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Letter to the Editor

Triggers Converting Ocular to Generalised Myasthenia Are More Diverse Than Anticipated

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In a recent article, Apinyawasisuk *et al.*, reported about a retrospective chart review on the factors triggering the conversion of seropositive ocular myasthenia (OM) to generalised myasthenia gravis (GM) in 71 patients (Apinyawasisuk, S. *et al.*, 2019). It was concluded that factors triggering the conversion OM/GM include not taking pyridostigmine or immunosuppressants, smoking, female gender, and thymic abnormalities (Apinyawasisuk, S. *et al.*, 2019). We have the following comments and concerns.

A shortcoming of the study is that emotional or physical stress was not taken into account as triggers of the conversion OM/GM. It is well appreciated that acute or chronic physical or emotional stress may worsen myasthenia (Blum, S. *et al.*, 2015) and may even increase serum titres of acetyl-choline receptor antibodies (AchR-abs) (Marcus, J. 1962).

A further shortcoming is that the titre of AchR-abs was not considered as a factor triggering the OM/GM conversion, although it is conceivable that high AchR-abs may predispose to OM/GM conversion. Since at least in some studies showed that there is a positive correlation between AchR-ab titres and severity of myasthenia (Masuda, T. *et al.*, 2012), it is conceivable that the amount of AchR-abs present in the serum may influence the time at which the conversion OM/GM may take place.

A third shortcoming is that drugs other than pyridostigmine or immunosuppressants were not taken into consideration as factors triggering the conversion OM/GM. From a number of compounds, such as opiods, calcium, carbamazepine, tobramycine, etc. it is well-known that they may worsen GM, why it is conceivable that they may also contribute to the conversion OM/GM. Thus, it is crucial that the entire medication the included patients were regularly taking is provided.

Additionally, it is crucial to know the condition of the 36 patients who converted at conversion. We particularly should know, how many had an infection, were not compliant with regard to the anti-myasthenic medication, took drugs worsening myasthenia, underwent surgery, or had severe physical or emotional distress.

A fourth shortcoming of the study is that the authors did not specify what they understand with "thymic abnormalities". We should know if they mean thymic hyperplasia, thymoma, adenoma, atrophy, calcification, bleeding, or infarcts. To assess the influence of thymic abnormalities on the conversion OM/GM it is crucial to know the exact abnormality found in the thymus of the included patients. Additionally, it is not mentioned if any of the 71 patients had undergone thymectomy prior to inclusion in the study already.

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Another triggering factor not considered is age at onset. It is conceivable that immune-competence declines with age that older patients with OM more frequently convert to GM than those with an early onset. It would be also interesting to know if those with short conversion interval more likely developed myasthenic or cholinergic crisis than those with prolonged conversion interval.

Overall, this interesting study has a number of shortcomings, which need to be addressed before drawing final conclusions. Emotional/physical stressors, entire current medication, age at onset, and AchR-ab titres need to be considered as factors triggering the conversion OM/GM.

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