Group A streptococcal meningitis: a case report and brief review

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ABSTRACT

Invasive Group A streptococcus (GAS) disease is an important cause of morbidity and mortality, and its incidence has been on the increase in industralised countries since the mid-1980s. Meningitis is an especially rare manifestation. We report one such case in a previously healthy 44-year old woman, followed by a brief review the epidemiology, pathogenesis, presentation, complications, and management of GAS meningitis within a New Zealand (NZ) context.

INTRODUCTION

Invasive Group A streptococcus (GAS) disease causes significant morbidity and mortality.[1] Meningitis is an especially rare manifestation of invasive GAS disease. We report one such case in a previously healthy woman and briefly review the literature on the topic.

CASE REPORT

A 44-year old female café worker from a rural area presented to our hospital with a 4-day history of generalised myalgia, headache and increasing lower back pain, and a 2-day history of fever and nausea. She denied rash, photophobia, recent ill contact, or animal contact, and divulged a travel history to Vanuatu two months ago. There was no significant past medical history or any regular medication.

On examination, she was restless, but afebrile and haemodynamically stable. There was mild pain on neck flexion but no nuchal rigidity, and no focal neurology. Detailed systemic examination was otherwise unremarkable, including normal otoscopy and throat examination.

Initial blood tests showed leukocytosis (14.4x109/L[Normal range 4-11x109/L]) and elevated C-reactive protein (237.2 mg/L[Normal range <6 mg/L]). Electrolytes, liver enzymes, renal function, and urinalysis were normal. Intravenous ceftriaxone 2g once daily was commenced empirically as well as to cover possible leptospirosis, which is prevalent in the Waikato in a NZ context.[30]

Overnight, the patient developed saddle anaesthesia but with preserved anal tone, as well as ataxia, and neck stiffness. Examination revealed subjective numbness in the soles of her feet, but a preserved spinothalamic sensory pathway. Whole spine and brain magnetic resonance imaging (MRI) was non-revelatory, apart from a mild, non-specific epidural fluid isointensity extending from T10 to L5. Specialist radiology and neurology opinion was sought, but these changes were thought to not be in keeping with an abscess, and likely represented non-specific meningeal reaction. Lumbar puncture following the scan revealed straw-coloured cerebrospinal fluid (CSF) consistent with bacterial meningitis on analysis, showing leukocytosis (176x109/L, 90% neutrophils), low glucose (<0.1 mmol/L [Normal range 2.8-4.4 mmol/L]) and elevated protein (4.6 g/L[Normal range 0.15-0.45 g/L]). Blood cultures taken on admission later grew GAS in both aerobic and anaerobic bottles, predictably sensitive to penicillin. Viral culture was negative, as was a leptospira panel.

The initial management with intravenous ceftriaxone was continued due to clinical response. Dosage was increased to twice daily for the next five, before being stepped down to a once daily regime to complete a 14-day course. The patient became mildly hyponatraemic later in the course of the admission (127 mmol/L, [Normal range 135-145 mmol/L]) attributed to inappropriate secretion of anti-diuretic hormone. Saddle anaesthesia persisted on discharge on day 14, but there were no other neurological or medical sequelae. A repeat whole spine MRI towards the end of admission was reassuring, with no further progress of the lumbar area signal change. The patient reported no change in saddle anaesthesia at follow up via phone consult a few months later.

DISCUSSION

Epidemiology

GAS, or Streptococcus pyogenes, is responsible for a variety of clinical syndromes, ranging from mild infection of the skin and upper respiratory tract, to severe disease such as toxic shock syndrome and necrotising fasciitis. Rheumatic fever is an important cause of S. pyogenes-related cardiac morbidity in NZ. Rarely, the inoculation of GAS into a sterile site in the body can lead to invasive disease, more commonly of soft tissue. Invasive GAS disease is associated with a high mortality rate.[1] Although GAS was a common cause of meningitis up to the early 20th century, it is now one of the least frequently reported forms of invasive GAS disease.[2-4] This shift coincided with the sharp decline in the general incidence of invasive GAS disease seen globally in the mid-20th century, variously attributed to the advent of modern antibiotics, the prevalence of less virulent strains, and improved living conditions.[1,4,5]

The past three decades, however, have witnessed a gradual reversal of this trend. A resurgence of invasive GAS disease has been reported in many industrialised countries, with an estimated annual rate comparable to that of invasive meningococcal disease at 4 to 6 per 100,000.1 NZ data from a recent Auckland study suggest a higher incidence at 8.1 per 100000 per annum in the general population.[6]

Meningitis has been estimated to occur 1-3% of cases of invasive GAS disease in two separate national surveillance studies from Denmark and Canada.[7,8] However, GAS has been implicated in less than 1% of all bacterial meningitis in two separate national-level prospective studies in the United States and the Netherlands across two decades.[9,10] Given its rarity, data on GAS meningitis have predominantly been based on analyses of individual case reports and series, primarily affecting children.[3,11-13]

Strain virulence

The M protein is an important feature of GAS virulence in human hosts, and is coded in the bacterial genome by the emm gene.[5] The M1T1 serotype has been implicated most consistently and in the majority of invasive GAS disease outbreaks internationally, including in NZ,[6,14] but other serotypes have also been reported.[15,16]

Subsequent typing analysis of our patient's GAS isolate by the Institute of Environmental Science and Research (ESR, Porirua, NZ) revealed it to be of the emm106 type, a rarely-reported strain first classified in 2002 following a bacteraemia case in Malaysia.[17] This emm type has previously been isolated from invasive GAS disease in NZ, albeit remaining an uncommon strain.[6] One Taiwanese study, however, reported a high prevalence of the emm106 type isolated from invasive disease in the elderly, whilst a further study from Taiwan found it to be significantly associated with a higher risk of invasive soft tissue disease compared to other emm types.[18,19] The emm106 was also found to be a common strain for invasive disease in a New Caledonian study.[20] Although it is difficult to extrapolate this data to the rest of the Melanesian sub-region, it is of some interest that our patient had traveled to neighbouring Vanuatu two months prior to her presentation.

Pathophysiology

Whilst haematogenous spread from the pharynx to the CNS is well-established in meningococcal meningitis, the pathogenesis of meningitis as caused by GAS, also a common pharyngeal commensal, is less well understood.[3,12] Reported predisposing factors for GAS meningitis include a focus of infection (especially otolaryngological), meningeal breach (such as basal skull fracture or neurosurgery), compromised immunity, and young age.[3,11,12,21] A systematic review in 1999 reported that a little less than two thirds of reported cases presented with predisposing factors.[11] As with our patient, GAS meningitis has also been reported in previously healthy adults.[22]

Presentation and management

Although our patient did not initially present with meningism, fever, or rash, this is not unusual for bacterial meningitis.[23] A large Dutch prospective study noted that fewer than half of patients with bacterial meningitis presented with a triad of neck stiffness, headache, and change in mental state, and only approximately one quarter presented with new rash.[9] There are no clinical features reported to distinguish meningitis as caused by GAS from typical organisms.[3,9,11] This highlights the importance of vigilance amongst clinicians in patients who present with non-specific symptoms. Penicillin is the antibiotic of choice in invasive GAS disease.[1]

In NZ, surveillance data by ESR suggest a minute percentage of GAS resistance to penicillin in 1998 (0.1%) and 1999 (0.2%), but this pattern has since virtually disappeared, including in the most recent report in 2011.[27] Erythromycin-resistance was relatively stable at 0.9% to 1.5% of GAS isolates between 1998 and 2005, but this rose to 6.4% in 2011.28 Tetracycline-resistance was 12.5% in 2001, with no clustering by source (hospital or community) or geographical location found.[29]

Course and complications

The course of GAS meningitis can be fulminant and severe, especially for children. Complications include seizures, coma, and focal neurological deficit.[3,11] The mortality rate for GAS meningitis is comparable to that of meningococcal and Haemophilus influenzae B meningitides, but post-meningeal sequelae may be higher.[11]

In a Dutch case series on GAS meningitis, hyponatraemia was observed in more than half of the 41 patients studied, a feature more often recognised with tuberculous and Staphylococcus aureus infection.[12] Hyponatraemia has also been reported elsewhere in the literature as a complication of GAS meningitis.[24,25] However, whether this is a consistent and clinically significant aspect of GAS meningitis is yet to be established.

GAS meningitis has previously been reported in NZ in the context of puerperal sepsis (one patient) and toxic shock syndrome (five patients).[6,26] To our knowledge, however, this patient is the first reported case in a previously healthy adult in NZ, and the first ever report of sacral radiculopathy complicating GAS meningitis. The initial presentation with severe lower back pain and subsequent finding of in lumbar spine MRI may explain the symptoms that evolved.

CONCLUSION

We have reported a case of GAS meningitis with no discernible predisposing factors, an atypical presentation and radiological evolution culminating in an overall positive outcome. The literature, however, highlights the significant morbidity and mortality associated with this disease in the majority of cases. We believe that the increasing incidence of invasive GAS disease in its multitude of forms is of more than just academic interest and remains an important public health issue internationally that NZ clinicians need to be aware of.

REFERENCES

1. Steer AC, Lamagni T, Curtis N, Carapetis JR.
Invasive group a streptococcal disease: epidemiology, pathogenesis and management.
Drugs 2012 Jun 18;72(9):1213-27.

2. Perera N, Abulhoul L, Green MR, Swann RA.
Group A streptococcal meningitis: case report and review of the literature.
J Infect 2005 Aug;51(2):E1-4.

3. Shetty AK, Frankel LR, Maldonado Y, Falco DA, Lewis DB.
Group A streptococcal meningitis: report of a case and review of literature since 1976.
Pediatr Emerg Care 2001 Dec;17(6):430-4.

4. Peterson C, Smith P, Loomis G, Osterholm R.
Group A streptococcal meningitis in an adult.
Nebr Med J 1985 Jul;70(7):233-5.

5. Cunningham MW.
Pathogenesis of group A streptococcal infections.
ClinMicrobiol Rev 2000 Jul;13(3):470-511.

6. Safar A, Lennon D, Stewart J, Trenholme A, Drinkovic D, Peat B, Taylor S, et al.
Invasive group A streptococcal infection and vaccine implications, Auckland, New Zealand.
Emerg Infect Dis.2011 Jun;17(6):983-9.

7. Luca-Harari B, Ekelund K, van der Linden M, Staum-Kaltoft M, Hammerum AM, Jasir A.
Clinical and epidemiological aspects of invasive Streptococcus pyogenes infections in Denmark during 2003 and 2004.
J Clin Microbiol 2008 Jan;46(1):79-86.

8. Tyrrell GJ, Lovgren M, St Jean T, Hoang L, Patrick DM, Horsman G, Van Caeseele P, et al.
Epidemic of group A Streptococcus M/emm59 causing invasive disease in Canada.
Clin Infect Dis 2010 Dec 1;51(11):1290-7.

9. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M.
Clinical features and prognostic factors in adults with bacterial meningitis.
N Engl J Med 2004 Oct 28;351(18):1849-59.

10. Schlech WF 3rd, Ward JI, Band JD, Hightower A, Fraser DW, Broome CV.
Bacterial meningitis in the United States, 1978 through 1981.
JAMA 1985 Mar 22-29;253(12):1749-54.

11. Baraldés MA, Domingo P, Mauri A, Monmany J, Castellanos M, Pericas R, Vázquez G.
Group A streptococcal meningitis in the antibiotic era.
Eur J ClinMicrobiol Infect Dis 1999 Aug;18(8):572-8.

12. van de Beek D, de Gans J, Spanjaard L, Sela S, Vermeulen M, Dankert J.
Group A streptococcal meningitis in adults: report of 41 cases and a review of the literature.
Clin Infect Dis 2002 May 1;34(9):e32-6.

13. de Almeida Torres RS, Fedalto LE, de Almeida Torres RF, Steer AC, Smeesters PR.
Group A streptococcus meningitis in children.
Pediatr Infect Dis J 2013 Feb;32(2):110-4.

14. Martin DR, Single LA.
Molecular epidemiology of group A streptococcus M type 1 infections.
J Infect Dis 1993 May;167(5):1112-7.

15. Steer AC, Law I, Matatolu L, Beall BW, Carapetis JR.
Global emm type distribution of group A streptococci: systematic review and implications for vaccine development.
Lancet Infect Dis 2009 Oct;9(10):611-6.

16. Lynskey NN, Lawrenson RA, Sriskandan S.
New understandings in Streptococcus pyogenes.
Curr Opin Infect Dis 2011 Jun;24(3):196-202.

17. Facklam RF, Martin DR, Lovgren M, Johnson DR, Efstratiou A, Thompson TA, Gowan S, Kriz P, Tyrrell GJ, Kaplan E, Beall B.
Extension of the Lancefield classification for group A streptococci by addition of 22 new M protein gene sequence types from clinical isolates: emm103 to emm124.
Clin Infect Dis 2002 Jan 1;34(1):28-38.

18. Chiang-Ni C, Wu AB, Liu CC, Chen KT, Lin YS, Chuang WJ, Fang HY, Wu JJ.
Emergence of uncommon emm types of Streptococcus pyogenes among adult patients in southern Taiwan.
J MicrobiolImmunol Infect 2011 Dec;44(6):424-9.

19. Lin JN, Chang LL, Lai CH, Lin HH, Chen YH.
Clinical and molecular characteristics of invasive and noninvasive skin and soft tissue infections caused by group A Streptococcus.
J ClinMicrobiol 2011 Oct;49(10):3632-7.

20. Le Hello S, Doloy A, Baumann F, Roques N, Coudene P, Rouchon B, Lacassin F, Bouvet A.
Clinical and microbial characteristics of invasive Streptococcus pyogenes disease in New Caledonia, a region in Oceania with a high incidence of acute rheumatic fever.
J ClinMicrobiol 2010 Feb;48(2):526-30.

21. Sommer R, Rohner P, Garbino J, Auckenthaler R, Malinverni R, Lew D, Kaiser L.
Group A beta-hemolytic streptococcus meningitis: clinical and microbiological features of nine cases.
Clin Infect Dis. 1999 Oct;29(4):929-31.

22. Ulug M, Ulug NC, Celen MK, Geyik MF, Ayaz C.
A case of meningitis caused by Streptococcus pyogenes in a previously healthy woman.
J Infect DevCtries 2009 Apr 1;3(3):241-4.

23. Attia J, Hatala R, Cook DJ, Wong JG.
The rational clinical examination. Does this adult patient have acute meningitis?
JAMA 1999 Jul 14;282(2):175-81.

24. Bruun T, Kittang BR, Mylvaganam H, Lund-Johansen M, Skrede S.
Clinical, microbiological and molecular characteristics of six cases of group A streptococcal meningitis in western Norway.
Scand J Infect Dis 2010 Sep;42(9):665-71.

25. Rezvani M, Yager JY, Hartfield DS.
Group A streptococcal meningitis as a complication of an infected capillary haemangioma.
Eur J Pediatr 2004 Jan;163(1):19-21.

26. Quinney RA, Ali MR, Thomas MG, Lang SD.
Post-partum streptococcal meningitis and septicaemia.
NZ Med J 1984 Oct 10;97(765):702-3.

27. Heffernan H, Woodhouse R, Maitra A.
Antimicrobials resistance trends in New Zealand, 2005.
Institute of Environmental Science and Research (Porirua). Accessed 4 February 2015. Available from: http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/AR/AR_Trends_2005.pdf.

28. Heffernan H, Rosemary S.
Antimicrobial susceptibility of Group A streptococci in New Zealand in 2001.
Institute of Environmental Science and Research (Porirua). Accessed 4 February 2015. Available from: http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/GAS_2001.pdf.

29. Public Health Surveillance.
Antimicrobial resistance data from hospital and community laboratories, 2011.
Institute of Environmental Science and Research. 2001. Accessed 4 February 2015. Available from: http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/AR/National_AR_2011.pdf.

30. Cowie G, Bell A.
A retrospective review of notified human leptospirosis cases in the Waikato region of New Zealand, 2004 to 2010.
NZ Med J 2012 Jul 29;125(1358):20-8.