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RESEARCH ARTICLE

COVID-19 AND MYASTHENIA: A CASE REPORT AND REVIEW OF MANAGEMENT STRATEGIES

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Abstract

Background: The COVID-19 pandemic poses unique challenges in managing patients with pre-existing autoimmune disorders, such as myasthenia gravis. This article presents a case report of a myasthenic patient who contracted COVID-19, providing insights into the clinical presentation, diagnostic workup, treatment approaches, and disease course.

Methods: A comprehensive review of the literature was conducted to examine the current understanding of the interaction between myasthenia gravis and COVID-19. The focus was on the challenges faced in managing these patients and the optimal therapeutic strategies.

Results: The case report describes a 42-year-old male with confirmed myasthenia gravis who presented with sudden-onset respiratory distress and flu-like symptoms. The patient's clinical course, including the utilization of immunomodulatory therapies and respiratory support, is discussed. The review of the literature highlights the increased risk of severe infection in myasthenic patients, the potential exacerbation of myasthenic symptoms, and the impact of immunosuppressive treatments on the course of COVID-19.

Conclusion: The management of myasthenia gravis patients with COVID-19 requires a tailored approach that considers the delicate balance between controlling the viral infection and preserving neuromuscular function. Early recognition, prompt diagnosis, and the integration of multidisciplinary care are crucial for optimizing outcomes in this patient population. Further research is needed to enhance our understanding of the underlying mechanisms and refine management strategies for these complex cases.

Introduction:-

The ongoing COVID-19 pandemic has presented unique challenges in the management of patients with pre-existing medical conditions, particularly those with autoimmune disorders such as myasthenia gravis. Myasthenia gravis is a chronic neuromuscular disorder characterized by fluctuating muscle weakness and fatigue. Patients with myasthenia

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gravis may be at an increased risk of severe COVID-19 infection and have a higher likelihood of developing complications associated with the disease.

In this article, we present a case report of a 42-year-old male patient with confirmed myasthenia gravis who contracted COVID-19. The patient exhibited sudden-onset respiratory distress, accompanied by flu-like symptoms and a significant decline in muscle strength. We describe the clinical presentation, diagnostic workup, treatment strategies, and the subsequent course of the disease in this particular case.

Furthermore, we discuss the current understanding of the interaction between myasthenia gravis and COVID-19, including the potential mechanisms underlying the exacerbation of myasthenic symptoms in the context of viral infection. We explore the available literature on the management of myasthenic patients with COVID-19, focusing on the challenges posed by the disease and the optimal therapeutic approaches. Additionally, we address the impact of immunosuppressive therapies commonly used in the management of myasthenia gravis on the course and outcomes of COVID-19 infection.

By presenting this case report and reviewing the existing literature, we aim to contribute to the growing body of knowledge regarding the clinical characteristics, management strategies, and outcomes of COVID-19 in patients with myasthenia gravis. This information will aid healthcare professionals in making informed decisions and optimizing the care of these vulnerable individuals during the pandemic.

Casepresentation

A 42-year-old male patient with confirmed myasthenia, confirmed on EMG with negative antibodies, was receiving oral corticosteroid therapy (prednisolone 20mg/day). He had no other significant medical history. The patient was admitted to the intensive care unit due to acute respiratory distress that had been progressing for 4 days, accompanied by unspecified fever. The admission interview revealed flu-like symptoms including myalgia, asthenia, generalized fatigue worsening in the evening, and after 12 hours, the patient experienced tachypnea and a sensation of suffocation, prompting him to seek medical attention 2 days later.

Upon admission, the patient was conscious and oriented, with a Glasgow Coma Scale score of 15/15 and no agitation. He presented with generalized muscle weakness rated at 2/5 in all four limbs, along with diplopia and ptosis. He exhibited tachypnea at 32 cycles per minute, intercostal retractions, thoracoabdominal paradox, perioral cyanosis, and an oxygen saturation (SpO2) of 41% in room air, which improved to 88% with a high-flow oxygen mask at 15L/min. The patient had a heart rate of 143 beats per minute and a blood pressure of 165/90 mmHg.

The patient was placed in a semi-upright position for stabilization and received non-invasive ventilation with spontaneous mode plus inspiratory assistance (PEP: 7, AI: 8, FiO2: 100%) using a helmet-type interface. The initial arterial blood gas analysis revealed severe respiratory acidosis secondary to acute respiratory distress syndrome, with a PaO2/FiO2 ratio of 49, pH of 7.10, PaCO2 of 67, and HCO3- of 30.

Initial laboratory findings showed significant inflammatory markers, including leukocytosis with a predominance of neutrophils (16,220/mm3 with neutrophils at 14,580/mm3) and lymphopenia (720/mm3). The patient's CRP level was 39.9 mg/L, D-dimer level was 4062 µg/mL, ferritin level was 938 mg/L, and fibrinogen level was 5.19 g/L. Additionally, the patient had acute renal insufficiency. A prostigmine test was performed and yielded positive results, leading to regression of diplopia and ptosis.

A thoracic CT scan was performed, revealing a ground-glass appearance in both lung fields consistent with a viral COVID-19 infection, estimated to involve 50% of the lungs. The diagnosis was confirmed by a positive COVID-19 PCR test.

The progression of the case was marked by worsening respiratory distress 3 hours after admission, leading to the decision to intubate and sedate the patient. The patient was placed on volume assist-control (VAC) ventilation mode with the following parameters: tidal volume (Vt) of 5ml/kg, respiratory rate (FR) of 24, FiO2 of 100%, positive end-expiratory pressure (PEP) of 16, and an inspiratory-to-expiratory ratio (I/E) of 1/1.

The patient received dual antibiotic therapy consisting of ceftriaxone 2g/day and levofloxacin 500mg/day. Additionally, he underwent a course of immunoglobulin therapy with a total dose of 2g/kg administered over 4 days,

along with corticosteroid therapy using methylprednisolone 120mg/day for 5 days. Subsequently, he was placed on long-term treatment for myasthenia with ambenonium chloride 20mg every 8 hours and corticosteroid therapy with prednisolone 60mg/day.

The patient's condition gradually improved, and sedation was discontinued on Day 6 after stabilization. However, in the absence of signs of awakening, an MRI was performed, revealing cortical signal abnormalities and supratentorial white matter involvement suggestive of hypoxic or viral encephalitis (Figure 1). Viral genome testing, including COVID-19 PCR and antibody analysis in the cerebrospinal fluid, yielded negative results, confirming the hypoxic origin of the encephalitic involvement.

The patient underwent percutaneous tracheostomy for weaning purposes and was gradually weaned off mechanical ventilation over a period of 30 days. He was declared ready for discharge on Day 46 of hospitalization while continuing his long-term treatment regimen.

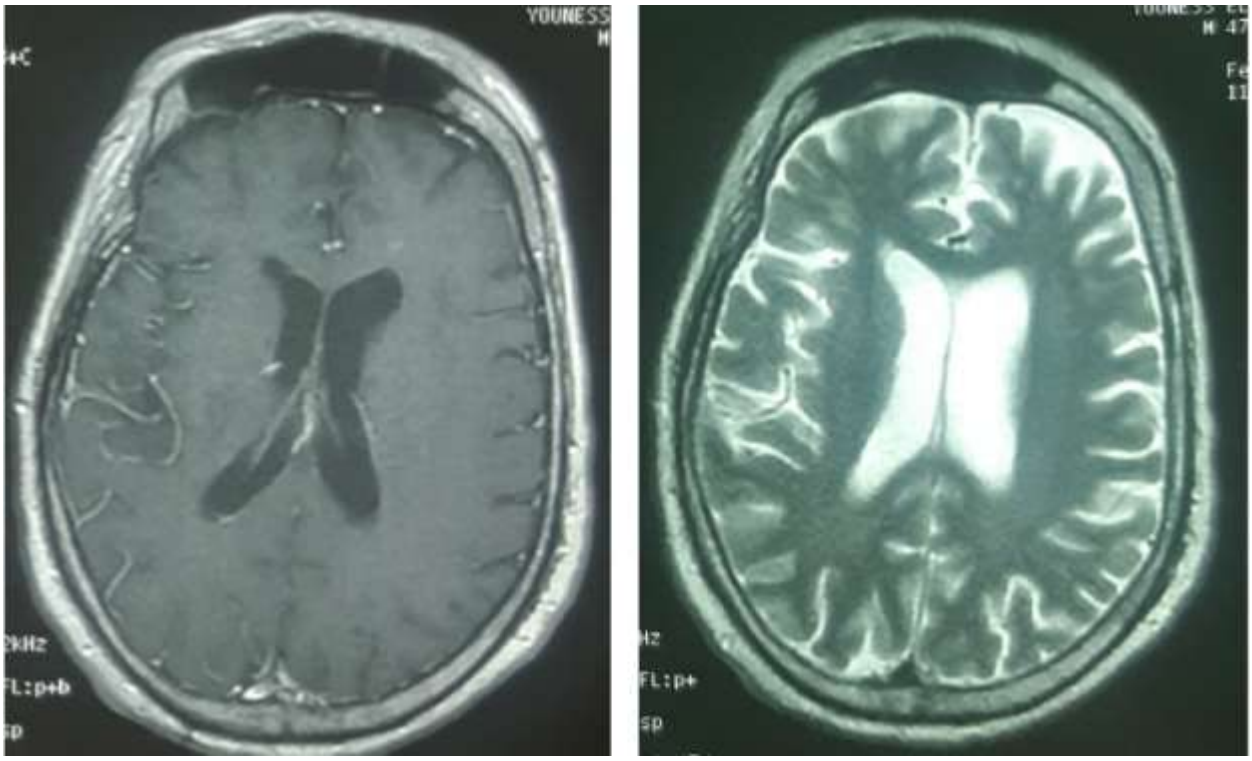

Figure 1:- Cerebral MRI, revealing cortical signal abnormalities and supratentorial white matter involvement suggestive of hypoxic or viral encephalitis.

Discussion:-

Several neurological complications have been directly associated with COVID-19 infection, such as seizures, Guillain-Barré syndrome, and ischemic stroke. Decompensation of myasthenia can be secondary to COVID-19 infection, and it can also be the cause of severe respiratory distress secondary to COVID-19.[1]

According to current knowledge, patients with pre-existing myasthenia are at a higher risk of developing severe forms of COVID-19 infection, with a significantly increased rate of intensive care unit (ICU) hospitalization and higher morbidity and mortality.[2] They are also more prone to developing neurological complications associated with COVID-19.

Multiple studies have reported ICU hospitalization rates ranging from 14% to 32.9%, with in-hospital mortality rates of 21% to 30%.[3,4] Initially, this higher rate of hospitalization and mortality was attributed to the immunosuppressive treatment used for myasthenia, as several other autoimmune diseases have a higher mortality rate compared to the general population in cases of severe COVID-19 infection.[5] This increased risk is explained

by the vulnerability to opportunistic bacterial and fungal infections, which can be life-threatening. Consequently, recommendations were established for the management of immunosuppressive treatments in myasthenic patients with COVID-19.[6] However, recent studies have highlighted the reality that immunosuppressive treatment may be protective by reducing the immune response to the infection, thereby limiting the inflammatory cytokine storm responsible for sepsis-like syndrome, clinical deterioration, and organ failure.[7,8] For example, a Brazilian serie of 15 myasthenic patients hospitalized with severe COVID-19 infection revealed a protective effect of intravenous immunoglobulin and corticosteroid therapy.[9]

One of the main challenges in managing these patients is the therapeutic management of treatments commonly used in protocols for severe COVID-19 infection or acute respiratory distress syndrome.

In terms of artificial ventilation, it is currently clear that early use of non-invasive ventilation, whether in CPAP or BIPAP mode, helps to limit the percentage of invasive ventilation and reduces the rates of intubation, sedation, and use of neuromuscular blockers.[10,11] Factors indicating respiratory insufficiency that necessitates the use of artificial ventilation include vital capacity less than 20 mL/kg, negative inspiratory force less than -20 cmH2O, or forced vital capacity less than 15 mL/kg.[10,11]Non-invasive ventilation should always be preferred before intubation, while following the usual safety measures due to the risk of virus transmission. It should be noted that COVID-positive myasthenic patients have a higher risk of requiring non-invasive ventilation or intubation (42.4%) for respiratory or neurological distress compared to the general COVID-positive population (2.3% and 33.1% according to studies).[11,12]

Regarding the use of azithromycin or hydroxychloroquine, these two medications have been clearly associated with myasthenia exacerbation,[9,13,14] so their use should be debated on a case-by-case basis, as current literature data do not provide clear recommendations. Furthermore, several studies have shown that continuous neuromuscular blockade in myasthenic patients is associated with increased mortality. Therefore, it is recommended to spare neuromuscular blockers whenever possible, and their use should be minimal and limited to the management of respiratory distress syndrome refractory to other therapeutic measures, using minimal effective doses.

For specific treatment, a literature review has highlighted that patients treated with intravenous immunoglobulins or plasmapheresis in addition to corticosteroids have significantly lower mortality and morbidity rates compared to patients treated with corticosteroids alone. Moreover, these combinations have been shown to reduce symptoms of myasthenic decompensation.[15,16]

Regarding routine treatment, the International MG/COVID-19 Working Group recommends continuing the use of the usual treatment, such as eculizumab (an immunosuppressant targeting the C5 fraction of complement) and pyridostigmine.[6,17,18]The only valid reason for temporarily discontinuing pyridostigmine appears to be excessive secretion in cases of intubation.[11]

Myasthenic patients should receive the COVID-19 vaccine according to local recommendations due to the significant risk of developing severe COVID-19.[19] However, the patients' immune status and immunosuppressive treatments should always be taken into consideration to maximize the benefits.[6,20] The use of inactivated vaccines is more recommended after reports of moderate myasthenia exacerbation in elderly patients following vaccination with a live attenuated vaccine.[19]

Conclusion:-

The case report presented here highlights the challenges faced in managing patients with myasthenia gravis who contract COVID-19. It underscores the increased risk of severe infection and the potential for exacerbation of myasthenic symptoms in these individuals. The management of such cases requires a comprehensive approach that considers the delicate balance between controlling the viral infection and minimizing the impact on neuromuscular function.

Our review of the literature emphasizes the importance of early recognition, prompt diagnosis, and tailored treatment strategies for patients with myasthenia gravis and COVID-19. The use of immunomodulatory therapies, such as immunoglobulins, in combination with corticosteroids, has shown promising outcomes in terms of reducing disease severity and improving myasthenic symptoms. Additionally, the judicious use of respiratory support,

including non-invasive ventilation techniques, can help mitigate respiratory distress and avoid unnecessary intubation.

Further research and larger studies are needed to elucidate the underlying mechanisms of the interaction between myasthenia gravis and COVID-19 and to optimize management strategies. The integration of multidisciplinary care, involving neurologists, intensivists, and infectious disease specialists, is crucial for achieving favorable outcomes in this vulnerable patient population.

Abbreviations:
COVID-19:Coronavirus Disease 2019
PEP: Positive expiratory pressure
AI: Pressure support
CT:Computed tomography
PCR: Polymerase Chain Reaction
MRI: Magnetic Resonance Imaging
ICU: Intensive Care Unit
CPAP: Continuous Positive Airway Pressure
BIPAP: Bilevel Positive Airway Pressure

Declaration section

- **Declaration of conflicting interests**

The authors declaredno conflictsofinterestwith respect to the research, authorship, and/or publication of this article.

- **Ethics Approval and consent to participate**

Not applicable.

- **Consent for Publication**

Written informed consent was obtained from the patientfor publication of the case report and any accompanying images.

- **Availability of supporting data**

All clinical finding and radiological results included in this case report can be found in the archived medical file of the patient.

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Authors' contributions
All authors have contributed to this work since conception, reading and endorsing the final version of the manuscript.

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