Local IgG production in aqueous humour in patients with idiopathic uveitis compared with MRI findings

We have previously reported an increased concentration of antibody to measles in the aqueous humour of patients with multiple sclerosis related uveitis.1 We further found a high frequency of asymptomatic multiple sclerosis-like lesions on MRI of the brain of patients with uveitis.1 There was a significant association between MRI lesions and high aqueous humour and blood concentrations of antimeasles antibodies.

The local production of oligoclonal IgG in the CNF has long been considered as a pathognomonic characteristic of multiple sclerosis, and also a good biological aid to its diagnosis.2 Oligoclonal production of IgG has also been suspected in the aqueous humour of patients with multiple sclerosis, on the basis of the ratio between albumin and IgG contents in both aqueous humour and serum.

The study was aimed at determining if the presence of white matter MRI lesions in patients with uveitis was linked to an increased content of IgG in the aqueous humour, and if this increase could be explained by the high concentration of antimeasles antibodies in the aqueous humour.

Sixty eight patients with idiopathic uveitis (23 males, 45 females, aged 15–49), all free of neurological symptoms, diabetes, and blood pressure problems, were submitted to both a brain MRI examination and a sampling of blood and aqueous humour. All patients gave informed consent to their participation in this study.

The presence of white matter lesions on MRI was determined in each patient by three independent radiologists according to Pany's multiple sclerosis diagnosis scale.4 Samples of aqueous humour and blood were assayed for albumin and total IgG by laser nephelometry and measles virus, herpes simplex virus (HSV), varicella-zoster virus (VZV), and cytomegalovirus (CMV) specific IgG by enzyme linked immunosorbent assay (ELISA). The following coefficients were calculated:2 albumin quotient = aqueous humour albumin/serum albumin; IgG quotient = aqueous humour IgG/serum IgG. IgG index = IgG quotient/albumin quotient.

The values of these three coefficients as well as optical densities in aqueous humour for each of the four virus assays were compared in patients with lesions on MRI (MRI+ ) and those without (MRI− ) by Wilcoxon's test. Partial Spearman correlations were calculated to assess if the relation between the local IgG production coefficients and MRI was related to a specific viral expression.

The results showed an association between the presence of brain lesions and high ocular IgG production as represented by the IgG quotient (P < 0.002; table). Albumin quotients did not differ significantly between the groups and the associated was due to differences in the values of the IgG quotient (P < 0.05).

Moreover, an optical density of aqueous humour of MRI+ patients was significantly higher than that of MRI− patients. (P < 0.001). We did not find a difference in VZV, HSV, or CMV optical densities between the two groups. The value of the measles optical density in aqueous humour were significantly correlated with both IgG quotient (P < 0.01) and IgG index (P < 0.04). Finally, when adjusting for the effect of optical density in aqueous humour, the partial correlation between IgG index and MRI remained significant (P < 0.05).

The well documented relation between multiple sclerosis and uveitis is difficult to evaluate from a clinical point of view. Asymptomatic forms of ocular inflammation have been variously described in multiple sclerosis. The local production of IgG in the CSF of patients with multiple sclerosis is also well documented.2 White matter lesions on MRI of the brain are present in various inflammatory diseases, but specially multiple sclerosis.

The aim of this study was to check if the IgG concentration was increased in the aqueous humour of patients with idiopathic uveitis. The albumin quotient measures the modifications of the blood ocular barriers and by comparing both albumin and IgG quotient, the local production of IgG (IgG index) can be evaluated. The association between a high IgG index in aqueous humour and the presence of white matter lesions in patients with idiopathic uveitis and without neurological symptoms might be a phenomenon similar to the local increase in the IgG index in the CSF of patients with multiple sclerosis.

Our study is based on a quantitative measure of IgG production that is less sensitive than the qualitative measure of oligoclonal IgG. We think, however, that the large number of patients studied compensates for the lower sensitivity of our measures, compared with studies based on qualitative measures that involve a smaller number of patients.

The common presence of measles anti-

bodies in the CSF of patients with multiple sclerosis is well known.1 After adjusting for the values of measles optic density in aqueous humour, the correlation between IgG index and MRI remained significant. This indicates that measles optical density in aqueous humour and IgG index are positively linked with MRI but the link between IgG index and MRI lesions is only partially explained by the link between measles optical density in aqueous humour and MRI. If measles has a role in the origin of multiple sclerosis and multiple sclerosis related uveitis, it may not be the only contributing factor.

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Central nervous system demyelination after vaccination against hepatitis B and HLA haplotype

Although very unusual, acute CNS complications may occur after vaccination against hepatitis B.1 We report a patient with evidence of severe demyelination in the CNS after hepatitis B vaccination.

Local production coefficients in MRI+ and MRI− patients with uveitis

| Coefficient | MRI+ (n = 21) | MRI− (n = 47) | P value *
|-------------|---------------|---------------|-------------
| Albumin quotient | 0.007 (0.003–0.011) | 0.006 (0.003–0.013) | NS |
| IgG quotient | 0.008 (0.006–0.024) | 0.004 (0.002–0.011) | 0.02 |
| IgG index | 1.13 (0.72–2.67) | 0.74 (0.43–1.00) | 0.002 |

*Wilcoxon test.

Results are medians (25th and 75th percentiles).