Title: Meningitis due to Gemella haemolysans in a pediatric case

Running Title: Gemella haemolysans meningitis

Author’s name: Murat Anıl¹, Nisel Ozkalay²*, Mehmet Helvaci¹, Neval Agus², Ozlem Guler¹, Aysu Dikerler¹, Berat Kanar¹

Author’s address: Department of Pediatrics¹ and Department of Microbiology², Tepecik Educational and Research Hospital, Yenisehir, Izmir, Turkey

*Corresponding author:
Mailing address : Department of Microbiology, Tepecik Educational and Research Hospital, Yenisehir, Izmir, Turkey.
Phone : 90 232 4696969
Fax : 90 232 4330756
E-mail : niseloz@yahoo.com
*Gemella haemolysans* is a rare pathogen in cases of bacterial meningitis. We present a case of meningitis due to *Gemella haemolysans* in a 17-month-old boy. This is the first reported case of *Gemella* meningitis in a child. The patient completely recovered following intravenous therapy with linezolid and chloromphenicol.
THE CASE

A 17-month-old boy who was diagnosed at the age of two months with complex congenital heart disease (perimembranous ventricular septal defect and a small patent ductus arteriosus) was admitted to the hospital with complaints of fever, vomiting and loss of appetite for two days. The physical examination revealed an ill-appearing baby with a head circumference of 46.5 cm, a weight of 10500 g, and a height of 77 cm. His body temperature was 39.2°C, his heart rate was 164/min, and his respiratory rate was 28/min. The anterior fontanelle was closed and he had a grade 2/6 systolic murmur at the left sternal border. There was no hepatomegaly or splenomegaly, and he had no sick contacts or trauma. He had received three times hepatitis B, polio, diphtheria, tetanus toxoids, pertussis, and first Bacille Calmette-Guerin (recommended in the childhood immunization schedule in Turkey) vaccines, and had not received *Haemophilus influenzae* type b vaccine (recommended in the childhood immunization schedule in Turkey for three months). His medications included digoxin and spironalactone because of heart disease. There was no family history of invasive bacterial infection.

Blood, cerebrospinal fluid (CSF) and urine samples were taken and sent to laboratory for culture and biochemical analyses. The complete blood count showed a white blood cell (WBC) count of 21830 /mm$^3$, of which 74% were neutrophils, 8% were bands, 16% were lymphocytes, and 2% were monocytes; a hemoglobin level of 11.9 g/dL; and a platelet count of 170.000 /mm$^3$. A serum basic chemistry was normal except for a glucose level of 183 mg/dL. The level of C-reactive protein was 30.4 mg/dL and the erythrocyte sedimentation rate was 56 mm/h. Serum immunoglobulin and subclass levels were normal and anti-HIV was negative. Urine analysis and the chest radiograph were normal.

Transthoracic echocardiography was negative for endocarditis. CSF analyses showed a protein concentration of 102 mg/dL; a glucose concentration of 11 mg/dL; a red blood cell count of 250 /mm$^3$; and WBC count of 4500 /mm$^3$, of which 88% were neutrophils, 12% were lymphocytes. The CSF was negative by Gram staining. He was diagnosed as suspected bacterial meningitis and empirical antibiotic treatment was started as; ampicillin (300 mg/kg per day) and cefotaxime (200 mg/kg per day) as part of our clinical protocol. Intravenous dexamethasone (0.6 mg/kg per day, 4 days) was given before the first administrated antibiotic dose. The CSF specimen was cultured on 5% sheep blood, eosin-methylene blue, and chocolate agars at 35°C in 5 to 10% CO$_2$ for 48-72 h. Because of suspicions of the endocarditis three pairs of aerobic and anaerobic blood cultures with each bottle containing 1-2 ml of the patient’s blood were obtained prior to initiating antimicrobial therapy. The blood cultures were incubated in a BACTEC 9120 instrument (Becton Dickinson and Company, Sparks, MD). The urine specimen was cultured on 5% sheep blood, eosin-methylene blue at 35°C in 5 to 10% CO$_2$ for 24 to 48 h. Blood and urine cultures were negative but from the CSF cultures, $10^3$ CFU/ml, small and grayish colonies grew on the sheep blood and chocolate agars after 72 h. Colonies were weakly alpha-hemolytic on the sheep blood agar. Gram staining of the colonies showed Gram-variable cocci. Additional standard conventional biochemical method (15) and the API 20 STREP identification system (bioMerieux, Marcy l’Etoile, France) were used to identify these colonies. The
organism was a nonmotile, oxidase-, catalase-, bile esculine reaction-negative, and failed to grow in broth containing 6.5% NaCl. In the API 20 STREP system the isolate gave biotype number 040011011000 with a probability of 99.5%, which was interpreted as “very good identification”. All tests showed that *Gemella haemolysans* was present in the CSF culture. The antimicrobial susceptibility testing was performed by Kirby-Bauer disk diffusion method using Mueller-Hinton agar supplemented with 5% sheep blood and incubated in 5% CO\(_2\) at 35°C (20). The susceptibility of the isolate to antimicrobial agents was determined by applying the Clinical and Laboratory Standards Institute susceptibility criteria used for viridans streptococci (4). The isolate was resistant to penicillin, ampicillin, ceftazidime, ceftriaxone, clindamycin, levofloxacin, and vancomycin (zone diameter: 14 mm) and susceptible to linezolid and chloromphenicol (Oxoid Limited, Hampshire, England) by the disk diffusion method. After the antimicrobial susceptibility test, intravenous linezolid (100 mg/kg/day) and chloramphenicol (20 mg/kg/day) were started on the 4th day as a substitute for ampicillin and cefotaxime. We stated E-test was performed while disk diffusion results were given. Later, we tested vancomycin MIC by the E-test according to the manufacturer’s recommendations (AB BIODISK, Solna, Sweden) method and found it susceptible (MIC, 1 µg/ml) but we did not change the treatment protocol. The patient’s clinical status progressively improved. Forty-eight hours after initiation of linezolid and chloramphenicol treatment the patient became afebrile. Subsequent CSF culture was negative on day 6. After an antibiotic treatment of 10 days, clinical evolution was found to be excellent, inflammatory indexes were normal, there was no evidence of neurologic sequelae and hearing assessment was normal.

*Gemella haemolysans* was first described by Thjötta and Böe as *Neisseria haemolysans* in 1938. Berger further showed that it was catalase and oxidase negative, and attacked carbohydrates fermentatively, unlike neisseriae. He considered that it should be allocated to a new genus *Gemella* (“little twin”) within the family *Neisseriaceae*, with a single species *Gemella haemolysans*. Nucleic acid hybridization studies showed no relatedness to members of *Neisseriaceae*. On the basis of these findings, the genus *Gemella* was transferred to the family of *Streptococcaceae* (7, 13, 14, 21). *G. haemolysans* is commensal of the upper respiratory, gastrointestinal and genitourinary tracts in humans (7, 14). However, as an “opportunistic pathogen”, *G. haemolysans* occasionally causes severe localized and generalized infections. Endocarditis (7, 8), central nervous system infections (1, 9, 12, 13, 16), eye infections (17), spondylodiscitis (11), thorax empyeme (6) and bacteremia (22) have been described. Endocarditis is the most common infection caused by this organism (7, 8). However, we did not find any clinical signs associated with endocarditis and any finding for endocarditis on echocardiography. And also, all of the blood cultures were negative. Interestingly, the infection site was the central nervous system not the heart in our case. The central nervous system infection due to *G. haemolysans* is very rare. To date worldwide, there are six documented cases of meningitis and a case of brain abscess due to *G. haemolysans*. Characteristics of previously reported cases of intracranial infections due to *G. haemolysans* are summarized in table 1. The most common primary
septic sites in the cases of intracranial *Gemella* spp. infections were the upper respiratory tract and the oral (9, 10, 12, 16, 19). In the present case, the portal of the entry of the infecting organism is uncertain.

Table 1. Characteristics of previously reported cases of intracranial infections due to *G. haemolysans*

<table>
<thead>
<tr>
<th>Reference</th>
<th>Primary septic site</th>
<th>Intracranial involvement</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Paranasal sinus</td>
<td>Meningitis</td>
<td>Good</td>
</tr>
<tr>
<td>9</td>
<td>Oral cavity</td>
<td>Brain abscess</td>
<td>Good</td>
</tr>
<tr>
<td>12</td>
<td>Paranasal sinus</td>
<td>Meningitis</td>
<td>Good</td>
</tr>
<tr>
<td>12</td>
<td>Unknown</td>
<td>Meningitis</td>
<td>Good</td>
</tr>
<tr>
<td>13</td>
<td>Unknown</td>
<td>Meningitis</td>
<td>Good</td>
</tr>
<tr>
<td>16</td>
<td>Oral cavity</td>
<td>Meningitis</td>
<td>Good</td>
</tr>
</tbody>
</table>

Infections caused by *G. haemolysans* in the pediatric age group are rare. In medline research, we found only three pediatric cases, but none of this involved the central nervous system (Table 2).

Table 2. Case reports of *Gemella haemolysans* infections in children

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Underlying condition or source of infection</th>
<th>Culture site</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>6</td>
<td>M</td>
<td>Endocarditis</td>
<td>Congenital truncal arteriosus, valvular surgery</td>
<td>Blood</td>
<td>Amoxicillin and gentamicin</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>M</td>
<td>Wound infection</td>
<td>Rheumatic heart disease</td>
<td>Blood</td>
<td>Cephalexin</td>
<td>Good</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>M</td>
<td>Pneumonia leading to renal failure</td>
<td>Operative repair of pectus excavatus. Transtorasic-fixating devices</td>
<td>Blood</td>
<td>Cefotaxime and hemodialysis</td>
<td>Good</td>
</tr>
<tr>
<td>PR</td>
<td>17 month</td>
<td>M</td>
<td>Meningitis</td>
<td>Complex congenital heart disease</td>
<td>CSF</td>
<td>Linezolid and chloromphenicol</td>
<td>Good</td>
</tr>
</tbody>
</table>

M: male; CSF: Cerebrospinal fluid; PR: Present report

Generally, human infections caused by *Gemella* species are associated with underlying conditions, including an immunocompromised state, cancer, heart disease, sinusitis, or poor dental condition, as
well as with previous invasive medical procedures. Some cases have been reported in immunocompetent patients and have even caused life-threatening conditions in previously healthy people (7, 11). In our case, the patient had an underlying chronic heart disease without a source of infection.

Infections due to *G. haemolysans* have been observed infrequently. During Gram staining, cells are easily decolorized and may, therefore, appear Gram-variable or even Gram-negative, and also, identification of the organism may be delayed owing to its slow growth and fastidious requirements. It is likely that Gram staining abnormality and morphological polymorphism are responsible for the misidentification of *Gemella* spp. They may exhibit alpha-hemolytic on blood agar, catalase negative and appear Gram-positive cocci. Therefore, it can be initially misidentified as a viridans streptococcus and reported as a normal flora. This again may explain why so few cases are reported (8, 18, 20, 21).

In most cases, the infections were successfully treated with antibiotic therapy, usually penicillin or amoxicillin associated with gentamicin (8). Species isolated from clinical specimens in the past were usually sensitive to penicillin G and ampicillin. However, recent data suggests an emerging resistance.

In 1993, a strain of *G. haemolysans* that was recovered from a blood culture was found to be sensitive to penicillin G, ampicillin, gentamicin, and cefuroxime and was resistant to vancomycin, teicoplanin, erythromycin, and tetracycline (21). Our isolate was highly resistant to most of the tested antibiotics but sensitive to vancomycin, linezolid and chloromphenicol.

In conclusion, although *G. haemolysans* is a rare pathogen in humans it may occasionally cause severe infections, including meningitis, endocarditis and bacteremia, and while *G. haemolysans* is highly susceptible to many antibiotics, our data may show a possible increasing resistance rate.

REFERENCES