

CASE REPORT

Diagnostic challenges with acellular bacterial meningitis

Y Moolla, MB ChB, FCP (SA), MMed; L Naidoo, MB BCH

Department of Internal Medicine, Addington Hospital, Durban, South Africa

Corresponding author: Y Moolla (moollayusuf@hotmail.com)

An immunocompetent adult presenting with acellular pneumococcal meningitis is a rare occurrence and may pose a diagnostic challenge.

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Acute bacterial meningitis is a medical emergency and requires prompt diagnosis because it is associated with significant morbidity and mortality.^[1,2] The incidence ranges from 5 per 100 000 persons in southern Africa to 12 per 100 000 in Africa.^[3,4] Up to 50% of survivors may suffer from long-term neurological sequelae.^[5-7]

Better outcomes have resulted from early initiation of appropriate therapy; however, this has to be balanced with prompt confirmation of diagnosis, as inappropriate empirical therapy carries the risk of side-effects, cost burden and increased nosocomial infection.^[8-11]

Case report

A 60-year-old woman with no comorbidities had complained of headache, fever, general malaise and photophobia. She had no symptoms of an upper respiratory tract infection and had not travelled recently. She had no surgical history of splenectomy and did not consume alcohol. This was her first presentation for medical care.

On examination she was haemodynamically stable with a temperature of 38°C. No rashes were present. She was alert and orientated. Signs of meningism were present, which included Kernig's and Brudzinski's signs. There were no cranial nerve palsies, and neither motor nor sensory abnormalities were elicited. Other systems were clinically unremarkable.

The laboratory investigations revealed a haemoglobin concentration of 9.5 g/dL, a normal platelet count ($352 \times 10^9/L$) and leucocytosis (white cell count $14.98 \times 10^9/L$). Her C-reactive protein (CRP) was markedly raised at 381 nmol/L and the plasma glucose level was 7.1 mmol/L. As no clinical signs of raised intracranial pressure were present, a lumbar puncture was performed. The findings of the cerebrospinal fluid (CSF) examination are shown in Table 1. Other tests performed included a non-reactive HIV ELISA and syphilis serology.

The patient was started empirically on high-dose intravenous ceftriaxone in view of the clinical suspicion of meningitis. Her symptoms resolved 2 days later, and she had an uncomplicated inpatient stay with no neurological sequelae.

Discussion

We were fortunate that our patient presented with the classic signs and symptoms of meningitis. It is integral to note that the symptoms of meningitis, which may include headache, nausea and vomiting, have poor sensitivity and specificity for the diagnosis of meningitis, as demonstrated in a meta-analysis of 845 patients.^[12] The classic clinical signs of Kernig and Brudzinski have value in ruling in the diagnosis of meningitis; however, these traditional signs have poor sensitivity and their absence cannot be used to rule out the disease.^[8,13,14]

The performance of a lumbar puncture is fundamental, as CSF examination is needed to establish the diagnosis.^[15] Consistent CSF findings with acute bacterial meningitis include a polymorphonuclear pleocytosis, hypoglycorrhachia and a raised CSF protein level.^[2,8,16] Despite our patient's reduced CSF glucose and raised protein, the inconsistent polymorph cell count was striking. Based on clinical suspicion, CSF and laboratory determinants, she was treated for acute bacterial meningitis. CSF Gram stains and culture results confirming *Streptococcus pneumoniae* were only available after 48 hours. While CSF Gram stain testing has a high specificity for bacterial meningitis, it lacks sensitivity and was proven to be helpful in only 30 - 40% of patients.^[17,18]

There have been documented cases of bacterial meningitis in the absence of pleocytosis, with a particular occurrence in children.^[19,20] Normal CSF meningitis may occur when underlying immunosuppressive states are present; however, this acellular phenomenon is exceptionally rare in an immunocompetent adult.^[15,21] We have noted only eight similar cases of acellular pneumococcal meningitis in the literature.^[21-28]

Additional markers that may assist in the diagnosis of acute bacterial meningitis exist, but their diagnostic role in the current guidelines is modest. The CSF glucose/blood glucose ratio is a simple marker that is often utilised, but it should be emphasised that it was shown to predict the presence of bacterial meningitis more precisely than routine CSF measurements.^[29] CSF lactate has the ability to differentiate bacterial meningitis from aseptic meningitis with robust

Table 1. Findings on CSF examination

CSF characteristics	
Appearance	Clear
Opening pressure (cm H ₂ O)	25
Glucose (mmol/L)	<1
Protein (g/L)	3.14
Polymorphs	0
Lymphocytes	0
Erythrocytes	0
Ratio CSF glucose/serum glucose	Very low
Gram stain	Positive
Culture	<i>Streptococcus pneumoniae</i> sensitive to penicillin G/ceftriaxone
Cryptococcal antigen test	Negative

accuracy; however, this test is often unavailable.^[30,31] Serum CRP and procalcitonin are useful markers as well, with the latter carrying a strong diagnostic odds ratio.^[32,33] Molecular diagnostic testing, such as nuclear acid amplification tests, has been shown to facilitate the diagnosis in 33% of patients in whom the diagnosis could not be made conventionally.^[34] Other future diagnostic aids may include immunochromographic testing, and the use of complement component 3, apolipoprotein A-1 and kinnogen-1.^[35]

Our experience highlights the rare occurrence of acellular bacterial meningitis in an immunocompetent adult. A heightened index of suspicion based on symptoms and clinical examination should prompt early appropriate antibiotic therapy. Swift, simple, highly sensitive investigations beyond routine tests may assist in supporting the diagnosis of meningitis in these challenging cases.

Learning points

- Acellular bacterial meningitis is rare in an immunocompetent adult.
- The CSF glucose/blood glucose ratio and CSF lactate may assist in the diagnosis of bacterial meningitis.
- Prompt empirical therapy improves outcomes.

1. Durand ML, Calderwood SB, Weber DJ, et al. Acute bacterial meningitis in adults: A review of 493 episodes. *N Engl J Med* 1993;328:21-28. DOI:10.1056/NEJM199301073280104
2. 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;351:1849-1859. DOI:10.1056/NEJMoa040845
3. Bill PLA, Bhigjee AI. Bacterial meningitis and viral infections of the nervous system. *CME* 1994;12:413-427.
4. O'Dempsey TJ, McArdle TF, Lloyd-Evans N, et al. Pneumococcal disease among children in a rural area of West Africa. *Pediatr Infect Dis J* 1996;15(5):431-437. DOI:10.1097/00006454-199605000-00010
5. Weisfelt M, Hoogman M, van de Beek D, de Gans J, Dreschler WA, Schmand BA. Dexamethasone and long-term outcome in adults with bacterial meningitis. *Ann Neurol* 2006;60(4):456-468. DOI:10.1002/ana.20944
6. De Gans J, van de Beek D. Dexamethasone in adults with bacterial meningitis. *N Engl J Med* 2002;347:1549-1556. DOI:10.1056/NEJMoa021334
7. Bohr V, Paulson OB, Rasmussen N. Pneumococcal meningitis. Late neurologic sequelae and features of prognostic impact. *Arch Neurol* 1984;41(10):1045-1049.
8. Boyles TH, Bramford C, Bateman K, et al. Guidelines for the management of acute meningitis in children and adults in South Africa. *South Afr J Epidemiol Infect* 2013;28(1):5-15.
9. Miner JR, Heegaard W, Mapes A, Biros M. Presentation, time to antibiotics, and mortality of patients with bacterial meningitis at an urban county medical center. *J Emerg Med* 2001;21(4):387-392. DOI:10.1016/S0736-4679(01)00407-3
10. Swinger G, Delpont S, Hussey G. An audit of the use of antibiotics in presumed viral meningitis in children. *Pediatr Infect Dis J* 1994;13(12):1107-1110. DOI:10.1097/00006454-199412000-00007
11. Parasuraman TV, Frenia K, Romero J. Enteroviral meningitis: Cost of illness and considerations for the economic evaluation of potential therapies. *Pharmacoeconomics* 2001;19(1):3-12. DOI:10.2165/00019053-200119010-00001

12. Attia J, Hatala R, Cook DJ, Wong JG. The rational clinical examination. Does this adult patient have acute meningitis? *JAMA* 1999;282(2):175-181. DOI:10.1001/jama.282.2.175
13. Fitch MT, van de Beek D. Emergency diagnosis and treatment of adult meningitis. *Lancet Infect Dis* 2007;7(2):191-200. DOI:10.1016/S1473-3099(07)70050-6
14. Waghdhare S, Kalantri A, Joshi R, Kalantri S. Accuracy of physical signs for detecting meningitis: A hospital-based diagnostic accuracy study. *Clin Neurol Neurosurg* 2010;112(9):752-757. DOI:10.1016/j.clineuro.2010.06.003
15. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. *Lancet* 2012;380(9854):1684-1692. DOI:10.1016/S0140-6736(12)61185-4
16. Van de Beek D, de Gans J, Tunkel AR, Wijdicks EF. Community-acquired bacterial meningitis in adults. *N Engl J Med* 2006;357:44-53. DOI:10.1056/NEJMra052116
17. Feigin RD, McCracken GH Jr, Klein JO. Diagnosis and management of meningitis. *Pediatr Infect Dis J* 1992;11(9):785-814. DOI:10.1097/00006454-199209000-00039
18. Spanos A, Harrell FE Jr, Durack DT. Differential diagnosis of acute meningitis: An analysis of the predictive value on initial observations. *JAMA* 1989;262(19):2700-2707. DOI:10.1001/jama.1989.03430190084036
19. Coll MT, Uriz MS, Pineda V, et al. Meningococcal meningitis with 'normal' cerebrospinal fluid. *J Infect* 1994;29(3):289-294. DOI:10.1016/S0163-4453(94)91197-5
20. Polk DB, Steele RW. Bacterial meningitis presenting with normal cerebrospinal fluid. *Pediatr Infect Dis J* 1987;6(11):1040-1042.
21. Fishbein DB, Palmer DL, Porter KM, Reed WP. Bacterial meningitis in the absence of CSF pleocytosis. *Arch Intern Med* 1981;141(10):1369-1372.
22. Domingo P, Mancebo J, Blanch L, Coll P, Net A, Nolla J. Bacterial meningitis with 'normal' cerebrospinal fluid in adults: A report on five cases. *Scand J Infect Dis* 1990;22(2):115-116. DOI:10.3109/00365549009023130
23. Uchiyama T, Ichikawa K, Yoshida S, Tsukagoshi H. Positive culture from normal CSF of *Streptococcus pneumoniae* meningitis. *Eur Neurol* 1996;36(4):234. DOI:10.1159/000117256
24. Gutiérrez-Macías A, García-Jiménez N, Sánchez-Muñoz L, Martínez-Ortiz de Zarate M. Pneumococcal meningitis with normal cerebrospinal fluid in an immunocompetent adult. *Am J Emerg Med* 1999;17(2):219. DOI:10.1016/S0735-6757(99)90074-8
25. Alvarez EF, Olarte KE, Ramesh MS. Purpura fulminans secondary to *Streptococcus pneumoniae* meningitis. *Case Rep Infect Dis* 2012;2012:508503. DOI:10.1155/2012/508503
26. Ris J, Mancebo J, Domingo P, Cadafalch J, Sanchez M. Bacterial meningitis despite 'normal' CSF findings. *JAMA* 1985;254(20):2893-2894. DOI:10.1001/jama.1985.03360200043019
27. Suzuki H, Tokuda Y, Kurihara Y, Suzuki M, Nakamura H. Adult pneumococcal meningitis presenting with normocellular cerebrospinal fluid: Two case reports. *J Med Case Rep* 2013;7:294. DOI:10.1186/1752-1947-7-294
28. Tamune H, Takeya H, Suzuki W, et al. Cerebrospinal fluid/blood glucose ratio as an indicator for bacterial meningitis. *Am J Emerg Med* 2014;32(3):263-266. DOI:10.1016/j.ajem.2013.11.030
29. Huy NT, Thao NTH, Diep Doan TN, Kikuchi M, Zamora J, Hirayama K. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: A systemic review and meta-analysis. *Crit Care* 2010;14(6):R240. DOI:10.1186/cc9395
30. Sakushima K, Hayashino Y, Kawaguchi T, Jackson JL, Fukuhara S. Diagnostic accuracy of cerebrospinal fluid lactate for differentiating bacterial meningitis from aseptic meningitis: A meta-analysis. *J Infect* 2011;62(4):255-262. DOI:10.1016/j.jinf.2011.02.010
31. Rajs G, Finzi-Yeheskel Z, Rajs A, Mayer M. C-reactive concentrations in cerebral spinal fluid in Gram-positive and Gram-negative bacterial meningitis. *Clin Chem* 2002;48(3):591-592.
32. Vikse J, Henry BM, Roy J, Ramakrishnan PK, Tomaszewski KA, Walocha AJ. The role of serum procalcitonin in the diagnosis of bacterial meningitis in adults: A systematic review and meta-analysis. *Int J Infect Dis* 2015;38(1):68-76. DOI:10.1016/j.ijid.2015.07.011
33. Parent du Châtelet I, Traore Y, Gessner BD, et al. Bacterial meningitis in Burkina Faso: Surveillance using field-based polymerase chain reaction testing. *Clin Infect Dis* 2005;40(1):17-25. DOI:10.1086/426436
34. Cordeiro AP, Pereira RAS, Chapeaurouge A, et al. Comparative proteomics of cerebrospinal fluid reveals a predictive model for differential diagnosis of pneumococcal, meningococcal, and enteroviral meningitis, and novel putative therapeutic targets. *BMC Genomics* 2015;16(5):1-9. DOI:10.1186/1471-2164-16-S5-S11

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