Jurnal Ners Volume 8 Nomor 2 Tahun 2024 Halaman 1151 - 1155
**JURNAL NERS**
Research & Learning in Nursing Science
http://journal.universitaspahlawan.ac.id/index.php/ners

# MANAGING REFRACTORY MYASTHENIA GRAVIS IN-DEPTH MULTIDISCIPLINARY EXPLORATION: CASE REPORT

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**Abstract**

Our case involves a 38-year-old female patient with refractory Myasthenia Gravis (MG), highlighting the intricate and evolving nature of the disease. She exhibits predominant cranial and upper respiratory muscle involvement, characteristic of ocular MG, with diurnal symptom variation. This case underscores the necessity for individualized therapeutic strategies to achieve disease stability and improve the patient's quality of life. It also stresses the urgent need for ongoing research and advancements in MG management, emphasizing tailored care and a multidisciplinary approach to effectively address refractory cases. Her clinical journey exemplifies the complexities and opportunities in managing refractory MG within contemporary medical practice. Through personalized treatment plans and collaborative efforts among healthcare providers, we can navigate the challenges of this condition. The case further illustrates the importance of patient-centered care and the continuous evolution of therapeutic interventions to meet the unique needs of each patient with refractory MG. By focusing on these elements, we can enhance outcomes and quality of life for those affected by this challenging condition.

**Keywords:** Myasthenia Gravis, Refractory, individualized therapy, multidisciplinary approach



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## INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder characterized by the production of antibodies that target proteins found on the postsynaptic membrane of the motor endplate. These antibodies disrupt the normal functioning of the acetylcholine receptor, leading to impaired neuromuscular transmission and resulting in skeletal muscle weakness. While MG is considered a rare condition, with a prevalence of fewer than 2 cases per 10,000 individuals in Europe, recent years have witnessed an increasing number of diagnoses, particularly in individuals aged over 50.(Dresser et al., 2021; Salsabila et al., 2023)

The term "gravis" is derived from the historical observation that MG often had a severe impact on morbidity and mortality rates, significantly affecting individuals' daily activities and quality of life. Nowadays, advancements in treatment options, including corticosteroids, conventional immunosuppressive drugs (such as azathioprine, mycophenolate mofetil, ciclosporin, tacrolimus, etc.), selective thymectomy in certain cases, and interventions like intravenous immunoglobulins (IVIg) or plasma exchange (PLEX) during clinical deterioration, have considerably improved outcomes. As a result, the majority of MG patients can maintain minimal or no symptoms with or without pharmacological interventions.(Rousseff, 2021; Sheikh et al., 2021)

Nonetheless, there exists a subset of patients who do not respond adequately to standard therapies, experiencing a condition known as refractory MG. These individuals continue to exhibit symptoms, frequent exacerbations, and adverse reactions to corticosteroid and immunosuppressive treatments. The exact prevalence of refractory MG remains uncertain, but it is estimated to affect approximately 10% to 20% of MG cases. Typically, these patients experience higher rates of myasthenic crises, hospital admissions, and emergency care utilization compared to those with non-refractory MG, significantly impacting their quality of life. Despite the importance of this subgroup of MG patients, research addressing their specific characteristics and needs has been limited. The principal aim of this case report is to offer a thorough and detailed clinical description of a patient diagnosed with refractory myasthenia gravis (MG). This report contributes to medical literature by providing a specific and in-depth analysis of the clinical characteristics and experiences of an individual with refractory MG, with a focus on their unique case within the context of the broader disease population.(Farrugia & Goodfellow, 2020; Gilhus et al., 2019)

## CASE REPORT

A 38-year-old female patient presented at the neurology outpatient clinic of RSUD RAA Soewondo Pati with a constellation of complaints that had been troubling her for the past year. Chief among her concerns was the sensation of pronounced heaviness in her left eyelid, coupled with the disconcerting occurrence of involuntary eyelid closure. These ocular symptoms had persisted for an entire year, markedly affecting her quality of life. In addition to these visual disturbances, the patient articulated a range of other distressing issues. She described her visual world as becoming strangely bifurcated, where objects or shadows would inexplicably appear as double images. This diplopia added a layer of complexity to her daily activities. Furthermore, the patient voiced significant difficulties in swallowing when partaking in meals, a symptom that had become increasingly bothersome. Her voice had also undergone an unwelcome transformation, manifesting as hoarseness and diminished vocal strength. This, in turn, had an impact on her ability to communicate effectively. Alongside these impairments in ocular, swallowing, and vocal functions, the patient reported a curious sense of stiffness in her back and hands, accompanied by a pervasive and frustrating tendency to rapidly tire during even the most modest physical exertions. These symptoms seemed to follow a diurnal pattern, with noticeable amelioration in the morning but a disconcerting exacerbation as the day wore on. Importantly, her symptoms exhibited a propensity to recede after periods of rest.

The origin of these distressing complaints could be traced back to February 2023, when the patient sought medical evaluation at the aforementioned outpatient clinic. Following a comprehensive assessment, she received a diagnosis of Myasthenia Gravis (MG), an autoimmune neuromuscular disorder characterized by muscle weakness and fatigue due to the body's production of antibodies that interfere with neuromuscular transmission. Consequently, the patient was admitted to the Tulip ward for a six-day hospitalization, during which a nasogastric tube (NGT) was inserted to aid in nutritional

support. Despite the initial hospitalization and treatment, the patient's condition took a concerning turn, leading to her readmission in October. During this subsequent hospitalization, she experienced a recurrence of her symptoms, raising questions about the effectiveness of her previous treatment regimen. It is noteworthy that the patient denied any accompanying limb weakness, shortness of breath, nausea, vomiting, or any appreciable weight loss over the past year, indicating that her symptoms were predominantly localized to the cranial and upper respiratory muscles.

Upon physical examination, the patient presented as moderately unwell, although her level of consciousness was fully intact, as reflected by a Glasgow Coma Scale (GCS) score of 15. Her vital signs were within normal ranges, with a blood pressure of 120/90 mmHg, a heart rate of 80 beats per minute, a respiratory rate of 20 breaths per minute, and a temperature of 36.7°C. No discernible abnormalities were noted on other aspects of the physical examination. However, the neurological examination yielded a spectrum of intriguing findings. The most prominent of these was unilateral ptosis, characterized by the drooping of the left eyelid, along with diplopia (double vision). The diplopia was associated with paresis (weakness) involving cranial nerves III (oculomotor), IV (trochlear), and VI (abducens). In addition to these ocular manifestations, the patient exhibited unilateral paresis of cranial nerve VII (facial nerve), resulting in distinct facial muscle weakness. Furthermore, her ability to swallow was compromised (dysphagia), and her vocal function was significantly impaired (dysphonia). Notably, at rest, her uvula exhibited lateralization to the right, a finding indicative of neurological involvement. Confirmatory testing revealed positive results for voice cord assessment and Wartenberg's test, further substantiating the presence of neuromuscular dysfunction in the cranial and upper respiratory muscles. The patient's presentation, characterized by a complex array of neurological symptoms and a history of inadequate response to initial treatment, underscores the challenging nature of her condition. This case serves as a valuable clinical illustration of refractory Myasthenia Gravis and highlights the need for a comprehensive and individualized management approach tailored to the unique characteristics of this patient's disease course.

## DISCUSSION

The intricate clinical presentation of this 38-year-old female patient with refractory Myasthenia Gravis (MG) calls for an in-depth medical discussion to elucidate the complexities and considerations involved in managing this autoimmune neuromuscular disorder. Myasthenia Gravis (MG) is characterized by the presence of autoantibodies that target acetylcholine receptors (AChR) at the neuromuscular junction, leading to impaired neuromuscular transmission and resulting in muscle weakness and fatigability. While MG can manifest in various ways, this patient's primarily cranial and upper respiratory muscle involvement aligns with the classical presentation of ocular MG.(Lazaridis & Tzartos, 2020b; Wang et al., 2018)

The clinical hallmarks of ocular MG, including left eyelid heaviness, unilateral ptosis, and diplopia, are evident in this case. These symptoms are attributed to the dysfunction of cranial nerves III (oculomotor), IV (trochlear), and VI (abducens), responsible for coordinated eye movements. Diplopia, in particular, has a substantial impact on the patient's daily activities requiring precise visual coordination. Diurnal symptom variation, characterized by symptom improvement in the morning and exacerbation in the afternoon, is a distinctive feature of MG. This phenomenon can be attributed to the transient nature of antibody binding to AChR, with receptor availability improving after periods of rest.(Jordan & Freimer, 2018; Menon et al., 2020) Moreover, the patient's reports of dysphagia and dysphonia highlight the involvement of the bulbar muscles, responsible for throat and voice box functions. These symptoms pose significant risks, including aspiration and aspiration pneumonia, necessitating careful assessment and management of her swallowing function. The rightward lateralization of the uvula at rest is indicative of weakness in the muscles innervated by cranial nerve X (vagus), which plays a pivotal role in swallowing and speech production. Positive results on voice cord assessment and Wartenberg's test further corroborate the presence of neurological dysfunction.(Alvin Oliver Payus, Justin Leow Wen Hsiang, Leong Jia Qian, Azliza Ibrahim, 2021; M amod, F chappel, L Ebbeling, L Fikizolo, n.d.)

Managing refractory MG, as observed in this patient, presents a formidable therapeutic challenge. Despite initial treatment and a prior hospitalization, her symptoms have recurred,

underscoring the complexity and unpredictability of the disease. In cases of refractory MG, a thorough reassessment of the treatment regimen is crucial. Immunomodulatory therapies, including corticosteroids, azathioprine, mycophenolate mofetil, and emerging agents like eculizumab, may be considered to suppress the autoimmune response responsible for neuromuscular dysfunction. The selection of the most appropriate immunomodulatory agent should be guided by the patient's clinical profile, comorbidities, and potential side effects, necessitating a personalized approach.(Mckenzye Dehart, Shital Patel, 2023; Tomasz Sobierajski, Anetta Lasek Bal, Marek Krzystanek, 2023; Yangtao Ling, Qianjin Kuang, Hongjin Li, Bo Liang, Jiaxin Lu, Qilong Jiang, n.d.) In the context of exacerbations and respiratory muscle involvement, continuous monitoring is essential. Swift interventions, such as intravenous immunoglobulins (IVIg) or plasma exchange (PLEX), may be necessary during myasthenic crises to stabilize the patient's condition and prevent life-threatening respiratory complications. This case underscores the critical importance of a multidisciplinary approach to MG management. Collaboration among neurologists, ophthalmologists, speech therapists, and other specialists is essential to optimize the patient's care. Regular clinical follow-ups, supported by objective measures of disease activity, are pivotal to gauge treatment response and disease stability. (Alzhraa Salah Abbas, Nicole Hardy, Sherief Ghozy, Mah, oud Dibas, 2022; Fan Jiang, Yue Su, 2023; Yelena SHames, Mimma Errante, 2022)

The complex clinical presentation of this refractory MG patient highlights the challenges and nuances involved in managing this autoimmune disorder. Personalized treatment strategies, guided by a multidisciplinary team, continuous monitoring, and the consideration of emerging immunomodulatory therapies, are key to achieving disease stability and improving the patient's quality of life. This case serves as a reminder of the ongoing need for research and a patient-centered approach in the management of MG. (A Mahmood, J Hawken, 2023; Lazaridis & Tzartos, 2020a)

## CONCLUSION

Clinical presentation of our patient with refractory Myasthenia Gravis underscores the multifaceted and dynamic nature of this autoimmune disorder. MG's propensity for heterogeneity in its manifestations and its unpredictable course necessitate individualized therapeutic strategies. The ultimate objective in MG management is to attain disease stability while enhancing the patient's overall quality of life. This case reiterates the critical importance of personalizing treatment plans to cater to the unique clinical profiles of MG patients. As exemplified by our patient's journey, the ability to fine-tune interventions based on specific symptomatology, treatment response, and patient well-being remains paramount in optimizing therapeutic outcomes. Furthermore, achieving and maintaining disease stability emerges as a primary goal in MG management. The fluctuating nature of the condition underscores the need for continuous monitoring, enabling prompt intervention when necessary to mitigate exacerbations and enhance long-term prognosis.

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