Reviewer’s report

Title: Subacute Sclerosing Panencephalitis: Results of the Canadian Paediatric Surveillance Program and review of the literature.

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Reviewer: Benedikt Weissbrich

Reviewer’s report:

General

In their paper Subacute sclerosing panencephalitis: results of the Canadian paediatric surveillance program and review of the literature, the authors report on the SSPE epidemiology in Canada. Four cases of SSPE have been identified between 1997 and 2000. After describing the details of these four clinical cases, the authors present a review of the literature about the SSPE epidemiology, pathophysiology, clinical features, outcome measures, and treatment. Especially the review of current treatment options should be useful to clinicians.

Major Compulsory Revisions

1. The clinical case reports are rather lengthy. Because there are many clinical descriptions of SSPE cases and also clinical reviews available in the literature, the case reports should be shortened to contain the most pertinent information and unusual aspects of the individual cases. Highlighting the reasons why the SSPE diagnosis was delayed, for example in case 2, and how this could have been prevented would add some instructive aspects to the case reports.

2. As stated in the introduction (last sentence), the review of the literature should focus on clinical issues and management of the disease. In addition, a more thorough review of the epidemiological literature appears appropriate, because the SSPE epidemiology in Canada is the focus of the paper by Campbell et al. In addition to the reports mentioned in the discussion and listed in Table 2, there is a considerable number of old and more recent epidemiological studies on SSPE, for example from Papua New Guinea, England and Wales, South China, Bulgaria, to name only a few. It is recommended, that these and other studies are included in the discussion.

3. While SSPE epidemiology should be discussed and reviewed in more detail, it is recommended that the review section on SSPE pathophysiology and Fig. 1 are deleted. The review section on SSPE pathophysiology contains several inaccuracies and is less than complete. Overall, the paper would profit from concentrating the literature review on epidemiology, clinical features and treatment.

4. Discussion, epidemiology section: The second paragraph should be clarified. One child contracted wild-type measles infection in the Philippines (case 1), one child in Canada (case 3), and one child in the Iraq (child 4). As to case 3, the possibility of a vaccine-associated SSPE case should be phrased much more cautiously. Today with the techniques of molecular epidemiology, it is possible to distinguish wild-type and vaccine virus with certainty when brain material is available. To my knowledge, vaccine virus sequences have not been detected in a single SSPE case, yet. Reports of SSPE cases that were only vaccinated but have no history of measles disease may represent cases of measles infection in the first year of life, when the course of measles may be
attenuated or atypical because of the presence of maternal antibodies.

5. The number of SSPE cases in Canada should be related to the number of acute measles cases in Canada starting from 1985, if these data are available. Is it possible to relate the number of Canadian SSPE cases to the number of measles infections in Canada?

Minor Essential Revisions

6. Introduction, line 6: The sentence about measles vaccine being the only exposure in some cases should be rephrased. As pointed out above, vaccine associated SSPE is currently only a theoretical possibility but has never been proven so far.

7. For better clarity of the case reporting with respect to the surveillance period, it would be helpful if the actual dates (month, year) of first presentation, SSPE diagnosis, survival etc. were listed with the cases rather than abstract indications of the time frame.

8. Case 2: When was the first presentation? When was the CSF analysis performed? When was the diagnosis of SSPE made? How long is the follow-up after the diagnosis? Is there any history of measles disease or measles contact within the first year of life?

9. Case 2, CSF findings (page 8): 662 mg/l instead of mmol/l?

10. Case 3: If this is a true case of SSPE, it is hard to believe that the CSF results were normal (page 9). There should have been oligoclonal bands and an increased IgG/albumin ratio in the CSF. Which studies were performed on the CSF, and what were the results?

11. Case 4: Why was a brain biopsy performed, in spite of the elevated measles antibody titers in serum and CSF and the suggestive clinical and EEG findings? If there was already suspicion of SSPE, has immunohistochemistry for measles antigen been performed on the brain biopsy?

12. Has the SSPE surveillance program been continued after 2000? Are there any additional data on SSPE cases in Canada after the year 2000?

Discretionary Revisions

13. Table 3: Separating Jabbours stages, NDI, and BAE in three tables might improve clarity

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory 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

Declaration of competing interests:

I declare that I have no competing interests.