Clinical implementation of anti-acetylcholine receptor antibodies

Dr Somnier summarises his experience with testing for antibodies to acetylcholine receptors in his 10-year clinical practice. He confirms the reference range obtained with a large number of disease controls. His data completely agree with our study on 193 validated disease controls. It is of interest that all of his 26 patients with myasthenic symptoms had titres within the reference range, contrasting with other reports. It is of interest to note that 80% clearly stands out. It is not obvious how these cases were validated as not having generalised myasthenia gravis at any time during their disease, which would put them into the other disease group. This group was not uncommon for ocular myasthenia gravis to start with ocular symptoms and signs of generalised myasthenia gravis to develop within the next months. On the other hand, some patients may have very mild generalised signs which may be too subtle to be detected by an inexperienced examiner. For diagnostic use in ocular cases (Osserman 1) it seems reasonable to come up with two sensitivity figures: in a case of recent onset, the prior chance to find elevated titres may be approximately 70% or even higher as stated by Somnier. If patients are observed over six or 12 months, some will have developed generalised myasthenia which shifts them into another group. In the remaining patients with long-standing, purely ocular myasthenia gravis, the test sensitivity will gradually decrease. By using these criteria we have indeed found a positivity rate of initially close to 70%, dropping to 45% (above 0-5 nM/l) or 53% (above 0-4 nM/l) (fig). It is that persistence that is difficult to establish in cases that pose considerable diagnostic problems.

Sensitivity figures for generalised myasthenia gravis are similar to the ones reported by Howard et al but higher than in our study. The reason may be that all patients were examined by one of our clinical research group and any questionable cases were excluded from this analysis. The definition of what remains to be "seronegative" is not trivial because permanent seronegativity often calls for tedious further studies to search for unusual myasthenias and myasthenic syndromes. In the few percent of negative cases some may have other types of autoantibodies, as discussed by Somnier and others or have low circulatory levels within the reference range. Seronegative patients with acquired autoimmune myasthenia gravis may indeed have autoreactive B cells capable of producing antibodies, as demonstrated by the elegant experiments of referring lymphocytes from patients to severe combined immunodeficiency mice. Furthermore, serum immunoglobulin of seronegative patients with ocular or generalised myasthenia gravis may increase degradation of junctional acetylcholine receptors.

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1 Somnier FE. Clinical implementation of anti-acetylcholine receptor antibodies. J Neurol Neurosurg Psychiatry 1993;54:496-504.

Dr Somnier replies: I am pleased to learn that my data completely agree with the experiences of Toyka and colleagues with the exception of the diagnostic sensitivity of the anti-acetylcholine receptor (AChR) antibodies assay in ocular myasthenia gravis. Ocular cases were validated as not having generalised myasthenia gravis exclusively on clinical or pharmacological criteria or both. (1) Complaints and signs of fatigability with or without weakness were located to extraocular muscles and eyelid (ptosis), and there were no symptoms of other striated muscles. (2) Unequivocal effect of cholinesterase inhibitors drugs (edrophonium, pyridostigmine, etc.) was observed at least on one occasion. (3) Neuropsychological signs of generalisation were not a disqualifying feature, that is, repetitive nerve stimulation (RNS) may or may not show a decrement of action potential or twitch in adductor pollicis, brachial biceps, or deltoid muscle. (4) All patients were assessed several times by an experienced examiner (the author).

In eastern Denmark, 202 incident cases of myasthenia gravis were identified during the 20-year period from 1 January 1970 to 31 December 1989. A total of 187 patients were followed for more than one year. Serum samples were obtained from 155 of these patients (group A). The number of long-standing, purely ocular myasthenia gravis was five (16%) among the 32 cases without a serum sample compared with 18 (12%) in group A. In the latter group many may therefore be taken as unbiased estimates of the whole patient population.

In cases of recent onset of myasthenia gravis, the chance to find elevated anti-AChR antibodies titres was 84-9% in ocular myasthenia gravis and 92-6% in generalised myasthenia gravis. After a duration of the disease longer than one year, the sensitivity of the anti-AChR antibodies assay was 77-8% in ocular myasthenia gravis compared with 92-7% in generalised cases. Re-defining ocular myasthenia gravis with a decrement at RNS as generalised myasthenia gravis (transferring four ocular cases to the other group), yielded a sensitivity of 78-6% in persistently ocular cases, in agreement with the observation that no prognostic conclusion can be drawn from non-longitudinal measurement of decrement. Toyka's observation that many patients with recent onset of myasthenia gravis will develop generalised disease was confirmed by the long-term assessment of group A (15 of 33 patients, 45%). The
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