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Perioperative cardiac risks in myasthenia gravis

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Abstract

Myasthenia gravis (MG) is an autoimmune disorder that affects the neuromuscular junction. The primary pathology in MG involves the presence of autoantibodies to acetylcholine receptors (AChRs), which results in qualitative and quantitative reductions in the availability of functional AChRs. Cardiac muscles are also affected, resulting in various perioperative cardiac complications. Antistriational antibodies are commonly reported in MG cases with cardiac involvement. In the presence of thymoma, the prevalence of cardiac manifestations in patients with MG increases to approximately 10%-15%. Cardiac involvement in MG may range from asymptomatic electrocardiogram changes to ventricular tachycardia, myocarditis, conduction disorders, heart failure, and sudden death. Increased incidence of atrial fibrillation, ventricular and supra-ventricular extra systoles, and prolonged QTc have also been reported in patients with MG. Clinicians should consider the evaluation of autonomic dysfunction and risk of cardiovascular disease in patients with MG.

Key Words: Myasthenia Gravis; Perioperative period; Receptors; Cholinergic; Anesthesia

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Core Tip: Current evidence shows that elderly patients with myasthenia gravis (MG) are more prone to developing perioperative cardiac complications. As healthcare professionals refine and evolve screening methods to identify patients with MG at risk of developing perioperative cardiac events due to autonomic dysfunction, the integration of screening for antistriational antibodies becomes crucial. In addition, assessing left ventricular function in the preoperative period may result in successful outcomes in these patients.

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INTRODUCTION

Myasthenia gravis (MG) leads to fatigue and progressive muscular weakness due to an autoimmune disorder affecting the neuromuscular junction[1]. With a maximal prevalence in the second-third decade in females and fifth-sixth decade in males, the approximate prevalence of MG is 1:7500[2].

The primary pathology in MG involves the presence of autoantibodies to acetylcholine receptors (AChRs)[1], which disrupts the function of AChRs by blocking the receptors, making conformational changes, activation of complements, and crosslinking. This leads to increased degradation of these receptors[1]. The qualitative and quantitative reductions in the availability of functional AChRs result in decreased motor endplate potential amplitude and failure in the initiation of muscle fiber contraction[1]. Skeletal muscles are primarily involved in MG. However, numerous studies[3-5] have shown that cardiac muscles are also affected, resulting in various perioperative cardiac complications. In the presence of thymoma, the prevalence of cardiac manifestations in patients with MG increases to around 10%-15%[3]. The AChRs autoantibodies do not bind to cardiac muscle receptors. Studies[5,6] have revealed that 48% of patients with MG and 97% of patients in whom MG is present along with thymoma, have antibodies against cardiac muscles[5]. The antistriational antibodies[6] (antititin antibodies, antiryanodine receptor antibodies, and anti-Kv 1.4 antibodies) are commonly reported in MG cases with cardiac involvement[5,6].

Cardiac involvement in MG may range from a normal sinus rhythm on an electrocardiogram (ECG) to various other pathologies myocarditis or heart failure and ventricular tachycardia to conduction disorders, with at times can lead to sudden death[2].

Myocarditis

Myocarditis has been reported in 37.5% of patients with MG who possess antistriational antibodies[4]. Suzuki *et al*[7] observed that anti-Kv 1.4 antibody influences cardiac function by complement activation and T cell proliferation; therefore, it can be a potential marker for the development of lethal autoimmune myocarditis. Giant cell myocarditis is frequently reported in patients with MG and is evidenced by the presence of myonecrosis[5] with increased age and thymoma being identified as risk factors[8].

Cardiomyopathy

Studies[5] have shown takotsubo cardiomyopathy, a stress-induced reversible and transient left ventricular dysfunction is often associated with MG, which is in the absence of significant coronary stenosis, takotsubo cardiomyopathy frequently presents as acute coronary syndrome and is aggravated by anything which causes a catecholamine surge, like emotional or physical stress, and suppresses myocardial function[9]. Mayor-Gomez *et al*[10] reported a case of heart failure with difficulty in weaning a patient off the ventilator after mitral valve replacement, which was retrospectively diagnosed as a myasthenia crisis. Similarly, Shukla *et al*[11] observed that with every episode of myasthenia crisis in an elderly female, she had recurrent takotsubo cardiomyopathy.

Cardiac arrhythmias

Increased in the incidence of atrial fibrillation, ventricular or supraventricular extra systoles, or prolonged QTc have been reported in different studies[5,12] in patients with MG and thymoma. Peric *et al*[12], in his study of patients with MG, observed that autonomic dysfunction was present in 20% of cases with thymoma and about 3% of cases without thymoma. He also concluded that antibodies to ganglionic AChRs were responsible for autonomic dysfunction in these patients[12]. Chiavistelli *et al*[13] showed that patients with MG had associated nonspecific changes in T waves, prolongations in QT interval and increase in the incidence of first-degree atrioventricular (AV) block during the perioperative period. Several other studies[2,14,15] have documented a positive correlation between anti-Kv1.4 antibody and perioperative fatal arrhythmias, which include sick sinus syndrome, ventricular tachycardias, complete AV block, and sudden cardiac death.

Coronary artery spasm

Various cases of coronary artery spasm have been reported in patients with MG. Yanagihashi *et al*[16] reported a case of intravenous immunoglobulin coronary spastic angina (CSA) that was relieved by glyceryl trinitrate. Hsu *et al*[17] also reported a case of diffuse coronary artery spasm with three vessels. Intracoronary isosorbide dinitrate and adenosine relieved the symptoms. Chuapakdee *et al*[18] also reported a case of CSA after pyridostigmine dose up-titration. Sublingual nitrate immediately relieved symptoms concomitantly with the resolution of abnormal electrocardiograph findings.

CONCLUSION

The heart, like other organs, is a potential target for immune attack in autoimmune disorders such as MG. The exact incidence of perioperative major adverse cardiac events in patients suffering from MG is not known, perhaps due to similar symptoms such as fatigue, dyspnea, and poor exercise tolerance, leading to lesser appreciation of cardiac manifestations. The current evidence mostly consists of retrospective case-control studies or case reports; these suggest that cardiac involvement in MG is often associated with thymoma, anti-Kv 1.4 antibodies, and advancing age. Therefore, it is necessary to conduct prospective studies before recommending cardiac screening in MG. However, antistriational antibodies highlight a fascinating potential connection between MG and cardiac diseases.

FOOTNOTES

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