Rare disease

Group-A-streptococcal meningitis in a 7-year-old child – a rare pathogen in a non-immune compromised patient

Leonarda Maria (LM) van Zitteren,¹ Niek LA Arents,² Feico Halbertsma¹¹Pediatrics Department, Máxima Medical Centre, Veldhoven, Netherlands;²Microbiology Department, Máxima Medical Centre, Veldhoven, Netherlands**Correspondence to** Dr Feico Halbertsma, f.halbertsma@mmc.nl**Summary**

A case is presented of meningitis in a 7-year-old female child caused by Group A streptococcus (GAS), a rare bacterial cause of meningitis, with a high rate of morbidity (46%) and mortality (10%). GAS is susceptible for empiric antibiotic therapy aimed at the most prevalent pathogens of meningitis. As GAS meningitis is typically associated with ear-nose-throat (ENT) infections, specific search for a reservoir is advised. Bacterial typification often demonstrates M-protein gene sequence type (EMM type) 1.0 associated with upper respiratory tract infections and also severe, invasive GAS infections. Follow-up investigation including neurologic developmental status and audiology testing is necessary. Although GAS is a very uncommon cause of acute bacterial meningitis in children, high morbidity and mortality have been reported. Being associated with ENT infections, a search for a GAS reservoir is proposed. GASs are susceptible for common empiric antibiotic therapies in meningitis. Follow-up investigation is necessary.

BACKGROUND

Group A streptococcus (GAS), also known as *Streptococcus pyogenes*, is one of the common pathogens usually causing mild infections of the upper respiratory tract, the skin and the soft tissue in children, such as acute pharyngitis, pneumonia, scarlet fever, impetigo and erysipelas.¹

Occasionally, GAS causes invasive infections. GAS infections are considered invasive when GAS are isolated from a sterile site and cause one of three clinically overlapping syndromes. The first two are most prevalent: GAS toxic shock syndrome and necrotising fasciitis. The third one is the group of focal and systemic infections, that does not meet the criteria of the first two, such as bacteremia without identified focus, osteomyelitis, peritonitis and very rarely, meningitis.²

We present a case report of a 7-year-old female child with classic symptoms of meningitis caused by a GAS infection, and discuss the diagnostic investigation, therapeutic considerations, follow-up and review the literature.

CASE PRESENTATION

A 7-year-old Caucasian, female child, presented at the emergency department of the Máxima Medical Centre in Veldhoven with progressive fever. She had been ill for 2 days with fever, headache and vomiting. There was no photophobia.

On examination, she had a normal level of consciousness. The ear temperature was 40.5 °C. Nuchal rigidity was seen with a positive Brudzinski and Kernig sign. The skin showed no petechia, purpura or rash. Examination of the ear, nose and throat area revealed an acute otitis media, without signs of mastoiditis. The remainder of the physical examination, including haemodynamic parameters was normal.

INVESTIGATIONS

Laboratory tests results showed a C-reactive protein of 68 mg/l (N: <6 mg/l) with a white blood cell count of $21.1 \times 10^9/l$ (87% neutrophils, 7% lymphocytes and 6% monocytes). Lumbar puncture revealed a nucleated cell count of 769/ μ l, a protein level of 1171 mg/l (N: 160–310 mg/l), a glucose level of <0.1 mmol/l (N: 2.6–3.8 mmol/l) and a lactate level of 8.66 mmol/l (N: 1.17–1.85 mmol/l). A Gram stain of the cerebrospinal fluid (CSF) showed Gram positive cocci and subsequently grew β -haemolytic Group A streptococci with T classification 1, EMM type 1.0 and exotoxine A, sensitive to penicillin, amoxicillin and gentamicin. Bloodcultures remained negative. A throat swab, obtained during antibiotic treatment, showed no hemolytic streptococci.

TREATMENT

The patient was admitted to the paediatric ward and intravenous ceftriaxone without dexamethasone was started immediately. Once GAS was identified in the CSF, antibiotics were switched to intravenous penicillin 6 times 825.000 IU a day. Antibiotics were continued for 2 weeks. No complications occurred during therapy.

OUTCOME AND FOLLOW-UP

She recovered completely without neurologic symptoms at examination after 2 months. Examination of ear, nose and throat was normal, as also her audiogram.

DISCUSSION

GAS accounts for only 0.8% of all cases of bacterial meningitis,³ the majority being caused by *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* serotype B. Up to 1994, these three bacteria represented 85% of all

cases of bacterial meningitis in children. In the Netherlands, nationwide immunizations for these three bacteria have reduced the occurrence of bacterial meningitis.⁴

Despite an increase in incidence of severe invasive GAS infections over the past decades, acute bacterial meningitis (ABM) caused by GAS remains rare.^{2–5} GAS ABM is associated with high morbidity and mortality. A mortality of 27% has been reported in the Netherlands in adults, which is in contrast with data from the literature that describe a mortality of 5 to 10%.⁶ Based on 29 reported cases of GAS ABM in children a mortality of 10% and morbidity rate of 46% can be estimated.⁷ Clinically, GAS meningitis can not be distinguished from meningitis caused by other pathogens. GAS are sensitive for all empiric therapies (usually containing a third generation cephalosporin (eg, ceftriaxone)), aimed at the most prevalent pathogens as mentioned above.^{8–9} Once GAS is isolated from the CSF, penicillin is the preferred choice of treatment, since it penetrates well into the CSF and resistance has never been described.¹⁰

The pathogenesis of GAS meningitis, as well as of other severe invasive GAS infections, is unclear but an association with exotoxins has been suggested.^{2–11} GAS produce a large variety of enzymes and toxins, including streptococcal pyrogenic exotoxins. Exotoxins A, B and C, and more, appear to be involved by stimulating T lymphocytes and macrophages to produce cytokines. These cytokines are capable of producing shock and tissue injury and are therefore responsible for the severe clinical picture of invasive GAS infections.² These exotoxins can be determined by PCR. In this case, the bacteria proved to produce exotoxin A known to be involved in severe GAS infections.

The M protein of this bacteria, a virulence factor displayed on its surface, is also important in the pathogenesis of GAS infections. More than 100 different M-protein gene sequence types (emm types) have been documented. The emm type is an important surveillance tool in investigations of the dynamics in GAS infections and each emm type is associated with specific presentation of a GAS infection, and therefore valuable for epidemiologic studies. Emm type 1.0 is the one most associated with streptococcal upper respiratory tract infection, as also associated with invasive GAS infection, as in our patient. In a Dutch study on emm types and GAS ABM, emm type 1.0 was one of three most prevalent types in 170 cases.¹¹

Once GAS is identified as cause of ABM, examination of the ear, nose and throat is required, to rule out a GAS reservoir such as a mastoiditis, an abscess or a fistula of the central nervous system.⁶

The clinical course is, due to the relative low prevalence, less well known than that of other bacteria causing ABM. However, also in GAS meningitis neurologic complications such as hearing loss, retardation, seizures, visual impairment and learning and behavioural problems are common.⁶ Neurologic sequelae have been described in 46%

of GAS ABM in children.⁷ Therefore, a follow-up study aimed at hearing and neurologic development is strongly suggested for all children.

We conclude that Group A streptococcus (GAS) is a very uncommon cause of ABM in children. Morbidity and mortality are high. As GAS ABM is associated with ear-nose-throat infections, a search for a GAS reservoir within the patient is proposed. Bacterial typification often demonstrates EMM type 1.0 associated with upper respiratory tract infections and also severe, invasive GAS infections. GASs are susceptible for common empiric antibiotic therapies in meningitis. Follow-up investigation including neurologic developmental status and audiologic testing is recommended.

Learning points

- GAS is a very uncommon cause of acute bacterial meningitis in children, with a high morbidity and mortality. Being associated with ear-nose-throat infections, a search for a GAS reservoir is proposed. GASs are susceptible for common empiric antibiotic therapies in meningitis.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Bisno AL**, Stevens DL. Streptococcal infections of skin and soft tissues. *N Engl J Med* 1996;**334**:240–5.
2. **Davies HD**, McGeer A, Schwartz B, *et al*. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. *N Engl J Med* 1996;**335**:547–54.
3. Rijksinstituut voor Volksgezondheid en Milieuhygiëne. *Hersenvliesontsteking*. The Netherlands: Nationaal Kompas Volksgezondheid; 4.3 2011.
4. Referentie Laboratorium voor Bacteriële Meningitis. The Netherlands: AMC Amsterdam 2009.
5. **Lamagni TL**, Darenberg J, Luca-Harari B, *et al*. Epidemiology of severe Streptococcus pyogenes disease in Europe. *J Clin Microbiol* 2008;**46**:2359–67.
6. **van de Beek D**, de Gans J, Spanjaard L, *et al*. Group A streptococcal meningitis in adults: report of 41 cases and a review of literature. *Clin Infect Dis* 2002;**34**:32–6.
7. **Shetty AK**, Frankel LR, Maldonado Y, *et al*. Group A streptococcal meningitis: report of a case and review of literature since 1976. *Pediatr Emerg Care* 2001;**17**:430–4.
8. **Tunkel AR**, Hartman BJ, Kaplan SL, *et al*. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis* 2004;**39**:1267–84.
9. **Arditi M**, Mason EO Jr, Bradley JS, *et al*. Three-year multicenter surveillance of pneumococcal meningitis in children: clinical characteristics, and outcome related to penicillin susceptibility and dexamethasone use. *Pediatrics* 1998;**102**:1087–97.
10. **Kaplan EL**, Johnson DR, Del Rosario MC, *et al*. Susceptibility of group A beta-hemolytic streptococci to thirteen antibiotics: examination of 301 strains isolated in the United States between 1994 and 1997. *Pediatr Infect Dis J* 1999;**18**:1069–72.
11. **Vlaamincx BJ**, Mascini EM, Schellekens J, *et al*. Site-specific manifestations of invasive group A streptococcal disease: type distribution and corresponding patterns of virulence determinants. *J Clin Microbiol* 2003;**188**:1578–86.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

van Zitteren LM, Arents NLA, Halbertsma F. Group-A-streptococcal meningitis in a 7-year-old child – a rare pathogen in a non-immune compromised patient. *BMJ Case Reports* 2011;10.1136/bcr.10.2011.4896, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow