Are MuSK antibodies the primary cause of myasthenic symptoms?

Triple-furrowed atrophic tongue: MuSK-antibody-positive patient

Selcen et al. report a childhood-onset, MuSK-seropositive myasthenic patient with reduced synaptic response to Ach but no endplate AChR or MuSK deficiency, trace IgG deposits at the endplates, and three polymorphisms in *MuSK*. They suggest that the anti-MuSK antibodies may not be the primary cause of myasthenic symptoms.

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MuSK antibody in Chinese and Japanese seronegative myasthenia gravis (SNMG)

Yeh et al. detected auto-MuSK antibodies kinase antibody in only 1 of 26 (4%) Chinese patients with generalized SNMG. This frequency is much lower than the 40% to 70% frequency reported in Caucasian SNMG.

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Ohta et al. detected anti-MuSK antibodies in 41% of 17 SN Japanese MG patients. In addition, they found a 10.5% MuSK positivity rate in AChR Ab-positive patients both with and without thymoma.

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"It is now critical to determine whether immunization of rodents with purified MuSK can cause loss of AChRs and muscular weakness."

The accompanying editorial by Jon M. Lindstrom notes that an explanation for muscular weakness of many of the 10 to 15% of "seronegative" MG patients who lack autoantibodies to AChRs had appeared to be autoantibodies to muscle-specific receptor tyrosine kinase (MuSK). MuSK mediates agrin-induced clustering of AChRs during synapse formation. These autoantibodies to the extracellular domain of MuSK inhibit its function in tissue culture.

These three articles cast doubt on MuSK autoantibodies as the explanation for seronegative MG: Autoantibodies to MuSK were not found where they were expected and were found where they were not expected. Moreover, they were found but do not seem to be the cause of weakness in the Selcen et al. case. Here, autoantibodies to MuSK appear to be incidental to unknown pathologic mechanisms which caused muscle weakness.

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Migraine practice patterns among neurologists

Lipton et al. surveyed US neurologists regarding migraine management relative to the US Headache Consortium Guidelines. Based on the survey, education initiatives should target the following: migraine diagnosis in the absence of unilateral pain, nausea, and aura; more appropriate use of neuroimaging; selection of acute treatment, including the cardiovascular contraindications to the triptans; medication overuse; and indications for preventive treatment.

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Seizures and calcific neurocysticercosis

Nash et al. summarize studies implicating calcified granulomas as an important cause of seizures in neurocysticercosis. The presence of associated perilesional edema is common, directly implicating calcified foci.

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High risk of stroke and MI risk after TIA

Hill et al. evaluated the risk of, and predictors for, stroke in patients presenting to Alberta Emergency Departments. Among 2,285 patients with a TIA, the risk of stroke was 9.5% at 90 days and 14.5% at 1 year. The risk of stroke, myocardial infarction, or death was 21% in 1 year. Hypertension, diabetes, and older age predicted stroke at 1 year.

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High blood pressure and cognitive decline

Hebert et al. investigated the relation of blood pressure to cognitive decline in a population-based study of older persons. They found that higher systolic or diastolic blood pressures at the beginning of observation were not associated with greater cognitive decline over the following 6 years.

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Genetic and environmental influences on episodic tension-type headache

Ulrich et al. estimated the relative effects of genes and environment in episodic tension-type headache in a study population of 5,360 twins. They found that environmental influence is of major importance for episodic tension-type headache and a genetic effect, if it exists, is minor. Their data distinguish episodic tension-type headache from migraine where a major genetic effect has been found.

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Antiepileptic drug (AED) use increases rates of bone loss

Ensrud et al. ascertained AED use and measured bone density in a cohort of 9,704 community-dwelling older women and followed them prospectively for changes in bone density. Women taking AEDs had a nearly twofold increase in the rate of bone loss at the calcaneus and hip.

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Anti-MOG antibodies in multiple sclerosis

Lampasona et al. using a newly developed ultrasensitive liquid-phase radiobinding assay reported that the frequency of positive samples with low titers of anti-MOG IgG ($\leq 5.7\%$) and IgM ($\leq 8.3\%$) was similar in multiple sclerosis patients (some of them at the onset of the disease) compared to patients with encephalomyelitis and healthy subjects, thus concluding that anti-MOG antibodies are not MS-specific.

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The accompanying editorial by Anthony T. Reder and Joel J.-F. Oger notes that MOG is a strong candidate as an MS antigen: it is unique to the brain, it is located on the outer lamellae of oligodendroglial membranes and myelin, it is highly immunogenic, and MOG immunization induces severe relapsing EAE in animals. A recent article proposed that anti-MOG antibodies were a marker for more rapid progression to MS in patients with their first symptoms raising the possibility of MS. The results of the Lampasona et al. study, likely caused by differences in techniques rather than study populations, raise questions about the role of these antibodies.

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Prevalence of marijuana use in patients with epilepsy

Gross et al. report that 21% of patients seen at a tertiary care epilepsy center had used marijuana in the previous year with 68% of users reporting beneficial effects on seizure severity.

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Clark et al. surveyed 220 patients in Nova Scotia with multiple sclerosis and found that 36% had used marijuana and that 29/205 (14%) were currently using smoked cannabis for self-reported improvement of stress, sleep, spasticity, and pain.

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"In order to use marijuana effectively and safely for clinical purposes, we need to be able to study its use in appropriately designed and conducted clinical studies. To do that, we must have a legal setting that permits unfettered scientific inquiry into the safety and efficacy of such a treatment."

The accompanying editorial by Joseph I. Sirven and Anne T. Berg notes that in July 2001, in a response to an appellate court decision, Canada implemented the Marijuana Medical Access Regulations, clearly outlining the circumstances and manner in which marijuana can be used therapeutically in that country. All patients must provide "a medical declaration that all conventional treatments have been reasonably tried or considered, and that the benefits of using marijuana outweigh any potential risks." While these studies demonstrate a high level of use of medical marijuana in Canada, it is of concern that there is a lack of evidence from randomized controlled trials demonstrating its effectiveness.

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