Meningoencephalitis due to *Gemella haemolysans*

Benjamin T. Galen,¹ David B. Banach,² Melissa R. Gitman³ and Terence K. Trow⁴

¹Department of Internal Medicine, Albert Einstein College of Medicine, Bronx, NY, USA
²Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, USA
³Pathology and Laboratory Medicine, Yale University School of Medicine, New Haven, CT, USA
⁴Section of Pulmonary, Critical Care and Sleep Medicine, Yale School of Medicine, New Haven, CT, USA

*Gemella haemolysans* is an uncommon but described cause of invasive disease in humans. We report a case of meningitis due to *G. haemolysans* that did not grow in cerebrospinal fluid culture, demonstrating a potential role for direct 16S rRNA gene PCR and sequencing in culture-negative cerebrospinal fluid when bacterial meningitis is suspected.

**Case report**

A 71-year-old man with hypertension, chronic obstructive pulmonary disease, pre-diabetes and chronic alcohol use presented from home to the Emergency Department with decreased responsiveness, nausea, vomiting, diarrhoea and subjective fever without headache. On presentation, his temperature was 97.8 °F, his heart rate was 150 min⁻¹ and his blood pressure was 160/94 mmHg. He subsequently suffered a grand-mal seizure necessitating intubation and initiation of intravenous lorazepam. Post-ictal laboratory examination was noteworthy for a serum bicarbonate of 17.4 mmol l⁻¹, lactic acid of 12 mmol l⁻¹ and a white blood cell count of 20 700 µl⁻¹ with 24 % bands. A computed tomography scan of the head was negative for acute stroke and he was admitted to the medical intensive care unit. In the Emergency Department, he had received ceftriaxone, vancomycin and clindamycin. During intensive care unit admission, the acid-base disturbances resolved, as did his leukocytosis. Electroencephalography did not demonstrate seizure activity. He was extubated on the second day of intensive care hospitalization and was alert and oriented but intermittently agitated and not at his baseline mental status off sedation. Lumbar puncture was performed the following day, which revealed an opening pressure of 44 cmH₂O, xanthochromia, protein 113 mg dl⁻¹, glucose 61 mg dl⁻¹ [serum glucose 161 mg dl⁻¹; cerebrospinal fluid (CSF): serum ratio of 0.38], and tube #4 revealed 1050 red blood cells and 773 nucleated cells with 85 % granulocytes. Gram stain was interpreted as 3+ Gram-negative diplococci (Fig. 1), and after blood cultures were obtained, the patient was continued on empiric antibiotics for bacterial meningitis comprising vancomycin, ceftriaxone and ampicillin. His mental status returned to baseline over the next 4 days and his final CSF and blood cultures remained without growth. He completed 7 days of ceftriaxone treatment for presumed meningococcal meningitis. He was discharged to home on day 9 of hospitalization with complete neurological recovery. Subsequently, direct 16S rRNA gene PCR amplification and sequencing of the CSF performed using a MicroSeq 500 system (Applied Biosystems) revealed *Gemella haemolysans* (99.83 % nucleotide identity). This patient has been seen in follow-up and remains neurologically intact without sequelae 6 months following discharge.

*G. haemolysans* is a rarely pathogenic, commensal Gram-positive coccus that colonizes the human respiratory and gastrointestinal tracts. Cases of invasive disease caused by this organism including endocarditis, endophthalmitis, spondylodiscitis, peritonitis and bacteraemia have been reported (Anil et al., 2007; Khan et al., 2004; Unal et al., 2009; Woo et al., 2003). To date, we are aware of only seven prior cases of meningitis due to this organism and one prior case of brain abscess (Anil et al., 2007). This patient probably presented with acute bacterial meningitis, but his diagnosis was delayed given plausible alternative diagnoses, including alcohol withdrawal in the setting of gastroenteritis. The failure of his CSF culture to grow was attributed to receipt of antibiotics prior to lumbar puncture. This patient's computed tomography scan of the head showed mucosal thickening of the maxillary sinuses, which might have provided a site of organism entry into the CSF. *G. haemolysans* may be difficult to identify on a Gram stain, as this organism is easily decolorized (Anil et al., 2007; Khan et al., 2004). Prior work suggests that β-lactam and glycopeptide antibiotics, which inhibit cell-wall synthesis, may induce cell-wall-deficient forms in Gram-positive bacteria; this could also potentially explain the results of the CSF Gram stain in this case (Woo et al., 2001). *G. haemolysans* was initially classified as *Neisseria haemolysans* in the family

**Abbreviation:** CSF, cerebrospinal fluid.
Neisseriaceae but later reassigned to the family Streptococcaceae (Anil et al., 2007). Resistance to antibiotics including β-lactams has been reported, but this patient’s complete clinical recovery with ceftriaxone did not prompt further therapy (Anil et al., 2007; Khan et al., 2004).

16S rRNA gene sequencing is an increasingly available technique for identifying clinical isolates with increased specificity compared with conventional means. This technique is able to detect a small quantity of organisms as well as the presence of non-viable organisms following the administration of antimicrobial therapy (Schuurman et al., 2004; Welinder-Olsson, et al., 2007). In one prior study, PCR was able to detect organisms in 19 cases of acute bacterial meningitis with culture-negative CSF, including 15 cases in which antibiotics were administered prior to lumbar puncture (Welinder-Olsson, et al., 2007).

Summary
This case adds to the literature supporting the use of 16S rRNA gene PCR testing in CSF analysis, specifically in cases of culture-negative CSF when antibiotics have been administered prior to lumbar puncture. To our knowledge, no prior publications describe the use of 16S RNA gene sequencing to make the initial diagnosis of Gemella spp. infection in the absence of growth on culture medium. Furthermore, clinicians should be aware that G. haemolysans is a rare cause of CNS infection in adults that may be misidentified by Gram staining.

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References