerol or radiofrequency is applied (Fig. 1B) (6–8). The procedure is considered safe, with postprocedural bacterial meningitis described in about 0.15% of cases (2).

*N. cinerea* was first recognized in 1905 by von Lingelsheim as *Micrococcus cinereus* (9) and was again described as an asaccharolytic commensal of the human oropharynx by Berger and Paepcke in 1962 (10). In 1984, *N. cinerea* was accurately characterized by Knapp et al. (11). It is a commensal of the human oropharynx and sometimes the urogenital tract with low pathogenic potential, although invasive infections are rarely reported. One case of posttraumatic meningitis and bacteremia (12), four episodes of bacteremia, two of these in immunocompromised patients and resulting in death (13–15), one case of endocarditis in an intravenous drug user (16), three episodes of continuous ambulatory peritoneal dialysis (CAPD)-associated peritonitis in two different patients (17, 18), two cases of pulmonary infections in immunosuppressed patients (19, 20), one case of proctitis (initially misidentified as *N. gonorrhoeae*) in a child (21), and several cases of purulent conjunctivitis in neonates (22) have been described so far.

Phenotypic identification of *N. cinerea* is difficult due to the limited number of expressed characteristics, and misclassification as *N. gonorrhoeae* has been reported (21, 23). Certain characteristics (i.e., no growth of *N. cinerea* on chocolate agar at 22°C or golden-brown pigmentation in many of the strains) allow identification, but none of these are reliable for accurate species identification (23).

Key reactions used for identification of *Neisseria* spp. include metabolism of different sugars. API NH and RapID NH (Thermo Scientific, Braunschweig, Germany) are examples of commercially available kits used for identification of *Neisseria* species within hours by testing similar enzymatic processes. However, as *N. cinerea* is one of the asaccharolytic species, specific identification by metabolic testing is difficult. *Neisseria meningitidis* can virtually be excluded with phenotypic tests, although misidentification of *N. meningitidis* is possible, as described recently (24).

As reported here, results of differentiation of *Neisseria* spp. by MALDI-TOF MS might not always be reliable. Misidentification of *N. polysaccharea* as *N. meningitidis* was recently reported (25). One systematic analysis of the performance of MALDI-TOF in the differentiation of *Neisseria* spp. has been published and showed good discrimination between pathogenic and clinically nonrelevant *Neisseria* spp., although the robustness of differentiation within the nonpathogenic subgroup was not studied in detail (26).

This report shows that *N. cinerea* is a potential source of severe disease following iatrogenic infection. Accurate differentiation of *Neisseria* spp. is mandatory due to serious medical, legal, and public health consequences (see, e.g., reference 21). As long as *Neisseria* species differentiation from a normally sterile specimen is pending, clinicians must consider invasive meningococcal disease, which implies the use of droplet isolation precautions for the first 24 h after the initiation of adequate antimicrobial treatment (27).

Although MALDI-TOF MS-based identification has become a quasistandard in the diagnostic microbiology laboratory (28), confirmation of identification results obtained with neisseriae with an independent diagnostic method (i.e., biochemistry, DNA-sequencing) is strongly advised.

**Nucleotide sequence accession number.** The 16S rRNA gene sequence was deposited in GenBank under accession no. KF646791.

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**REFERENCES**


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**TABLE 1 MIC for the isolated *Neisseria cinerea* strain by broth dilution**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (µg/ml)</th>
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<tbody>
<tr>
<td>Penicillin</td>
<td>0.25</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>0.125</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&lt;0.016</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.016</td>
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**FIG 2** Phylogenetic tree of related *Neisseria* 16S rRNA gene reference sequences compared to *N. cinerea* sequence KF646791 (1,486 bp) using ClustalW algorithm.

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Haqqie SS, Chiu C, Bailie GR. 18.


Knapp JS, Totten PA, Mulks MH, Minshew BH. 11.

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