

CLINICAL CASE REPORTS

Group A Streptococcal Meningitis in a Healthy Child: A Case Report Highlighting Diagnostic and Therapeutic Challenges

Ema Freitas^{1,2} , Clara Picão de Carvalho^{2,3} , Mariana Nogueira² , Isabel Esteves⁴ , Hugo de Castro Faria² 

ABSTRACT

Group A *streptococci* commonly causes non-invasive infections like tonsillitis and skin infections, but rarely causes invasive infections, such as bacteraemia and meningitis. Invasive streptococcal disease increased in Europe in 2022 and 2023, but rates returned to pre-pandemic levels in 2024. GAS meningitis remains rare. This case highlights a 13-month-old healthy child with fever, irritability alternating with periods of prostration, and petechial rash, diagnosed with Group A *streptococcal* meningitis. She was treated initially with ceftriaxone and vancomycin and later with penicillin based on culture results. Despite clinical and analytical improvement, persistent fever prompted further investigations, ruling out complications or other infections. The fever resolved after switching to ceftriaxone, suggesting drug-induced fever due to penicillin hypersensitivity. No neurological sequelae were detected in this case. Although rare, Group A *streptococcal* meningitis poses significant risks of morbidity and mortality, emphasising the need for prompt recognition and appropriate treatment.

Keywords: drug-induced fever; group A *Streptococcus* bacterial meningitis; penicillin

1. Pediatric Department, Unidade Local de Saúde de São José, Hospital Dona Estefânia. 1169-045 Lisbon, Portugal. emafreitas@gmail.com
2. Child and Adolescent Intermediate Care Unit, Hospital Cuf Descobertas. 1998-018 Lisbon, Portugal. emafreitas@gmail.com; clara.p.oliveira@jmellosaude.pt; mariana.s.nogueira@jmellosaude.pt; hugo.faria@jmellosaude.pt
3. Pediatric Department, Unidade Local de Saúde de Santa Maria. 1649-035 Lisbon, Portugal. clara.p.oliveira@jmellosaude.pt
4. Pediatric Infectious Diseases Department, Hospital Cuf Descobertas. 1998-018 Lisbon, Portugal. isabel.castro.menezes@gmail.com

INTRODUCTION

Group A *streptococcus* (GAS) is a common pathogen that frequently causes non-invasive infections such as tonsillitis, scarlet fever and skin infections. However, invasive infections like bacteraemia, streptococcal toxic shock syndrome, necrotizing fasciitis and less frequently meningitis, arthritis and osteomyelitis can occur.⁽¹⁾ An increase in the incidence of invasive streptococcal disease was observed, particularly in Europe, during 2022 and 2023, with rates returning to pre-pandemic levels in 2024.⁽²⁾ Nevertheless, GAS meningitis remains a rare clinical entity.

We present a case of GAS meningitis with a favourable outcome in a previously healthy child, to raise awareness of this rare meningitis pathogen.

CASE REPORT

A healthy, immunised 13-month-old-girl presented to our emergency department with a two-day history of high fever, maximum temperature of 40°C every seven to eight hours, associated with irritability alternating with periods of prostration. Additionally, she had two episodes of vomiting and one of diarrhoea without blood or mucus. She received a single dose of oral amoxicillin due to acute otitis media diagnosed the previous day. There were no respiratory symptoms. She had contact with a cousin with scarlet fever two weeks before the onset of symptoms.

On admission, she was hemodynamically stable, afebrile, conscious, and responsive but lethargic with a GCS of 13 and with preferred head position to the right side. A small anterior fontanelle was noted. Neck stiffness was difficult to assess; Kernig test was negative and Brudzinski sign was dubious. She had a petechial rash on her torso and abdomen. Her tonsils were hypertrophied and hyperemic, and otoscopy revealed bilateral hyperemic tympanic membrane without bulging. Physical exam was, otherwise, unremarkable.

Blood analysis revealed leukocytosis of 19400/uL with 86,6% neutrophils and elevated CRP at 36.76 mg/dL and elevated PCT at 37.78 ng/mL. A throat swab for group A *streptococcal* bacteria was positive. Brain CT was normal. A lumbar puncture was performed under sedation with ketamine, propofol and midazolam, yielding a clear cerebrospinal fluid (CSF). Empirical antibiotic therapy was initiated with ceftriaxone 100 mg/Kg/day every 24 hours. CSF analysis revealed 2499 cells/mm³ with predominance of polymorphonuclear cells, decreased glucose at 6 mg/dL (pre-procedure glycemia of 107 mg/dL) and elevated protein concentration of 500 mg/dL. Due to the suspicion of bacterial meningitis vancomycin 60 mg/Kg/day every six hours was associated. At day three of admission group A *streptococcal* bacteria sensitive to penicillin and ceftriaxone was isolated on CSF culture. Blood cultures were negative. Antibiotics were adjusted according to antimicrobial susceptibility testing and so ceftriaxone and

vancomycin were discontinued and penicillin 400.000 U/Kg/day every four hours was initiated. Due to the need for prolonged therapy a central venous catheter was placed in the left brachiocephalic trunk. The patient progressively improved neurologic symptoms and infectious parameters, however she maintained fever. At day eight of admission a brain MRI was performed, which didn't show any sign of complications. Other causes of fever were excluded, including viral and hospital acquired infections. Additionally, cultures of the catheter tip, catheter, and blood were all negative. Since inflammatory markers were decreasing, a chest radiograph, urinalysis, and repeat blood cultures were not performed. The persistent fever was attributed to penicillin hypersensitivity. Penicillin was discontinued after nine days and switched to ceftriaxone to complete 14 days of intravenous antibiotic therapy, and 48 hours later the fever disappeared. Considering a follow-up of three months, no neurological sequelae has been detected, and she is scheduled to repeat audiologic tests.

DISCUSSION

Bacterial meningitis due to group A *streptococcal* bacteria is very rare, accounting for 2% of cases.⁽³⁾ It is more prevalent in young children, particularly under one year old.^(4,5) Since GAS central nervous system infection is uncommon, the exact pathophysiology is still unclear and needs further studies.^(3,5) It is thought to be secondary to bacteraemia or contiguous infection from the ear and upper respiratory tract infections (otitis, tonsillitis, pharyngitis, sinusitis); however, there have been reported cases with no primary infectious focus found.^(3,6) In our case, the blood cultures were negative, which may be attributed to the previous single dose of amoxicillin. There are some risk factors associated with GAS infections of the nervous system such as the neonatal period, neurosurgery, skull fractures, CSF leaks, the presence of ventriculo-peritoneal shunt, skin lesions (varicella, impetigo, erysipelas), and immunocompromising conditions.^(7,8) Despite this, there have been reported cases in healthy children without any risk factors, as was the case with our patient.⁽⁸⁾ The clinical symptoms and CSF analysis of GAS meningitis are not different from other types of bacterial meningitis.^(8,9)

In our case, the patient initiated empirical treatment for bacterial meningitis according to our protocol. Afterwards, with the isolation of *S. pyogenes* in the CSF, the antibiotic was switched to penicillin, with a good outcome, and without admission in the intensive care unit. A CF multiplex PCR assay was performed; however, *S. pyogenes* wasn't among the pathogens tested. We believe it should be included due to its rapid result, allowing for the initiation of more appropriate antibiotic therapy.

The preferred antibiotic therapy is high dose of intravenous penicillin G owing to its potent bactericidal effect and the absence of reported cases of resistance to this drug.⁽⁸⁾ In the presence of meningeal inflammation, its penetration

through the blood-brain barrier increases, and also inhibits the penicillin efflux pump, augmenting its concentration in the brain.^(10,11) Although adjunctive clindamycin has been advocated in invasive Group A Streptococcus infections, particularly in toxin-mediated disease due to its inhibitory effect on toxin production, no clinical evidence of toxic shock syndrome was present in this case.⁽²⁾ Therefore, considering both the clinical presentation and the limited cerebrospinal fluid penetration of clindamycin, penicillin monotherapy was maintained.

As an alternative in cases of non-type I hypersensitivity to penicillin, ceftriaxone can be used.⁽⁸⁾ In the absence of complications, the treatment should last 10 to 14 days; however, if complications are present, the duration of treatment should be extended.⁽⁵⁾

An important difference observed in a study performed with children and adults revealed that morbidity and mortality is higher in children (44%) when compared to adults (7%).⁽⁵⁾ When compared with other bacterial agents, GAS meningitis mortality is lower than *pneumococcal*, group B *streptococcal*, and gram-negative meningitis, and similar to *H. influenzae* and *meningococcal* meningitis.^(5,9) Regarding sequelae post-GAS meningitis, they were more frequently observed than with other bacterial pathogens such as group B *streptococcal*, *pneumococcal*, and *meningococcal* meningitis.^(5,9) The majority of sequelae were neurological, described in 46% of cases, and included hearing loss, cognitive impairment, seizures, visual impairment and behavioural problems.⁽¹²⁾ Our patient had no neurological sequelae, but will require long-term follow-up over the next few years.

Also, in our case, despite clinical and analytical improvement with penicillin, she maintained fever. For that reason, an MRI was performed, which excluded associated complications. Drug-induced fever is a diagnostic of exclusion and a common cause of prolonged fever in clinical practice. It can be caused by several medications, including antibiotics, most frequently beta-lactams (such as penicillin), vancomycin and isoniazid. The fever's onset is variable but typically begins seven to ten days after initiating therapy in a patient with otherwise good clinical evolution.^(13,14) The diagnosis can only be reached by trial and error, realising that apyrexia is reached 48 hours after discontinuation of the drug and reappears after drug reintroduction.⁽¹⁴⁾

So, in our case, other possible sites of infection were excluded, making the drug-induced fever a more probable diagnosis. For that reason penicillin was discontinued and switched to ceftriaxone. Less than 48 hours after penicillin discontinuation, the patient became afebrile, which supported the suspicion of drug-induced fever. Further evaluation, including a future assessment for penicillin allergy, may be warranted to better clarify the presence of drug hypersensitivity.

In conclusion, it is crucial to recognize that GAS meningitis, though a rare agent of bacterial meningitis, poses a significant risk due to its high morbidity and mortality. We also point out

that persistent fever should prompt a thorough evaluation for potential complications and other sources of infection, and if these are excluded, drug-induced fever should be considered.

AUTHORSHIP

Ema Freitas - Conceptualization; Writing - Original Draft; Writing - Review & Editing

Clara Picão de Carvalho - Conceptualization; Writing - Original Draft; Writing - Review & Editing

Mariana Nogueira - Supervision; Validation; Writing - Review & Editing

Isabel Esteves - Supervision; Validation; Writing - Review & Editing

Hugo de Castro Faria - Supervision; Validation; Writing - Review & Editing

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CORRESPONDENCE TO

Ema Freitas
Pediatric Department
Unidade Local de Saúde de São José
Hospital Dona Estefânia
Rua Jacinta Marto
1169-045 Lisbon
Email: emafreitasc@gmail.com

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