Periodic weakness of the diaphragm as the sole manifestation of bulbar onset myasthenia

Josef Finsterer, PhD[1], Carla Alexandra Scorza[2], MD, Fulvio Alexandra Scorza, MD[2], Ana Claudia Fiorini[3], MD

[1]Krankenanstalt Rudolfstiftung, Vienna, Austria, [2]Disciplina de Neurociência. Escola Paulista de Medicina/Universidade Federal de São Paulo/. (EPM/UNIFESP). São Paulo, Brasil, [3]Programa de Estudos Pós-Graduado em Fonoaudiologia. Pontifícia Universidade Católica de São Paulo (PUC-SP). Departamento de Fonoaudiologia. Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP). São Paulo, Brasil

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Letter to the Editor

We read with interest the article by Tan et al. about a 25 years old female with recurrent broncho-pulmonary infections requiring intubation and mechanical ventilatory support each time since 3 years earlier.[1] The patient was finally diagnosed with bulbar onset myasthenia gravis and improved from treatment with pyridostigmine, steroids, and azathioprine.[1] We have the following comments and concerns.

Since myasthenic crises occurs along with mydriasis,[2] we should know if the patient also presented with dilated pupils during any of the episodes with respiratory insufficiency. Since the repetitive nerve stimulation was inconclusive, we would like to know if single-fibre needle electromyography (SF-EMG) was carried out, and if there was increased jitter with or without blockings in any of the bulbar muscles.

If myasthenia manifests exclusively in the respiratory muscles, it can be detected upon low-frequency repetitive nerve stimulation of the phrenic nerve.[3] We would like to know if this investigation showed an abnormal decremental response. We would also like to know if the patient ever underwent lung function testing during any episode of pneumonia and respiratory insufficiency during the three years prior to the diagnosis of myasthenia. It should be stated if low-frequency repetitive nerve stimulation during facial diplegia showed an abnormal decremental response upon facial nerve stimulation and if the eventually abnormal decremental response resolved with the application of pyridostigmine, steroids, and azathrioprin. Since immune-mediated myasthenia typically manifests with exercise intolerance, we would like to know if the patient was able to perform sport activities or any form of endurance training. Since patients with thymoma may react with an increased sensitivity to pancuronium,[4] it should be reported if intubation and ventilation required the administration of muscle relaxants, if so which muscle relaxants were used, and if weakness of respiratory muscles increased upon application of muscle relaxants. Furthermore, it would be interesting to know if ever an infectious agent was isolated during any of the recurrent aspiration pneumonias which required intubation each time. Missing in this report are the results of cerebral imaging. We would like to know if there was a lesion in the brainstem on cerebral magnetic resonance imaging (MRI). Since the patient was diagnosed with thymic hyperplasia, and this can be associated with myasthenia,[5] and since patients from ages 20 to 60 years benefit from thymectomy, we would like to know if the patient underwent thymectomy and benefitted from the intervention. It is worthwhile to know if the AChR antibody titer declined after initiation of immune-modulating therapy. Since bronchiectasias were attributed to recurrent microaspirations during the 3 years, we would like to know if they resolved after administration of the anti-myasthenia treatment. Since titers of AChR-antibodies may be false positive, we would like to know if the antibody titers truly declined upon application of the drug treatment.

Overall, this is an interesting report which can be improved by addressing the above issues before establishing the diagnosis and starting treatment. Since the patient had thymic hyperplasia, thymectomy should be considered.

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RESPONSE

We would like to thank Prof. Josef Finsterer et al. for their great interest in our recent case report (Tan TL, Tan HJ, Cheah CF, Kumaresh R, Azzahra NA. Silent microaspirations: The forerunner to the diagnosis of bulbar onset myasthenia gravis in a young woman. Med J Malaysia. 2020;75(3):295-297) and their comments. First and foremost, we would like to take this opportunity to update

Corresponding Author: Josef Finsterer
Email: fifigs1@yahoo.de

the progress of our patient. Twenty-two months have elapsed since the diagnosis of bulbar onset myasthenia gravis (MG). We are glad to inform readers that our patient has remained in remission until now and she is expecting her second baby at the time of writing. These observations lend credence to the efficacy of first line MG treatment as well as reaffirm the diagnosis of MG.

Lung function test was done after the patient's first encounter with the pulmonologist involved in the management of this case, during which time, the patient was free of any clinical evidence of active infection, and denied any weakness, nasal regurgitation or exertional dyspnoea. However, it was noted that she had dysphonia and reduced gag reflex, thus prompting a referral to a speech therapist and otorhinolaryngologist. Review of the high-resolution computed tomography (HRCT) thorax on the day of consultation raised the possibility of aspiration bronchiolitis/ bronchiolectasis, further substantiating the need for a speech therapist and otorhinolaryingology review. A lung function testing was performed on 4th of June 2018. Spirometry revealed a restrictive ventilatory defect (the rounded peak and sudden termination at the end of expiration was suggestive of an extraparenchymal origin). The body plethysmography demonstrated a reduction in total lung capacity with a mild increment in residual volume; given the spirometry findings, this is consistent with an extraparenchymal restriction. Her single-breath nitrogen washout (SBN2) test had mild ventilatory heterogeneity. Unfortunately, the patient was unable to perform the carbon monoxide diffusing capacity of the lung (DLCO) manoeuvre on that day and our Respiratory Muscle Strength apparatus was not functioning. Those 2 tests would have been crucial to demonstrate an extrapulmonary mechanism. However, the evidence provided by the spirometry and body plethysmography strongly pointed to an extraparenchymal aetiology.

With regards to the neurophysiological study, we concur with the commenters' opinions. Retrospective review of the clinical notes revealed that suxamethonium was used as the muscle relaxant during the past admission. Hypersensitivity response towards muscle relaxants and mydriasis were not recorded during her stay in the intensive care unit. To note, Streptococcus pyogenes, Streptococcus pneumonia and Pseudomonas aeruginosa were among the organisms cultured from the endotracheal aspiration samples.

We share a different view with their comment pertaining to repeating acetylcholine receptor antibody. Based on the clinical presentation of the patient and treatment response, it is rather unlikely that the initial acetylcholine receptor antibody could be false positive results. On a side note, we would consider anti-muscle specific kinase antibody instead if the acetylcholine receptor antibody was negative in the first place. Anti-muscle specific kinase antibodies are more commonly present among seronegative MG with bulbar manifestation.

Regrettably, certain tests that mentioned by the commenters were not performed on our patient. Firstly, the single-fibre EMG performed was only limited to the right biceps, and the bulbar muscles were not tested as our subject was unable to tolerate the pain induced during the procedure. Secondly, magnetic resonance imaging of the brain was not done in this case as there is no clinical suspicion of brainstem pathology. Thirdly, HRCT thorax was not repeated as clinically there was no diagnostic or therapeutic indication at this juncture. At the present time, control of the symptom takes precedence, and performing thymectomy will be discussed after the patient has delivered her baby. In accord with the commenters' view, we agree that thymectomy should be offered as it could contribute to a reduction of immunosuppressives needed as well as stabilising the MG disease in the long run.

Thai Lun Tan, MRCP
Department of Internal Medicine,
Hospital Seri Manjung, Perak,
Malaysia