Group A streptococcal septicemia, meningitis and cerebral abscess: case report and literature review

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Group A streptococcus (GAS) is a global bacterial pathogen. It is a rare cause of central nervous system infections and accounts for about 1% of all childhood meningitis. Otitis media or sinusitis has been reported as a risk factor for brain abscess in invasive GAS diseases. We present the case of a previously healthy boy with GAS sepsis and meningitis. He subsequently developed a brain abscess and needed a prolonged course of intravenous antibiotics.

Key words: group A streptococcus, meningitis, cerebral abscess, sepsis.

Group A streptococcus (GAS) is a major bacterial pathogen affecting children globally1. GAS can cause a wide range of clinical pathologies in humans and can be subdivided into superficial, invasive, toxin-mediated, and post-infectious diseases. However, pharyngitis and cellulitis remain the most common infections caused by GAS in children. There has been a recent increase in invasive GAS diseases, although bacterial meningitis caused by this pathogen remains fairly uncommon2,3. We describe the case of a healthy 3.5-year-old boy who presented with GAS septicemia and meningitis and later developed a cerebral abscess, followed by a review of the microbiological aspects of GAS and a literature review.

Case Report

ZP, a healthy 3.5-year-old boy born to non-consanguineous parents presented to the pediatric unit with a temperature of up to 40°C and two episodes of vomiting, and appearing generally unwell. One week prior to the admission, ZP suffered a sore throat lasting one day that was associated with a high fever and was managed with antipyretics (paracetamol and ibuprofen alternatively) by the general practitioner.

The initial assessment showed him to be pyrexial and tachycardic with a few non-blanching petechial spots on the face. His airway, breathing and circulation were stable, and he had congested tonsils and a pink tympanic membrane on the left. The clinical impression was of a viral illness or sepsis and he was started on intravenous (IV) ceftriaxone 80 mg/kg once daily. This dose was prescribed according to the British National Formulary for Children, 2010.

Initial blood investigations showed increased inflammatory markers with a C-reactive protein (CRP) of 222 mg/L (reference 0-10 mg/L), white cell count of 34 x 10^9/mm^3 (4.5-11.5 x 10^9/mm^3) and neutrophil count of 29 x 10^9/mm^3 (1.5-7.5 x 10^9/mm^3). The serum electrolytes and calcium were reported within normal limits.

As he remained tachycardic, pyrexial and irritable, a lumbar puncture was performed 24 hours after the antibiotics were started. The cerebrospinal fluid (CSF) was turbid in appearance. Initial examination of the CSF showed a white cell count of 7040/mm^3, of which 78% were polynucleated, and a red cell count of 140/mm^3. No organisms were seen on the gram stain. The CSF glucose was reported as 2.2 mmol/L (3–4.5 mmol/L) (random blood glucose was 5.2 mmol/L) and protein was 1.2 g/L (0.2–1.0 g/L). The serum electrolytes and calcium were reported within normal limits.

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Intravenous (IV) amoxicillin was added to the existing regimen of ceftriaxone (continued at the high dose of 80 mg/kg) to cover for
a possible Listeria, in line with the local antibiotic policy and in view of the lack of initial response to IV ceftriaxone in the first 24 hours. Penicillin-resistant or intermediate pneumococci are extremely rare in the region, and there was no relevant travel history.

The blood culture result was available at 48 hours and showed a growth of GAS. The IV ceftriaxone was continued and the amoxicillin was changed to IV benzylpenicillin at a dose of 50 mg/kg qds. The CSF study showed no growth after 48 hours; however, it may be noted that the CSF sample was obtained 24 hours after administration of the first dose of IV ceftriaxone. The inflammatory markers during the course of the illness are presented in Table I.

The patient started showing signs of improvement, and a peripheral long line was inserted for a definitive longer term access, as the plan was to treat him with IV antibiotics for two weeks. As the child showed signs of continuous improvement, on day 10 of the antibiotic treatment, benzylpenicillin was discontinued with a plan to complete a full two-week course of IV ceftriaxone. The ceftriaxone was continued as the GAS in the blood culture was sensitive to ceftriaxone, and monotherapy was considered adequate in this case.

However, on day 11, the patient began spiking a temperature of >39°C, and IV teicoplanin was started to cover the possibility of long-line sepsis as per the hospital protocol. A computed tomography (CT) scan showed a left-sided cerebral abscess (Fig. 1). He was transferred to the regional neurosurgical unit, where a magnetic resonance imaging (MRI) brain scan confirmed the CT scan findings. At this time, he was also found to have left-sided mastoiditis, and subsequently underwent drainage of his left mastoid. The wound swab culture showed no bacterial growth.

The antibiotic regimen was changed to IV cefotaxime and clindamycin, which was completed in his local hospital. He again started to spike a temperature on day 19 of hospitalization, and the long line was removed and a course of IV/intramuscular (IM) teicoplanin was given for a further four days. The choice of teicoplanin was in accordance with the local antibiotic policy for central line sepsis.

He remained afebrile for 72 hours and was discharged home on day 22. He was reported to have returned to normal health at a clinic follow-up two months later. However, he had developed left-sided sensorineural hearing loss and is under audiology follow-up. His development is reported to be normal six months after the infection.

### Discussion

Group A streptococcus (GAS) was discovered by Louis Pasteur in 1879. The entire genome of an M1 strain of GAS was sequenced in 2001, and a further eight strains have been sequenced since then. In the early part of the 20th century in the pre-antibiotic era, GAS was the second commonest cause of meningitis after pneumococci.

Pharyngitis and cellulitis are the most common infections caused by GAS in children. Broken skin or IV insertion sites can serve as an entry site leading to GAS invasive conditions. In a prospective population based study in Ontario, Canada, invasive GAS was found to occur in 1.9 per 100,000 children, and chicken pox infection was found to increase the risk of invasive GAS diseases, accounting for about 15% of all pediatric invasive GAS diseases. Invasive GAS occurs when the bacterium is isolated from a normally sterile site, for example pneumonia, meningitis, peritonitis, etc. Pre-existing chronic health conditions, for instance cardiac or respiratory, neoplasms, human

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**Table I. The Inflammatory Markers During the Course of the Illness**

<table>
<thead>
<tr>
<th>Inflammatory marker</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 11</th>
<th>Day 12</th>
<th>Day 24</th>
<th>Day 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCC (x10⁹/mm³)</td>
<td>34.1</td>
<td>43.3</td>
<td>21.5</td>
<td>17.2</td>
<td>3.6</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (x10⁹/mm³)</td>
<td>30.1</td>
<td>37.9</td>
<td>18.7</td>
<td>10.8</td>
<td>2</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Platelets (x10⁹/mm³)</td>
<td>599</td>
<td>544</td>
<td>587</td>
<td>616</td>
<td>303</td>
<td>286</td>
<td></td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>222</td>
<td>466</td>
<td>153</td>
<td>50</td>
<td>226</td>
<td>25</td>
<td>42</td>
</tr>
</tbody>
</table>

WCC: White blood cells. CRP: C-reactive protein.
immunodeficiency virus, and diabetes increase the risk of GAS infections. Bacteremia without a focus is found in 15% of cases of invasive GAS disease. In a study of 52 invasive GAS diseases in children who had primary varicella infection in the United States, an association was found between ibuprofen use and invasive GAS infection.

GAS Meningitis and Cerebral Abscess

Despite the increase in invasive GAS, bacterial meningitis due to GAS accounts for less than 1% of all cases of meningitis in children. Reports have suggested that a focus for initial GAS infection can be identified in 68% of cases, otitis media being the commonest. Children with cochlear implants are at increased risk, and a change in the child's hearing is often noted first. Streptococci and staphylococci are the most commonly identified organisms causing brain abscess.

Cerebral abscess is rarely seen in GAS meningitis. A suspicion should arise in cases with features of intracranial involvement such as regular spikes in temperature, headache, lethargy, vestibular symptoms, or deteriorating levels of consciousness. However, it may present without any clear signs or just as recurrence of temperature spikes after an initial improvement, as seen in the case report. In a study of 52 pediatric patients in the United States, a statistically significant association was observed between non-necrotizing invasive GAS infection and ibuprofen use. A CT scan may be needed in the case of a child with GAS infection who keeps spiking a high temperature or in the presence of signs of intracranial involvement.

Group A streptococcus (GAS) meningitis has higher rates of neurological sequelae, such as epilepsy, new motor deficits, learning disorders, hearing loss, visual field defects, etc., reported between 36% and 46%, one of the highest amongst the major bacterial meningitis. There is need for long-term follow-up.

Diagnosis

Group A streptococcus (GAS) may be demonstrated in throat or oropharyngeal swabs. In a study of 27 children in Zagreb, Croatia with blood culture-confirmed GAS bacteremia, respiratory infections were considered to be the primary focus in the majority of cases, and throat swab was positive for GAS in 17 out of the 25 samples sent for study. A suspicion of invasive GAS disease should initiate a complete workup with inflammatory markers and blood culture. In a case series of 30 patients with GAS meningitis recorded over 25 years, 59% of the cases grew GAS in the blood culture.

Lumbar puncture should always be done if a suspicion of GAS meningitis arises. An interval lumbar puncture (done after starting antibiotics) would reveal raised white cell count and low CSF sugar, but may not grow organisms, as was evident in this case report.

Management

Group A streptococcus (GAS) has been found to be sensitive to all beta-lactam antibiotics, with no published report of resistance thus far. Intravenous benzylpenicillin remains the drug of choice in GAS meningitis. However, third generation cephalosporins like cefotaxime or ceftriaxone are also suitable drug alternatives. A public health team needs to be involved when an invasive GAS disease is diagnosed. Clinical trials are currently in progress for a GAS vaccine.

In conclusion, GAS meningitis and cerebral abscess remains an unusual manifestation of invasive disease. It most commonly occurs in association with otitis media; however, GAS meningitis in the absence of a recognizable focus is possible. Clinical suspicion and early
administration of antibiotics are necessary. We hope this article provides a heightened awareness of this relatively rare but serious pathology. Public health control measures are aimed at decreasing the overall spread of invasive GAS diseases.

REFERENCES