A case of recurrent pneumococcal meningitis, establishing the (w)hole picture

BIA Annual Conference 26/05/22

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Background: Pneumococcal Meningitis

Pneumococal meningitis carries a significant risk of morbidity and mortality in both children and adults.[1,2]
The incidence of pneumococcal meningitis and other forms of Invasive Pneumococcal Disease have reduced in multiple age groups since the widespread introduction of pneumococcal conjugate vaccines in childhood immunisation programs.[3]
Recurrent Pneumococcal Meningitis is rare (1.5% of cases of Pneumococcal Meningitis) and is defined as recurrence >1 month after the initial episode.[4]

Case: A 5 year old female presents to ED…

She has a history of confusion and headache. On examination, she is febrile with evident neck stiffness. She is started on empiric IV Ceftriaxone. Lumbar puncture and bloods are performed and show:

CSF Cell count	WCC 2700, Neut 95%,
CSF Biochemistry	Glucose 0.3, Protein 2.1
CSF Gram Stain	Gram positive diplococci
CSF culture	No growth
CSF PCR	S. pneumoniae positive
Blood Culture	S. pneumoniae

She is treated with 14 days of IV Ceftriaxone and a full recovery is apparent at follow-up.

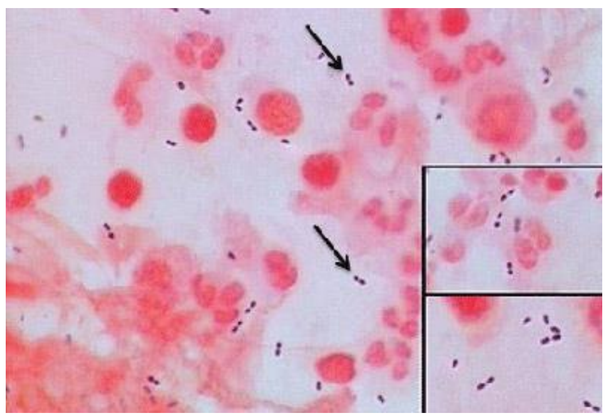

Figure 1:
Gram stain of S. pneumoniae in CSF [5]

Recurrence: 2 years later…

The same child presents to ED with fever, headache and vomiting.
Clinical signs of meningitis are again elicited on examination.
This time, investigations show:

CSF Cell count	WCC 952, Neut 60%
CSF Biochemistry	Glucose 0.7 Protein 1.8
CSF Gram Stain	Gram positive diplococci
CSF Culture	No growth
CSF PCR	S. pneumoniae positive
Blood Culture	No growth

Full history was re-visited:
This child has received all childhood immunisations including 2 doses of PCV-13. They are fit and well with no other past medical history. No history of recurrent or opportunistic infections. There is no family history of note.

Investigating the cause for recurrence

Immunodeficiency screen was undertaken, but did not yield a cause:

Serum Complement	Within normal limits
Serum Immunoglobulins	Within normal limits
Pneumoccocal Specific Functional Antibodies	Within normal limits
T and B Lymphocyte Subsets	Within normal limits
HIV p24 antigen/antibody	Negative
Ultrasound Abdomen	Normal appearances of the spleen

Neuroimaging was therefore undertaken:
Computed Tomography was performed, which showed a *'defect in the cribriform plate, continuation of the ethmoid sinus with the CSF space and a persistently full sinus - consistent with CSF leak.'*

<u>Diagnosis:</u>
Recurrent meningitis secondary to defect at the cribriform plate causing CSF breach.
History was re-visited at follow-up, and **trauma to the nose** was noted in retrospect.

Literature: CSF Breach and Meningitis

Hénaff F, Levy C, Cohen R, et al 2017: [6]
Retrospective cohort analysis of children 5-15 years of age with a *single episode* of pneumococcal meningitis:
70/316 (23%) had an anatomical defect causing CSF breach
47/316 (18%) had an underlying immunodeficiency

Tebruegge M, Curtis N 2008: [7]
Literature review of cases of adults and children with *recurrent* meningitis:
101/363 (28%) of cases of recurrent bacterial meningitis had an acquired anatomical defect causing CSF breach
Streptococcus pneumoniae was isolated in 72% of culture positive episodes of recurrence

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Van de Beek D et al 2019: [8]
Prospective cohort of adults with community-acquired bacterial meningitis and CSF leakage:
38/65 (59%) of cases had recurrent meningitis
Remote head trauma accounted for the cause of CSF leakage in 31% of cases

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Darmoun L et al 2019: [9]
Multi-centre case-control study of children with pneumococcal meningitis:
Cerebrospinal fluid leakage **was more frequent in cases with recurrent meningitis** versus controls with a single episode of meningitis (83% vs. 10%, $P < 0.01$)

Identification and Management

Imaging:
Thin section CT in multiple planes (coronal/sagittal/axial) of the skull, temporal bones and sinuses is first-line.[10,11]
Where this does not show an intra-cranial defect and suspicion remains high T2-weighted MRI should be considered.[11]
Repair:
Endoscopic exploration with the use if intra-thecal fluorescein and repair is highly successful (94-98%) for most defects, with some exceptions such as the frontal sinuses. Other surgical approaches e.g. transcranial may be considered.[11]

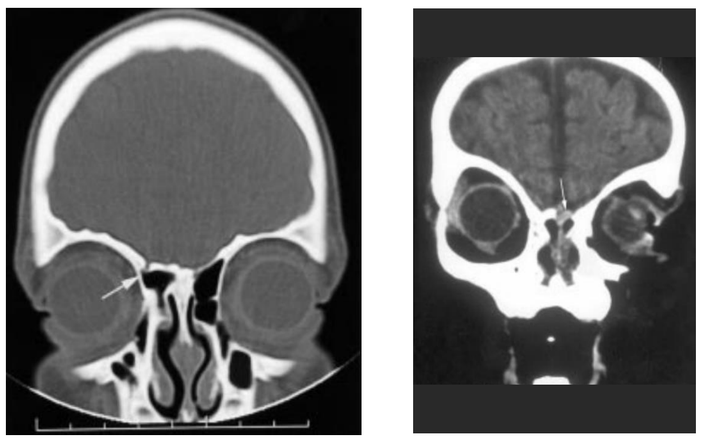

Figure 2
Examples of CT demonstrating anatomical defects:
L: Defect in ethmoid plate
R: bony defect in crista galli [10]

Key Learning Points

Assessment of patients of any age with pneumococcal meningitis requires:
- Thorough history and examination to identify symptoms of CSF breach such as oto/rhinorrhoea, plus risk factors such as previous surgery or head trauma
(NB Head trauma can be remote, and CSF breach can remain asymptomatic for a long time)
- Full immunodeficiency work-up in any vaccinated child with IPD (acquired and congenital causes, immunoglobulins, lymphocyte subsets, imaging of spleen)

Cranial imaging is critical in those with recurrent episodes, OR a single episode with symptoms of/history concerning for CSF leak due to high risk for recurrent meningitis, in particular - pneumococcal meningitis

Thin slice CT in multiple planes is preferred, and T2-weighted MRI should be considered as second-line.

Management involves referral to ENT/Neurosurgery for endoscopic repair and prophylactic penicillin.

References

1. Christie D, Viner RM, Knox K, et al. Long-term outcomes of pneumococcal meningitis in childhood and adolescence. Eur J Pediatr. 2011;170:997–1006.
2. Koelman DLH, Brouwer MC, Ter Horst L, Bijlsma MW, van der Ende A, van de Beek D. Pneumococcal Meningitis in Adults: A Prospective Nationwide Cohort Study Over a 20-year Period. *Clin Infect Dis*. 2022;74(4):657-667. doi:10.1093/cid/ciab477
3. Fitzwater SP, Chandran A, Santosham M, et al. The worldwide impact of the seven-valent pneumococcal conjugate vaccine. Pediatr Infect Dis J. 2012;31:501–508.
4. Darmaun, Laura MD*; Levy, Corinne MD, PhD†,‡,§,¶; Lagrée, Marion MD*,‡; Béchet, Stéphane MSc†,§,¶; Varon, Emmanuelle MD‡,‖; Dessein, Rodrigue MD, PhD**; Cohen, Robert MD†,‡,§,¶,‡‡; Martinot, Alain MD*,‡,††; Dubos, François MD, PhD*,‡,††; for the ACTIV-GPIP Study Group Recurrent Pneumococcal Meningitis in Children, The Pediatric Infectious Disease Journal: September 2019 - Volume 38 - Issue 9 - p 881-886 doi: 10.1097/INF.0000000000002358
5. (https://www.cdc.gov/meningitis/lab-manual/chpt06-culture-id.html)
6. Hénaff F, Levy C, Cohen R, et al.; French Group of Pediatric Infectious Diseases (GPIP). Risk factors in children older than 5 years with pneumococcal meningitis: data from a National Network. Pediatr Infect Dis J. 2017;36:457–461.
7. Tebruegge M, Curtis N. Epidemiology, etiology, pathogenesis, and diagnosis of recurrent bacterial meningitis. Clin Microbiol Rev. 2008;21:519–537.
8. Ter Horst L, Brouwer MC, van der Ende A, van de Beek D.‗Community-acquired bacterial meningitis in adults with cerebrospinal fluid leakage [published online July 12, 2019]. *Clin Infect Dis*. doi:10.1093/cid/ciz649
9. Darmaun L, Levy C, Lagree M, et al. Recurrent pneumococcal meningitis in children: a Multicenter Case-Control Study. Pediatr Infect Dis J. 2019;38:881–886.
10. Carrol ED, Latif AH, Misbah SA, et al. Lesson of the week: recurrent bacterial meningitis: the need for sensitive imaging. BMJ. 2001;323:501–503.
11. Le, Christopher et al. Management of Anterior Skull Base Cerebrospinal Fluid Leaks. *Journal of neurological surgery. Part B, Skull base* vol. 77,5 (2016): 404-11. doi:10.1055/s-0036-1584229