Reviewer's report

Title: Autoantibodies Against Retinal Proteins in Paraneoplastic and Autoimmune Retinopathy

Version: 1 Date: 5 February 2004

Reviewer: miles R stanford

Reviewer's report:

General This paper describes the prevalence and specificity of anti-retinal antibodies in 193 patients with suspected para-neoplastic or autoimmune retinopathy. The authors found that there was an overall prevalence of 47% of antibody detection, and that this prevalence was higher in patients with paraneoplastic disease. Overall this paper is well written, relevant and gives new information about this little recognised condition.

---------------------------------------------------------------------------------------------------------------------------------

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

none

---------------------------------------------------------------------------------------------------------------------------------

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

Abstract It would be useful to describe the phenotype in full in the Methods section. In line 2 of results add 'ed' to present.

Introduction penultimate line on p 4 - what does the word 'reasonable' mean in the context of the sentence?

Methods Did the control patients have the same physical exam ie., visual fields/ electrodiagnostic tests as the patients?

In the immunocytochemistry studies, it would be useful to know who evaluated the sections and that they were blinded to the diagnosis. Was any grading other than positive or negative applied to the sections? Did the authors attempt to quantitate by serial dilution the antibody titres of positive sera on Westerns or by immunocytochemistry?

On line 3 p8 ,insert 'were' for 'are'

In the cytotoxicity assay, the authors should state how the IgG was purified and emphasise that the control sera were/were not pre-selected for antibody positivity.

Results On line 5, 2nd para, p9 'prevalence' should be substituted for 'incidence'. In the 79 control sera, 15 were positive. How many of these were women? Was there any difference in titre of antibody between patients and controls? In the cytotoxicity assays we need to know how many sera were taken from each group. The only explanation for the statistical anomaly (a lower p value in the autoimmune group than the paraneoplastic group, despite lower cell survival), would be if there were different numbers in each group.

---------------------------------------------------------------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)

Abstract Do the authors know the identity of p35 (last line p2) - if so, could this be inserted. The authors might wish to consider that the production of the antibodies is a result rather than a cause of the disease. Was there any phenotypic difference (either in erg results or clinical findings) between patients who were antibody positive and those where it was not present?

Methods The authors should describe the visual field defects of their patients. Similarly it would be
of interest to know whether there was a specific association between the findings on ERG recording and the type of antibody found. Accordingly it would be useful to have a broad outline of the ERG abnormalities encountered.

In the ELISA experiments, the authors may wish to comment on the justification for using bovine rather than human recoverin.

Results In the second paragraph, it would be nice if the authors could express the average age as a median rather than a mean. How do the authors explain the converse of their findings that they have 50% of their patients with a typical picture (the inclusion criteria) and yet no evidence of anti-retinal autoimmunity?

In the report of the follow-up study the authors give the example of 1 CAR patient (p11, l3 from bottom) who, 2 lines later, has no cancer! I assume there was a cancer present at initial diagnosis. The relationship between antibody titre and visual worsening is weak. We are not told the nature of the visual worsening - was this acuity alone, visual field or ERG worsening.

Discussion

On p13, line 4 the authors state that there was a similar cytotoxic effect on the retinal cells whether the serum was derived from the AR or PR patients. Whilst this effect was not as great when the cells were incubated with 'control' serum, it was still seen. It is not clear if the 'control' sera were pre-selected for antibody positivity (15/79 patients) - see above.

On p 14 , the authors suggest that the heterogeneity of antibodies may give rise to the complex variation of clinical signs - do they have at least ERG data to support this, or is the ERG data also markedly heterogenous?

The references are appropriate to the text

What next?: Accept after minor essential 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:

one