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CASE REPORTS

Resolution of Severe Obstructive Sleep Apnea after Treatment of Anti-Muscle Kinase Receptor-Positive Myasthenia Gravis Despite 60-Pound Weight Gain

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Obstructive sleep apnea (OSA) in patients with myasthenia gravis (MG) may be caused by reduced pharyngeal dilator muscle activity. We report a patient with anti-muscle kinase receptor MG with severe OSA and hypoventilation that resolved upon successful treatment of MG despite a 60-lb weight gain.

Keywords: myasthenia gravis, obstructive sleep apnea, anti-musk antibody, hypoventilation

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Myasthenia gravis (MG) may contribute to development of obstructive sleep apnea (OSA) by inducing pharyngeal dilator muscle weakness, although not all studies have demonstrated this association.[1-3] MG is often caused by acetylcholine receptor antibodies (AchR-Abs) blocking neuromuscular transmission. However, approximately 40% of MG patients who do not have AchR-Abs have anti-muscle kinase receptor antibodies (anti-MuSKR-Ab). This likely alters clustering of acetylcholine receptors during neuromuscular junction formation.[4] MG has a variable clinical course that may be exacerbated by stress including infection, exertion or various drugs that may lead to "myasthenic crisis" with respiratory compromise.

REPORT OF CASE

A 45-year-old female with 6 months of headaches, weakness, dysarthria, dysphagia, and 60-pound weight loss (BMI 26 kg/m^2) was admitted for hypercapnic respiratory failure (ABG-supplemental O_2: pH 7.27 / PCO_2 60 mm Hg / PO_2 99 mm Hg / $HCO3^-$ 28 mmol/L). Neurological evaluation showed fatigable diplopia, ptosis, and bi-facial and genioglossus weakness. Neck flexor and extensor and proximal extremity muscles were spared. Formal swallowing evaluation confirmed dysphagia. However, AchR-Abs were negative. Electromyography, nerve conduction studies and repetitive nerve stimulation (no decremental response) were not consistent with MG. No definitive neurological diagnosis was made. The patient was discharged on nocturnal bilevel positive airway pressure for treatment of persistent hypercapnia (ABG after 2 weeks: pH 7.34 / PCO_2 62 mm Hg / PO_2 84 mm Hg / $HCO3^-$ 35 mmol/L). Pulmonary function assessment revealed a moderate restrictive ventilatory defect (FEV1 61%, FVC 63% predicted, FEV1/FVC% = 79%), reduced maximum inspiratory and expiratory pressures (-52, +36 cm H_2O). Split-night polysomnography (PSG) showed OSA with an apnea-hypopnea index (AHI) of 31/h, with T90% = 31%. Nocturnal noninvasive ventilation was optimized with average volume adjusted pressure support (AVAPS) to treat OSA and hypoventilation with a targeted tidal volume of 400 mL, EPAP 8 cm H_2O, IPAPmax 25, IPAPmin 12 cm H_2O.

Although hypercapnia improved (ABG: pH 7.38 / PCO_2 47 mm Hg / PO_2 77 / $HCO3^-$ 27 mm Hg), fatigue, dyspnea, and weakness persisted. Subsequent serology revealed anti-MuSKR-Abs prompting treatment with plasma exchange, maintenance mycophenolate mofetil and prednisone, which normalized her neurological exam and muscle weakness. After 3 months, despite a 60-lb weight increase (BMI 35 kg/m^2), repeat diagnostic PSG showed resolution of OSA and nocturnal hypoventilation (AHI = 1/h; T90% = 0) with normal serum $HCO3^-$ (25 mmol/L).

DISCUSSION

Both insufficient neural drive to upper airway dilator muscles and anatomic factors that compromise the upper airway contribute to the pathophysiology of OSA. In MG, muscular strength varies based on muscle exertion, fluctuating levels of autoantibodies that affect neuromuscular junction transmission, and other factors. The impact of MG may not be uniformly distributed, as greater effects are often manifested in specific muscle groups.[4] In our patient, the exacerbation and improvement of MG, manifested by development and resolution of fatigable diplopia, ptosis, bi-facial and genioglossus weakness, dysarthria, and dysphagia paralleled the course of OSA and hypercapnic respiratory failure. Despite gaining 60 pounds after successful MG treatment, OSA and hypercapnia resolved. Only one study reported improvement of OSA after treatment of MG, but with thymectomy.[1] Our patient represents the first report of OSA resolution after treatment of anti-MuSKR-Ab-positive MG.

Several studies have shown an increased prevalence of OSA in MG with AchR-Abs.[3] In one study of 100 AchR-Ab-positive MG patients, 36% had an AHI > 5.[2] In contrast, a study of 17

AchR-Ab-positive MG patients found no correlation between MG and OSA.[3] However, these studies did not report anti-MuSKR-Ab-positive MG.

Anti-MuSKR-Ab occurs in approximately 4% of patients with MG, compared with 90% of patients with AchR-Abs. Disease onset can be at any age, with female predominance. Weakness can be more severe than in AchR-Ab-positive MG. The diagnosis can be challenging since nerve conduction studies and electromyography are often normal. Further, anti-MuSKR-Ab MG is associated with distinct patterns of weakness compared to AchR-Ab-positive MG. One type presents with faciopharyngeal weakness. The other is associated with neck extensor, respiratory, and proximal muscle weakness.[4] Acetylcholinesterase inhibitors are less effective in this form of MG. Therapeutic response is better with plasma exchange and immunosuppressive therapy.

Patients with MG who present with sleep related complaints should be evaluated for OSA and nocturnal hypoventilation. Neurologists and sleep medicine professionals should be aware of the association between MG, OSA, and hypoventilation and consider testing for Anti-MuSKR-Ab if AchR-Abs are negative. Variations in disease state and antibody types of MG may influence the severity of sleep disordered breathing. Likewise, treatment of MG may result in improvement of MG, OSA, and hypoventilation.

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