Reviewer's report

Title: Low CD4 Count plus Coma Predicts Cryptococcal Meningitis in Tanzania

Version: 1 Date: 22 December 2006

Reviewer: Íñigo Corral

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General
This is a well performed study on cryptococcal meningitis (CM) in Tanzania. An appropriate methodology, the number of patients included in the study, and a fine statistical analysis make this report valuable.

The information provided by the study has a solid scientific support, although the report gives only some new data on CM. The major new conclusion of the study is the confirmation of the high incidence of CM among patients with HIV infection presenting with headache or altered mental status in Tanzania. High incidence of CM has previously been reported in other African countries. There are other interesting results regarding outcome and response of CM to high dose oral fluconazole.

Other main conclusions of the study come to confirm other known facts: 1) CM presents in severely immunodepressed HIV-infected patients, with CD4 counts usually under 100; and 2) The clinical presentation of CM is non-specific, as it is the rule with opportunistic infections of the central nervous system in AIDS, and the diagnosis can not be sustained only on clinical data or cerebrospinal fluid (CSF) parameters.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

There are some concerns about the justification of the study, expressed in page 4 (lines 9-12) and 7 (lines 6-8), that must be clarified in the introduction section.

Physicians working in developed countries cannot sometimes even imagine the conditions of daily clinical practice in some African regions. The possibility of an empirical management of patients with clinical suspicion of meningitis based only on clinical data will surely be rejected by hospital ethics committees in any developed country. In these countries, such a practice will even have medical-legal consequences. It seems clear that this approach is only theoretical and that it is firmly rejected by the authors in the discussion and conclusion sections, based on the results of the study. But the specific conditions that would eventually make necessary treatment decisions in suspected meningitis without CSF analysis (i.e., lack of 24-hour laboratory or lack of economical resources for microbiological investigations or for lumbar puncture) should also be clarified for the reader in the introduction section.

There is also some apparent contradiction between the goal of avoiding lumbar puncture and cryptococcal antigen testing due to limited economical resources, and the possibility of offering empirically a costly treatment as fluconazole, based only on clinical features, which a priori will have low specificity and will cause drug waste in many patients without CM. A brief economical analysis comparing costs of cryptococcal antigen assay with the cost of treatment with fluconazole for each patient, would be valuable in the introduction. If fluconazole is provided freely, this should also be mentioned.

Another negative counterpart of this approach, which is not considered by the authors, is the fact that without lumbar puncture other treatable conditions (for example tuberculous meningitis) would be missed.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

METHODS: Please, explain that CT scan was not available.
RESULTS: Although it is not essential for the purposes of the study, the reader will appreciate a list of alternative diagnoses of the patients, including the number of patients with a diagnosis of non-cryptococcal meningitis. What was the incidence of tuberculous meningitis?

DISCUSSION: The difficulties in differentiating CM from tuberculous meningitis (a presumably common cause of meningitis in African AIDS patients) by clinical or CSF data merit some comments in the discussion.

What next?: Accept after discretionary revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests