Are muscle cramps in Isaacs' syndrome triggered by human immunoglobulin?

Ishi et al reported the clinical evaluation of plasma exchange and treatment with high dose intravenous immunoglobulin (IVIg) in a patient with Isaacs' syndrome.1 The rationale for either treatment in this syndrome was a possible autoimmune etiology.2 The differential treatment response was remarkable, as IVIg in plasma exchange and intravenous immunoglobulin (IVIg) administration may cause adverse effects of muscle cramps that improve with intravenous globulin. Neurology 1994;57:859-61.

We would like to draw attention to an unusual response to intravenous immunoglobulin and muscle cramps. Although muscle cramps are generally not reported as adverse effects of IVIg treatment, they may be observed. This patient might be due to an altered excitability of motor terminals in this syndrome.2

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5 Hayashi et al reply: We thank van Engelen et al for their comments on our paper.1 In that paper, we reported that we had anticipated that IVIg treatment would be helpful for Isaacs' syndrome, but unexpectedly, the IVIg treatment actually worsened the symptoms of our patient. These symptoms (myokymia, cramps, fasculations, and muscle cramping) were not different from the previous ones, but were more intense.

The findings suggest that our patient may exhibit a hypersensitive immune response to human immunoglobulin. In other words, some trigger zones sensitive to immunoglobulin apparently exist in our patient. The mechanism is yet unclear, and thus it is important to find out where the trigger zone for immunoglobulin is. The letter of van Engelen et al gives an important clue.

One candidate for the trigger zone is the muscle tissue itself. Nagashima et al reported on the presence of a complex in the muscle fibre membrane and motor endplate from immunofluorescence studies on muscle biopsy samples from a patient with Isaacs' syndrome.1

Another candidate may be the nerve terminal, because morphological abnormalities, such as sprouting of the intramuscular nerve, have been reported in Isaacs' syndrome.1,3 Oda et al reported that there were extensive terminal arborisations in the endplates, and that some of these were extended away from the original endplate area.4 They suggested that terminal nerve abnormal discharge was in the distal segment of the intramuscular nerve axon, including the nerve terminal.

Our report is the first study of the use of IVIg in Isaacs' syndrome, and thus we cannot really assess the effectiveness of this treatment. There is, however, one patient with Isaacs' syndrome who improved with IVIg treatment (Wintzen et al and A R Wintzen, personal communication). It would seem, therefore, that the effect of IVIg may be dependent on the specifics of each case. There is likewise the possibility that the effect may be altered by the type or dose of human immunoglobulin.

Isaacs' syndrome has been considered as an autoimmune disorder. Arimura et al studied antibodies acting on the cell membrane of PC12 in serum taken from patients with Isaacs' syndrome1 and showed the suppression of potassium channels in the neuronal cell line in serum taken from such patients, including our case.4

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6 Wintzen AR, Dik JR, Brand A. Neuromyotonia with early response to plasmapheresis associated with maximal action myoclonus with late response to plasmapheresis. Muscle Nerve 1994;suppl 1:S221.

Somatisation in neurological practice

I was interested to read the article by Ron1 on somatization in neurological practice. The inability to make a specific diagnosis in neurological outpatient practice is something that I referred to in a paper published in this Journal in 1989.2 An analysis of 7836 successive new referrals to my clinics established that some 26-5% did not have a specific diagnosis, even in some cases after extensive investigation. Ron might be interested to know that among the same number of patients 297 or 3-8% had some evidence of conversion hysteria. Based on an earlier study, also published,1 one would have expected probably some 50% of these

Complementary alterations in the CSF of patients with amyotrophic lateral sclerosis

Recently, Tsuboi and Yamada1 reported increased CSF concentration of C4d and increased C4d index values in patients with amyotrophic lateral sclerosis and suggested that this finding may be due to complement activation that could play a part in motor neuron degeneration. Since 1985,2 we have found high levels of C3c but not changes in C3c index values and other complement fractions in CSF from patients with amyotrophic lateral sclerosis. The results of our study indicate that the CSF protein concentrations. We proposed that the increase in C3c fraction could be in part to leakage through the altered blood-brain barrier but also to decreased binding to specific complement receptors on CNS lymphocytes that leads to complement deposition in nervous tissues. This interpretation focuses on the biochemical and functional changes in cell membranes from patients with amyotrophic lateral sclerosis. The role of the immunological alterations in amyotrophic lateral sclerosis pathogenesis needs further investigation.

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4 Sonoda OH, Vestfahl IR. Reduction of brain insulin receptors in amyotrophic lateral sclerosis correlates with reduced insulin sensitiv-


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