Reviewer's report

Title: Spectrum of Centrosome Autoantibodies in Childhood Post Varicella Acute Cerebellar Ataxia

Version: Date: 11 August 2003

Reviewer: Anne M Connolly

Reviewer's report:

General:
There are three results of note in this well done small study of serum of children with ACA.

1. Autoantibodies to a variety of centrosome autoantibodies are common in ACA, ACA siblings, varicella without ataxia and other presumed post infectious conditions and as a whole are not specific.
2. A single autoantibody, pericentrin, had some specificity for ACA but had low sensitivity (5/12 ACA versus 0/5 varicella without ataxia).
3. Antiphospholipid autoantibodies had specificity but again, had very low sensitivity.

Discretionary Revisions (which the author can choose to ignore)

1. Discussion: The pericentrin autoantibodies are not sensitive for ACA, and while specific in this cohort, because they are also not entirely specific for this disease entity. The authors point out, they are well described in sclerosis. Therefore, they should acknowledge the fact that pathogenesis of autoantibodies to these intracellular targets is unclear. Non the less, they appear to be a clear marker in this disease and as the authors point out, further work may address pathogenesis.
2. RESULTS: RE: The centrisome staining in Figure 3. The figure a (child's sera) clearly shows immunostaining adjacent to the Purkinje cells and, as the authors note, in many nuclei in the molecular and granular cell layer, but it is less clear to this reviewer that intra-Purkinje cell staining is clearly demonstrated by panel b (Yo plus pericentrin autoantibody). The Purkinje cells seem spared. Perhaps a higher magnification of a single Purkinje cell would be more convincing to demonstrate this intracellular staining. Obviously, the size of the Purkinje cell may make it likely that one would miss the centrisome within the cell. This point does not necessarily detract from this paper though the discussion, which focusses on the Purkinje cell as the target may be overstated as many many nuclei throughout cerebellum are immunostained.

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. Background has a typographical error; Paragraph #2 (microtubule)
2. Methods section: As the authors note that parfin fixed tissue is more sensitive for the detection of autoantibody than commercially available HELA cells, the results in their laboratory for the numbers of healthy normal controls (ie numbers of people with presumed natural autoantibodies) to this prep should be stated.
3. Methods section: Authors should state that all "acute" sera for disease and healthy siblings with varicella were drawn within the same time frame as the ACA children. IE within 7-10 days?
4. Results has an error (5/12 is listed as 33%; it is correct in the table (42%)

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Results state that overall centrosome autoantibodies drop in convalescent sera to 4/12 for the ACA children; but do not state what happened to the one specific autoantibody; the pericentrin which was present in 5/12 initially. If these autoantibodies remit completely with resolution of the ataxia, this is a stronger point regarding potential pathogenesis in this subset of children.

Advice on publication: Accept after minor compulsory revisions

Level of interest: A paper whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Declaration of competing interests: None