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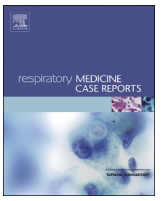

Case Report

A case of acute hypercapnic respiratory failure secondary to late onset nemaline rod myopathy: A multi-disciplinary approach

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ABSTRACT

Background: Nemaline rod myopathy (NRM) is a rare muscle disorder defined by muscle weakness, respiratory insufficiency, and dysphagia. Respiratory muscle involvement can lead to acute hypercapnic respiratory failure, posing significant challenges in management.
Case presentation: Our patient is a 73-year-old male with a history of polymyositis, who presented with acute hypercapnic respiratory failure secondary to a suspected polymyositis flare. Despite initial management, the patient experienced complications, including dysphagia, thrombocytopenia, and altered mental status. Neurological consultations revealed conflicting opinions regarding the primary diagnosis, suggesting inclusion body myositis. The patient's condition continued to deteriorate, prompting discussions about prognosis and palliative care options. This case highlights the challenges in managing respiratory failure in patients with late-onset nemaline myopathy and the importance of multidisciplinary care in addressing complex medical needs.
Conclusion: This case emphasises the complexity of managing respiratory failure in patients with late-onset nemaline myopathy and the significance of adopting a multidisciplinary approach. Timely interventions, including respiratory support, dysphagia management, and palliative care discussions, are vital in optimizing patient care and quality of life. Further research is warranted to elucidate optimal management strategies and improve outcomes in this patient population.

1. Introduction

Nemaline rod myopathy (NRM) is a rare muscle disorder defined by the presence of eosinophilic rod-shaped inclusions or nemaline bodies in muscle fibers. It is classified into various subtypes based on age of disease onset and severity of muscle weakness.

This disorder is mostly congenital resulting from genetic mutations and they present with muscle weakness and hypotonia. It may follow an autosomal dominant or recessive inheritance pattern [1]. In adults, nemaline myopathy can be either hereditary, symptomatic in adulthood or present in adulthood without a hereditary pattern. The case under discussion is of an adult-onset form also known as late onset nemaline rod myopathy.

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2. Case presentation

Our patient is a 73-year-old male with a past medical history of polymyositis, hypertension, constipation, and insomnia, who presented to the emergency department with dyspnea. He had been experiencing weakness and changes in mental status since his last intravenous immunoglobulin (IVIg) treatment. Initial assessment revealed hypothermia, bradycardia, and hypoxia, prompting admission for acute hypercapnic respiratory failure secondary to a possible polymyositis flare.

Upon admission, he received supportive care including fluid resuscitation, oxygen therapy, and antibiotic coverage. Patient was started on corticosteroids, bronchodilators, and bilevel positive airway pressure (BiPAP) for respiratory support. Investigations were undertaken to identify the cause of his respiratory distress, including blood cultures, urine analysis, and imaging studies, which were largely unremarkable.

His clinical condition improved temporarily, but not soon after, he developed altered mental status owing to hypercapnia. An arterial blood gas analysis revealed respiratory acidosis with a compensatory increase in bicarbonate levels. A comprehensive plan was devised for continued management, including transitioning to home non-invasive ventilation (NIV). Shortly thereafter, he developed shingles and further complications arose, such as dysphagia confirmed on modified barium swallow study, thrombocytopenia, and debility requiring full assistance for activities of daily living.

Consultations with neurology and rheumatology raised questions about the primary diagnosis of polymyositis, with a strong clinical suspicion for inclusion body myositis. In addition, the pattern of weakness and atrophy was more suggestive of inclusion body myositis than polymyositis. Further discussions with the patient's previous neurologist shed light on his extensive medical history, muscle biopsy report and IVIg therapy.

Despite initial stabilization, his respiratory status deteriorated, necessitating transfer to the intensive care unit for closer monitoring and adjustment of his respiratory support. He tolerated BiPAP well during his ICU stay.

Throughout his hospitalization, efforts were made to address his thrombocytopenia, constipation, and dysphagia. Oncology consultation was sought for further evaluation of his thrombocytopenia, while palliative care discussions were initiated given the complexity of his medical condition and declining respiratory status. Possible intubation, tracheostomy, and code status were elaborately discussed with the patient and family, following which the patient expressed a preference for a DNR/DNI order.

Despite challenges with BiPAP adherence, patient showed improvement with consistent use of the device, leading to discussions on discharge planning. Physical therapy recommended a transfer to a subacute rehabilitation facility, but the patient wished to be discharged home. Arrangements were made for home health services, including physical therapy, and visiting nurse support.

Prior to discharge, the patient's medication regimen was adjusted. Dietary modifications were recommended to address his dysphagia, and precautions were advised to prevent aspiration. Also, a tyrosine rich diet was recommended, which has been proven beneficial in patients with nemaline myopathy [2]. Patient's discharge plan emphasized the importance of continued respiratory support with BiPAP, along with close follow-up with his primary care provider and neurologist. Home equipment, including cough assistance and suction devices, were provided to aid in airway clearance and ensure a safe transition to home care.

3. Discussion

Nemaline myopathy is named after the characteristic fine, thread-like rod bodies observed on muscle biopsy. The prefix “nema-” is derived from Greek and means “thread-like.” Nemaline myopathy is most commonly caused by mutations in the nebulin (NEB) gene [3] and skeletal muscle alpha-actin (ACTA1) gene [4].

Nemaline myopathy is a rare genetic muscle disorder with a wide range of severity and variable presentation. The spectrum of clinical phenotypes of nemaline myopathy is wide, even in individuals with mutations in the same gene.

Congenital myopathies typically manifest with slowly progressive or stable clinical courses. Early signs include hypotonia (“floppy infant syndrome”), muscle weakness, hypotrophia, and delayed motor milestones. Some patients exhibit a myopathic face, ptosis and pronounced facial weakness, and may even need a feeding tube, especially in neonates. Facial and skeletal deformities are common [5].

Sporadic late-onset nemaline myopathy (SLONM) is a rare, subacute adult-onset non-hereditary myopathy. The earliest reported case dates back to 1966 [6]. SLONM most often presents with bilateral proximal muscle weakness and atrophy. Of note, the creatine kinase level is usually normal or mildly elevated [7]. The severity of the disease determines the clinical course. Respiratory involvement is associated with an unfavourable prognosis [8]. SLONM may be seen in conjunction with HIV (SLONM-HIV); J Maytal et al. reported a case of progressive nemaline myopathy in a patient coinfected with HIV-1 and HTLV-2 [9].

The diagnosis of nemaline myopathies involves a multidisciplinary approach with careful clinical, pathological and genetic correlations. Recent advances in genetic testing for the diagnosis of nemaline myopathy employs a next generation sequencing targeted gene panel [10]. Although invasive, histopathological and ultrastructural studies of muscle biopsy specimens may still prove valuable. Also, muscle magnetic resonance imaging (MRI) has become a significant tool for diagnosing and revealing specific patterns of muscle involvement [11].

Rod bodies, the pathologic hallmark of nemaline rod myopathy are best visualized on modified Gomori trichrome staining [12] as dark red/purple structures against a blue-green myofibrillar background. It is interesting to note that, a study conducted by E Malfatti et al. [13] demonstrated that the amount of nemaline bodies appears to be inversely correlated with clinical severity. These peculiar inclusions are derived from Z-discs [14] and have a similar composition [15].

Supportive care, including physical therapy, respiratory physiotherapy and nutritional support are essential in managing nemaline myopathy. Although no specific drug targets nemaline myopathy, intravenous immunoglobulin (IVIg) therapy and immunosuppressive agents may be considered for their anti-inflammatory effects in select cases. However, evidence supporting their efficacy in

the management of nemaline myopathy is limited. The approach to therapy is tailored to the patient's symptoms. Management of nemaline myopathy necessitates a multidisciplinary approach.

Cases of late-onset nemaline myopathy presenting with respiratory failure, which align closely with the clinical patterns and course of our patient have previously been reported [16,17]. Isolated muscular weakness without signs of upper or lower motor neuron involvement, raises clinical suspicion for myopathy. Further assessment of relevant risk factors and extramuscular symptoms is mandated to determine the type of myopathy [18].

Respiratory failure in nemaline myopathy can occur due to weakness and dysfunction of the respiratory muscles, such as the diaphragm and intercostal muscles. Muscle weakness can impair ventilation, causing hypercapnia and consequent hypoxemia [19].

As disease advances, individuals may require ventilatory support, such as non-invasive ventilation (NIV) or mechanical ventilation to assist with breathing. Regular monitoring of oxygen levels and respiratory function is crucial in identifying signs of respiratory compromise early. Management involves adopting a multidisciplinary approach, including respiratory therapy, physical therapy, and in severe cases, long-term ventilatory support may be required.

The authors declare no conflict of interest.

CRediT authorship contribution statement

Chandana Madala: Writing – original draft. **Srilakshmi Giridharan:** Writing – review & editing. **Dr Anthony Vacchio:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

None.

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