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CASE REPORT

Appearance of anti-acetylcholine receptor antibodies after COVID-19

Aparecimento de anticorpos antirreceptores de acetilcolina após COVID-19

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ABSTRACT

Objectives: In this paper, we report a case of Myasthenia Gravis (MG) exacerbated by COVID-19 that was initially anti-acetylcholine receptor (AChR) negative and after 9 months became positive for anti-AChR antibodies. **Methods:** We performed a review of the medical records and clinical follow-up of a patient followed at the Neurology service of Walter Cantídio University Hospital. **Results:** A 37-year-old female patient presented with mild dysphonia, ptosis and diplopia. Three months later, she was admitted to the hospital with respiratory failure associated with COVID-19. The patient received a clinical diagnosis of MG and anti-AChR and MuSK antibodies were negative at that moment. Nine months after initial presentation, serum anti-AChR antibodies were positive. **Conclusion:** We reported a patient who presented seroconversion for anti-AChR antibodies after COVID-19. There have been some reports of possible viral triggers for myasthenia, but controversy over this matter still remains.

Keywords: Myasthenia Gravis, COVID-19, SARS-CoV-2.

RESUMO

Objetivos: Neste artigo, relatamos um caso de Miastenia Gravis (MG) exacerbada por COVID-19 que inicialmente apresentava anticorpos antirreceptor de acetilcolina (AChR) negativos e após 9 meses tornou-se positivo para anticorpos anti-AChR. **Métodos:** Foi realizada revisão de prontuário e seguimento clínico de uma paciente de 37 anos acompanhada no serviço de Neurologia do Hospital Universitário Walter Cantídio. **Resultados:** Paciente do sexo feminino iniciou quadro de leve disfonia, ptose e diplopia. Três meses depois apresentou quadro de insuficiência respiratória associada à COVID-19. Após melhora do quadro respiratório, recebeu diagnóstico clínico de MG e naquele momento os anticorpos anti-AChR e MuSK foram negativos. Nove meses após a apresentação inicial, os anticorpos anti-AChR séricos tornaram-se positivos. **Conclusão:** Houve alguns relatos de possíveis gatilhos virais para miastenia, mas a controvérsia sobre esse assunto ainda permanece. Há também um relato anterior de miastenia anti-MuSK após infecção por SARS-CoV-2, mas não há relatos anteriores de soroconversão para anti-AChR.

Palavras-chave: Miastenia Gravis. COVID-19. SARS-CoV-2.

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INTRODUCTION

Myasthenia gravis (MG) is the most common disease of the neuromuscular junction. It is an autoimmune disorder with a diverse clinical presentation and cardinal characteristics of symptom fluctuation and fatigability. It has a bimodal distribution, with a peak incidence at 30 and 50 years of age,[1,2] and an estimated prevalence of 10 to 20 cases per 100,000 people.[3]

MG is classified according to the antibodies related to the disease, such as antibodies against the acetylcholine receptor (anti-AChR), muscle-specific tyrosine kinase (anti-MuSK) and lipoprotein-related protein 4 (anti-LRP4),[4] and may also be negative for the 3 antibodies investigated and referred to as seronegative MG.

As for the clinical presentation, MG can be divided into the ocular form and the generalized form. Up to 70% of patients with the pure ocular form will progress to the generalized form within 2 years of symptom onset.[5] The positivity of anti-AChR antibodies is 85% in generalized forms and 50% in pure ocular forms. Up to half of Anti-AChR negative patients may be anti-MuSK positive.[6]

Numerous neurological complications caused by SARS-CoV-2 infection have been documented since the start of the new coronavirus pandemic, involving the central nervous system and peripheral nervous system, including the neuromuscular junction. Other viral diseases, such as cytomegalovirus, have been reported as possible triggers for the onset of acetylcholine receptor (AChR) antibody positive myasthenia gravis (MG), although the underlying mechanisms are not yet fully understood.[7] There is also one report of anti-muscle-specific tyrosine kinase (MuSK) MG associated with COVID-19.[8] We report a previously described[9] patient with initial symptoms of MG occurring within months of COVID-19 diagnosis, who 9 months later presented anti-AChR antibodies.

METHODS

Data were reviewed using patient medical records. Outpatient follow-up was carried out at the Neurology service of the Walter Cantídio University Hospital, and the patient provided informed consent for publication. The study was approved by the local ethics committee under the number 4.881.736.

CASE REPORT

A 37-year-old female patient started with mild dysphonia, ptosis, diplopia and dyspnea. There were no prior illnesses or neurological conditions in the family. Three months later, her dyspnea suddenly got worse, and the next day she needed to be intubated. A study of arterial blood gases showed hypercapnic respiratory failure. Real time-PCR was positive for SARS-CoV-2 infection. Five days later, after waning of sedation, bilateral ptosis, facial weakness and ophthalmoparesis were perceived, and a clinical diagnosis of MG was suggested. Anti-AChR and MuSK antibodies were negative, but a marked decremental response on repetitive nerve stimulation (RNS) was present. Response to pyridostigmine was poor and she was submitted to PLEX (Plasm Exchange) with temporary improvement. She received Rituximab followed by oral azathioprine 150mg/day and prednisone 60mg/day and her disease stabilized. Nine months after initial presentation, serum anti-AChR antibodies became positive. Chest CT scans did not show thymic abnormalities.

DISCUSSION

In this patient, symptoms suggestive of myasthenia gravis began before the diagnosis of COVID-19, but anti-AChR antibodies were initially negative and became positive after 9 months. A seroconversion rate of 15.2% at 12 months has been reported for initially seronegative AChR autoimmune MG.[10] It is possible that SARS-CoV-2 infection and the appearance of anti-AChR MG were a coincidence, but given the predisposition of this virus to cause immune dysregulation we have to consider the possibility that SARS-CoV-2 precipitated or worsened a complex autoimmune response that resulted in seroconversion for anti-AChR myasthenia gravis.

CONCLUSION

Myasthenia Gravis may worsen with infections, and it is believed that infections may function as triggers for the onset of a neuromuscular junction disorder. The positivity of antibodies linked to the pathophysiology of the disease may occur at different times of clinical presentation, but there were no previous reports of seroconversion to anti-AChR MG after infection with SARS-CoV-2. This understanding may lead to repeating the search for autoantibodies during the follow-up of initially seronegative MG, especially after well-documented viral infections. We believe that more studies are needed to provide better evidence of the relationship between SARS-CoV-2 infection and anti-acetylcholine receptor antibody seroconversion.

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