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Management of immune checkpoint inhibitor–related acute hypoxic neuromuscular respiratory failure using high-flow nasal cannula

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ABSTRACT

Immune-related adverse events are increasingly associated with the use of immune checkpoint inhibitors for treatment of cancers. While neurological immune-related adverse events are rare, immune-related myasthenia gravis and immune-related myositis can lead to myasthenic crisis and acute respiratory failure. High-flow nasal cannula is an emerging alternative in critically ill patients for early treatment in neuromuscular acute hypoxic respiratory failure as well as for those who cannot endure noninvasive positive pressure ventilation with face mask. We describe use of high-flow nasal cannula in a patient with acute hypoxic respiratory failure and psychological distress due to the immune-related adverse event of myasthenic crisis.

KEYWORDS High-flow nasal cannula; immune checkpoint inhibitors; immune-related adverse events; myasthenic crisis; noninvasive positive pressure ventilation

Immune checkpoint inhibitors (ICIs) are becoming the new standard of therapy in oncology, and the frequency of immune-related adverse events (irAEs) is increasing as ICIs are utilized more often.[1,2] Neurological irAEs are uncommon, representing <3% of all irAEs.[1] Immune-related myasthenia gravis and immune-related myositis can lead to myasthenic crisis and acute respiratory failure (ARF).[1] Standard treatment for ARF starts with supplemental oxygen administration, frequent pulmonary care using cough assistive devices and suctioning of secretions, and noninvasive positive pressure ventilation (NIPPV), with endotracheal intubation and invasive mechanical ventilation as a last resort. There is emerging evidence that high-flow nasal cannula (HFNC) can be used in patients who are either unable to tolerate NIPPV or refuse endotracheal intubation.[3] We report a case of irAE myasthenic crisis and the use of HFNC in the management of hypoxic ARF in a patient with psychological distress.

CASE DESCRIPTION

A 68-year-old man with left ocular melanoma, who progressed to enucleation of the left eye and metastatic disease involving the liver and peritoneal carcinomatosis, received his first cycle of immunotherapy with the ICIs nivolumab and ipilimumab. One week later, he had progressive ascending myalgias and arthralgias, culminating in severe muscle weakness, dyspnea, ptosis, and extraocular muscle weakness. He was anxious and tearful about "dying," with hypophonic speech, a respiratory rate of 35 to 50 breaths/minute, accessory muscle use, and oxygen saturation of 70% to 89% with speaking or activity. Spirometry was notable for forced vital capacity 1.1 L and negative inspiratory force −20 cm H_2O. Arterial blood gas analysis on nasal cannula 4 L/min oxygen included a pH of 7.37; partial pressure of carbon dioxide, 30 mm Hg; partial pressure of oxygen, 87 mm Hg; and bicarbonate, 17.4 mmol/L. A chest radiograph showed low lung volumes with bibasilar atelectasis. Magnetic resonance imaging of the brain did not demonstrate findings to explain his weakness. Significant laboratory tests included creatinine kinase >5400 U/L, positive acetylcholine receptor antibody testing, elevated liver function tests, and elevated troponins. Based on his clinical presentation, laboratory results, and imaging, he was diagnosed with irAEs secondary to immunotherapy, specifically immune-related myasthenia gravis,

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immune-related myositis, acute immune-mediated hepatitis, myocarditis, and atrial fibrillation.

In the neurocritical care unit, the patient refused endotracheal intubation, fearing it would be a terminal intubation, and refused NIPPV with face mask due to claustrophobia. He was placed on HFNC with humidified oxygen at 50 L/min and fraction of inspired oxygen of 50% with immediate improvement in his work of breathing, phonation, and oxygenation. Myasthenic crisis treatment involved high-dose methylprednisolone, therapeutic plasma exchange, and pyridostigmine, with improvement of his respiratory mechanics, dysphagia, and extremity strength. Electromyography, a nerve conduction study, and muscle biopsy were discussed with the patient, but he refused further medical procedures until therapeutic plasma exchange was completed.

The day after completion of therapeutic plasma exchange, the patient had multiple panic attacks due to end-of-life despair; unfortunately, he was declined further treatment options for his cancer due to the severe neurotoxicity he developed to the ICIs. With discussions of further goals of care, comfort care became the primary focus. He died <2 weeks from admission to the hospital due to irAEs, only 1 month after administration of his first round of ICIs. Autopsy was declined by the family. Prior to transition to full comfort care, the patient and his spouse expressed their gratitude for his improved comfort with implementation of the HFNC as an alternative to a noninvasive respiratory support system in managing both his respiratory distress and his psychological state of mind.

DISCUSSION

This case illustrates the multifaceted concerns with irAE neuromuscular complications and psychological distress at the end of life in malignancy. Although neuromuscular irAEs are rare, they occur early during the therapy and are associated with mortality rates up to 26% due to recurrent cancer, comorbidities, and treatment complications.[2,4] Treatment of irAEs includes discontinuing the culpable agent, initiating immunomodulatory therapy, and supportive care.[2] The objective is to maintain a balance between effective treatment of the malignancy and the management of irAEs. While most patients with neurological irAEs can improve with appropriate treatment, the parameters of when it is safe to restart ICIs is not well defined, as some patients experienced relapse of neuromuscular complications upon rechallenge.[2]

The administration of frequent anxiolytics and analgesics for cancer pain applied in this patient's case would otherwise be atypical for non-irAE myasthenic crisis ARF given the medication-induced reduction in accessory muscle strength. HFNC has been shown to alleviate the suffering from shortness of breath at the end of life in patients with advanced cancer.[5] It can generate flows that match or exceed a patient's demand, thereby minimizing the nasopharyngeal resistance and decreasing the work of breathing.[3] It can also maintain constant delivery of fraction of inspired oxygen, generate positive end-expiratory pressure, decrease physiologic dead space, and improve mucociliary clearance.[5] HFNC has previously emerged as an effective method for early treatment of hypoxic ARF from acute heart failure, obstructive sleep apnea, and other various underlying reasons.[6] When there is an additional focus on comfort, early use of HFNC should be considered in patients with irAE neuromuscular hypoxic ARF in the absence of hypercapnia.

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