Reviewer’s report

Title: Impact of the clinical context on the 14-3-3 test, based on the analysis of a Spanish cohort of suspected sporadic CJD patients

Version: 1 Date: 26 April 2006

Reviewer: Alison J Green

Reviewer’s report:

General
This is an important study into the added value of 14-3-3 analysis in the diagnosis of sporadic CJD in a large cohort of patients and highlights the importance of the clinical context on the interpretation of a positive 14-3-3 result. The cohort of patients is separated into those with probable, possible and those without enough signs and symptoms to be considered as possible sporadic CJD (termed non-CJD) at initial investigation. The impact of the 14-3-3 analysis on the final diagnosis is then assessed. However the inclusion of cases initially classified as probable sporadic CJD is not appropriate, as a positive CSF 14-3-3 acts as a supportive investigation and a negative CSF 14-3-3 is unlikely to alter the diagnosis. It is only in the group of possible sporadic CJD and non-CJD cases that a CSF 14-3-3 influences the final diagnosis and as such these are the groups of patients that this study should focus on. Indeed the title of the paper refers to suspected sporadic CJD and a classification of probable sporadic CJD based on the WHO criteria even without CSF 14-3-3 results is more than a suspect case. Despite this the data that the authors present is important and is of value not only to those in the field of CSF 14-3-3 analysis but also to clinicians who may be investigating patients with rapidly progressive dementia.

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

The inclusion of patients initially classified as probable cases should be omitted and the data re-analysed

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

1. Page 6 and Table 4: What was the final diagnosis in the 6 patients who were initially classified as probable sporadic CJD and had a negative CSF 14-3-3? They presumably had PSWCs, so were they diagnosed with an alternative diagnosis on the basis of their clinical course? Have any of the patients died without a post-mortem, and if so how can you be sure they did not have sporadic CJD?

2. Table 4: There were 5 patients initially classified as possible sporadic CJD with a negative CSF 14-3-3 who were finally classified as sporadic CJD, 1 had a post-mortem so did the others have PSWCs on their EEGs? It would be interesting to describe these cases, were they young and did they have long disease durations, did they have changes on their MRI scan, was the PRNP codon 129 genotype investigated? In Table 4 the sensitivity for CSF 14-3-3 in the possible CJD cases is only be calculated using definite CJD cases and those probable cases where there are PSWCs on the EEG. This should be clarified in the notes under the table. This also applies to Table 2.

Discretionary Revisions (which the author can choose to ignore)

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

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests