

Letter to the Editor

The Spectrum of Comorbidities in Myasthenia Gravis Is Broad

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In a recent article, Misra *et al.*, reported about immunological (n=8) and miscellaneous comorbidities (n=71) in 48 early-onset (<40y) and 33 late-onset patients with myasthenia gravis retrospectively investigated for autoimmune disease, arterial hypertension, diabetes, hyperlipidemia, and chronic obstructive lung disease (Misra, U.K. *et al.*, 2019). Twenty-eight patient experienced a myasthenic crisis, of which 5 had autoimmune and all miscellaneous comorbidities (Misra, U.K. *et al.*, 2019). The study raises the following comments and concerns.

A repeatedly reported complication of myasthenia gravis, and particularly myasthenic crisis, is Takotsubo syndrome (TTS) (Douglas, T. M. *et al.*, 2018). TTS is defined according to the Mayo Clinic criteria and characterised by transient left ventricular systolic dysfunction due to adrenergic overstimulation (Zhang, L., & Piña, I.L. 2019). An apical type, mid-ventricular type, basal type and global type of TTS are differentiated (Zhang, L., & Piña, I.L. 2019). TTS mimics myocardial infarction clinically, chemically, and electrocardiographically, but contrary to acute myocardial infarction coronary arteries are normal. The apical type of TTS is the most frequent and characterised on echocardiography and cardiac MRI by ampullar widening of the left ventricle with regional or global akinesia, hypokinesia, or dyskinesia of the left ventricular wall. Thus, we should be informed how many of the included patients, including those with myasthenic crisis, developed cardiac complications and underwent echocardiography and determination of troponin and pro brain natriuretic peptide levels. Particularly in the patient with myocardial infarction it should be reported if coronary angiography was

abnormal and if myasthenic crisis was the trigger of the cardiac problem or vice versa.

A shortcoming of the study is that the differentiation between myasthenic crisis and cholinergic crisis is unclear (Misra, U.K. *et al.*, 2019). According to table 2, which lists precipitating factors of myasthenic crisis, myasthenic crisis was triggered by a cholinergic crisis in two patients. This is contradictory and requires clarification. Myasthenic and cholinergic crisis need to be thoroughly differentiated as the therapeutic management differs considerably between the two. A cholinergic crisis is typically associated with miosis and bradycardia, whereas a myasthenic crisis is typically associated with mydriasis and tachycardia (Adeyinka, A., & Kondamudi, N.P. 2019 Mar 24). Since a myasthenic crisis may be associated with high titers of acetylcholine-receptor (AChR-ab) (Kanzato, N. *et al.*, 1999), we should be informed about the AChR-ab titers in the 70 patients with elevated AChR-ab titers and particularly those with myasthenic crisis.

Interestingly, 7 patients had neither AChR-ab nor anti-MUSK-antibodies (Misra, U.K. *et al.*, 2019). We should be informed how myasthenia was diagnosed in these 7 patients, if they were diagnosed upon repetitive nerve stimulation or the pyridostigmine test. If myasthenia was diagnosed solely upon either of these two tests, it should be considered that the pyridostigmin test as well as repetitive nerve stimulation may be false positive.

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Other comorbidities of myasthenia which were not considered include alopecia, thrombocytopenia, hypogammaglobulinemia, nephrotic syndrome, insomnia, anxiety, and obstructive sleep apnea.

In conclusion, this interesting study may profit from clarification of some inconsistencies, from differentiation between myasthenic and cholinergic crisis, from providing AchR-ab titers, and from considering TTS and other entities as a possible complication of myasthenia gravis.

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