Reviewer’s report

Title: A Systematic Review of Cases of Meningitis in the Absence of Cerebrospinal Fluid Pleocytosis on Lumbar Puncture

Version: 0 Date: 26 Aug 2018

Reviewer: Pamela Palasanthiran

Reviewer's report:

This is a review of the literature of case reports of CSF non-pleocytosis in acute meningitis (bacterial, viral and fungal) in pediatric and adult populations (ages 0 - 86 years). To an extent, this is a reworking of a relatively recent review on lack of CSF pleocytosis in bacterial meningitis alone (ref 6, Hase et al, 2014) where a case was reported and cumulative cases from 16 articles reviewed. The same cases are included in this current article. This study adds another 35 articles to the 16 (accounting for an extra 98 cases of "meningitis"), with the additional ones including fungal and viral meningitis, and one case series of tuberculous meningitis. In addition, both immune incompetent and immune deficient populations are reported, with an additional neonatal series. Some of the articles are in languages other than English, some in journals which were difficult to access for verification. The details presented in Table 1 are in-depth, and painstakingly tabulated - the authors are congratulated on this table. What this article adds over the Hase 2014 article is the inclusion of fungal and viral meningitis (and one TB), and the inclusion of immune-incompetent groups e.g. HIV infection, and a series of newborns.

Overall, this is a useful article as it explores an important clinical entity, provides a useful summation of the current reported literature with the largest case number for "meningitis without CSF pleocytosis". The findings are useful for clinical practice. However, the information presented is in part confusing as all age groups are reported equally and is no distinction between immune competent and non-immune populations. In short: the data could be better organised into the specific age groups e.g. paediatrics versus adults. Ideally - into neonates as a separate group but impractical as some articles have neonates and children together. The immune competent and immune deficient patients should be treated as separate entities. This does raise a question: is there data on CSF profiles in immune deficient groups with meningitis e.g. CSF in oncological patients with meningitis (not cancer cells in the CNS) adn whether or not there is a general absence of pleocytosis anyway if neutropenic. This of course then impacts on some re-organisation of the results, and the table and discussion. I think I struggled a bit with the lack of perspective wrt to the significance of the organisms and patient populations; perhaps seeking some input from an infectious diseases expertise could assist with this.

1) Method:
Inclusion criteria: This needs further clarity.
a. Clarify that there was no restriction in age range. It is unclear the study relates to all ages from pediatric (including neonates) and adult cases until the Results section
b. Need to clarify that teh review is in both immune competent and immune deficient population
c. please what years were included in the search (I think 1973 (ref. 19) was the earliest report in the
table and the latest was 2014 - as far as I can see
d. Please state publications in "All languages " were sourced
e. The reference cited for CSF white cells cut offs per age group [Roberts J et al: Ref 59: - Is there a more accessible reference ?

2) RESULTS
a. Table 1:
- comprehensive: - congratulations
- It is difficult to know how the data is organised (it does not seem to have a structure wrt age gps, immune - competent vs immune-deficient
- For the viruses: are they "cultures" or molecular diagnosis (PCR)?

b)Table 3: I think the impact/significance of the information is lost somewhat by not organising the organisms into the "standard" bacteria that cause meningitis (GBS, N meningitidis, pneumococcus, haemophilus etc) firstn and then organisms that are unusual e.g bacteroides, S parasangionis etc etc. The unusual bugs must be related to those with depressed immune systems , newborns or CNS devices?

3) Discussion is satisfactory

4) References:
a) Error in the year of publication for ref 4: Lin et al - The year of publication is 2016, not 2014
b) References such as no. 59 and 60: these are books and not able to be sourced readily by most readership.
c) several other articles are not accessible

Table 1:
- Please check abbreviations are explained. The legend misses some of the abbreviations: e.g. "e" (is this a typo). , n/a - must mean "no available"?
b) Typo: Ziehl-Neelsen stain

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable

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