EJCRIM
European Journal of Case Reports in Internal Medicine

ATEZOLIZUMAB-INDUCED MYASTHENIA GRAVIS IN METASTATIC HEPATOCELLULAR CARCINOMA: A CASE REPORT AND LITERATURE REVIEW

Rajani Gubbala[1], Arumugam Ponnuswamy[1], Nikhileshwar C. Reddy[2], Sanath Kandem[3], Nikhil Pathi[3], Senthil J. Rajappa[3]

[1] Department of Critical Care and Internal Medicine, Basavatarakam Indo-American Cancer Hospital & Research Institute, Hyderabad, India
[2] Department of Neurology, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, India
[3] Department of Medical Oncology, Basavatarakam Indo-American Cancer Hospital & Research Institute, Hyderabad, India

Corresponding author's e-mail: armugamp@gmail.com

Received: 18/07/2026
Accepted: 23/07/2026
Published: 24/08/2026

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: Written informed consent was obtained from the patient's daughter to publish this case report.
This article is licensed under a CC Attribution-NonCommercial-NoDerivatives 4.0 License

How to cite this article: Gubbala R, Ponnuswamy A, Reddy NC, Kandem S, Pathi N, Rajappa SJ. Atezolizumab-induced myasthenia gravis in metastatic hepatocellular carcinoma: a case report and literature review. EJCRIM 2026;13:doi:10.12890/2026_007356

ABSTRACT

Immune checkpoint inhibitors (ICIs) have transformed the management of advanced malignancies but are associated with immune-related adverse events (irAEs), including rare neurological complications. We report a case of a 60-year-old male with metastatic hepatocellular carcinoma who developed severe myasthenia gravis (MG) following treatment with atezolizumab and bevacizumab. The patient was diagnosed with multifocal hepatocellular carcinoma in April 2025 and initiated on combination therapy with atezolizumab (1200 mg) and bevacizumab (600 mg) in May 2025. Approximately 2 weeks after receiving the first treatment cycle, he developed progressive fatigability, breathlessness, and dysphagia.

During hospitalization, he experienced acute respiratory deterioration leading to cardiac arrest, requiring successful resuscitation and intensive care support. Subsequently, he developed unexplained hypercapnic respiratory failure during ventilator weaning attempts. Neuroimaging and cerebrospinal fluid analysis were unremarkable. Repetitive nerve stimulation demonstrated a postsynaptic neuromuscular junction disorder, and serum acetylcholine receptor antibodies were positive. A diagnosis of ICI-induced MG was established. The patient was treated with intravenous immunoglobulin, corticosteroids, and pyridostigmine. Despite therapy, respiratory failure persisted, necessitating prolonged ventilator support. His clinical course was further complicated by myocarditis, demyelinating motor-sensory axonal polyradiculoneuropathy, and sepsis, and he ultimately succumbed to his illness. This case highlights the importance of early recognition and prompt management of neurological irAEs, particularly in patients presenting with unexplained respiratory failure after initiation of ICI therapy.

KEYWORDS

Immune-related adverse events, myasthenia gravis, atezolizumab, hepatocellular carcinoma, neurotoxicity

EFIM European Federation of Internal Medicine

Publisher smc media srl

LEARNING POINTS

- Immune checkpoint inhibitor-induced myasthenia gravis is a rare but potentially fatal complication that can present with rapidly progressive bulbar symptoms and unexplained hypercapnic respiratory failure soon after initiation of therapy. In patients receiving atezolizumab who develop ptosis, dysphagia, or ventilator weaning failure, early recognition, prompt discontinuation of immunotherapy, and timely initiation of intravenous immunoglobulin or plasma exchange are critical to improving outcomes.

INTRODUCTION

Immune checkpoint inhibitors (ICIs) targeting programmed cell death-1 (PD-1), programmed death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) have significantly improved outcomes across a variety of malignancies[1,2]. However, activation of the immune system may result in immune-related adverse events (irAEs) affecting virtually any organ system.

Neurological irAEs are uncommon, occurring in less than 5% of treated patients, but are associated with substantial morbidity and mortality. Among neurological irAEs, myasthenia gravis (MG) is one of the most severe and potentially life-threatening complications[3]. Compared with idiopathic MG, ICI-induced MG typically follows a more fulminant course and frequently presents with bulbar dysfunction, respiratory compromise, and overlap syndromes involving myositis and myocarditis[3,4].

Although most reported cases have been associated with PD-1 inhibitors such as nivolumab and pembrolizumab, atezolizumab-associated MG remains relatively uncommon. We report a fatal case of atezolizumab-induced MG occurring shortly after initiation of treatment for metastatic hepatocellular carcinoma and review the relevant literature.

CASE DESCRIPTION

A 60-year-old male physician with a history of diabetes mellitus was diagnosed with multifocal metastatic hepatocellular carcinoma in April 2025. He was initiated on combination immunotherapy with atezolizumab (1200 mg) and bevacizumab (600 mg) in May 2025.

Approximately 2 weeks after receiving the first cycle, he developed progressive fatigability, breathlessness, and dysphagia and was admitted for further evaluation. On examination, he was dyspnoeic at rest, although his vital signs remained stable. Respiratory, cardiovascular, and abdominal examinations were otherwise unremarkable.

Initial investigations revealed normal complete blood counts, serum electrolytes, and renal function tests. Electrocardiography and transthoracic echocardiography were within normal limits. Upper gastrointestinal endoscopy was unremarkable. A computed tomography scan of the chest and abdomen showed no evidence of pulmonary pathology or disease progression.

On the second day of hospitalization, the patient experienced sudden worsening of breathlessness followed by cardiac arrest. Cardiopulmonary resuscitation was performed, resulting in return of spontaneous circulation. He was subsequently intubated and transferred to the intensive care unit for mechanical ventilation.

Following intubation, arterial blood gas analysis was initially unremarkable, and he remained conscious with stable haemodynamics. Cardiac evaluation and computed tomography pulmonary angiography did not identify a cause for his deterioration. As his clinical condition appeared to improve, ventilator weaning was attempted. During a spontaneous breathing trial, however, he became unresponsive and was found to have severe hypercapnia with a partial pressure of carbon dioxide in arterial blood of 121 mmHg, consistent with type II respiratory failure.

Magnetic resonance imaging of the brain and electroencephalography were unremarkable. No focal neurological deficits were identified apart from bilateral ptosis. Given the unexplained hypercapnic respiratory failure and ocular findings, a neuromuscular junction disorder was suspected. Repetitive nerve stimulation

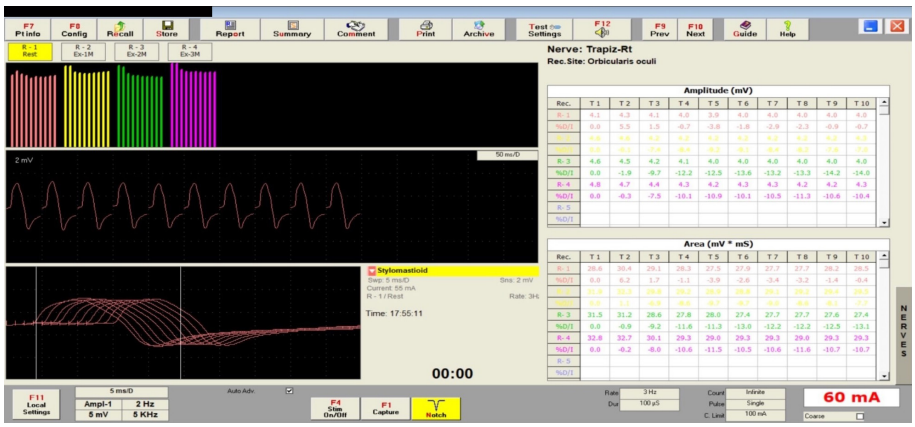


Figure 1. Repetitive nerve stimulation recordings from the right orbicularis oculi demonstrating decremental responses following repetitive stimulation.



Figure 2. Repetitive nerve stimulation recordings from the right nasalis demonstrating decremental responses following repetitive stimulation.

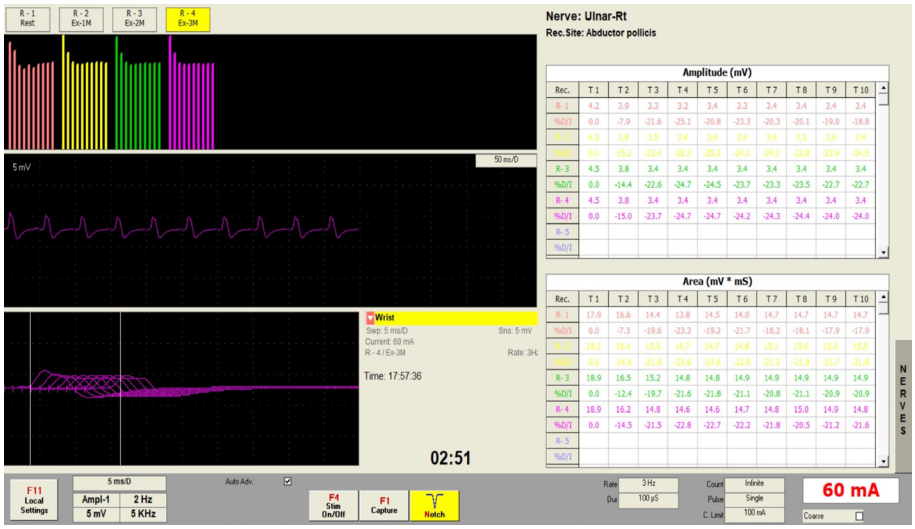


Figure 3. Repetitive nerve stimulation recordings from the right abductor pollicis brevis demonstrating a significant decremental response (>20%), consistent with a postsynaptic neuromuscular junction disorder.

testing performed on the right nasalis, orbicularis oculi, and abductor pollicis muscles demonstrated a significant decremental response, consistent with a postsynaptic neuromuscular junction disorder as seen in *Figure 1, 2 and 3*.

The most pronounced decrement was observed in the ulnar nerve–abductor pollicis recording, with a decrement exceeding 20%, fulfilling electrophysiological criteria for MG.

The formal neurophysiology report concluded that the findings were suggestive of a postsynaptic neuromuscular junction disorder. Serum acetylcholine receptor antibody was more than 6 nmol/l (normal <0.4 nmol/l) confirming the diagnosis. The diagnosis of ICI-induced MG was established based on the temporal relationship to atezolizumab exposure, characteristic clinical presentation, electrophysiological findings, positive acetylcholine receptor antibodies, and exclusion of alternative aetiologies. In the absence of structural, infectious, or metabolic causes, the event was classified as a grade 4 neurological irAE.

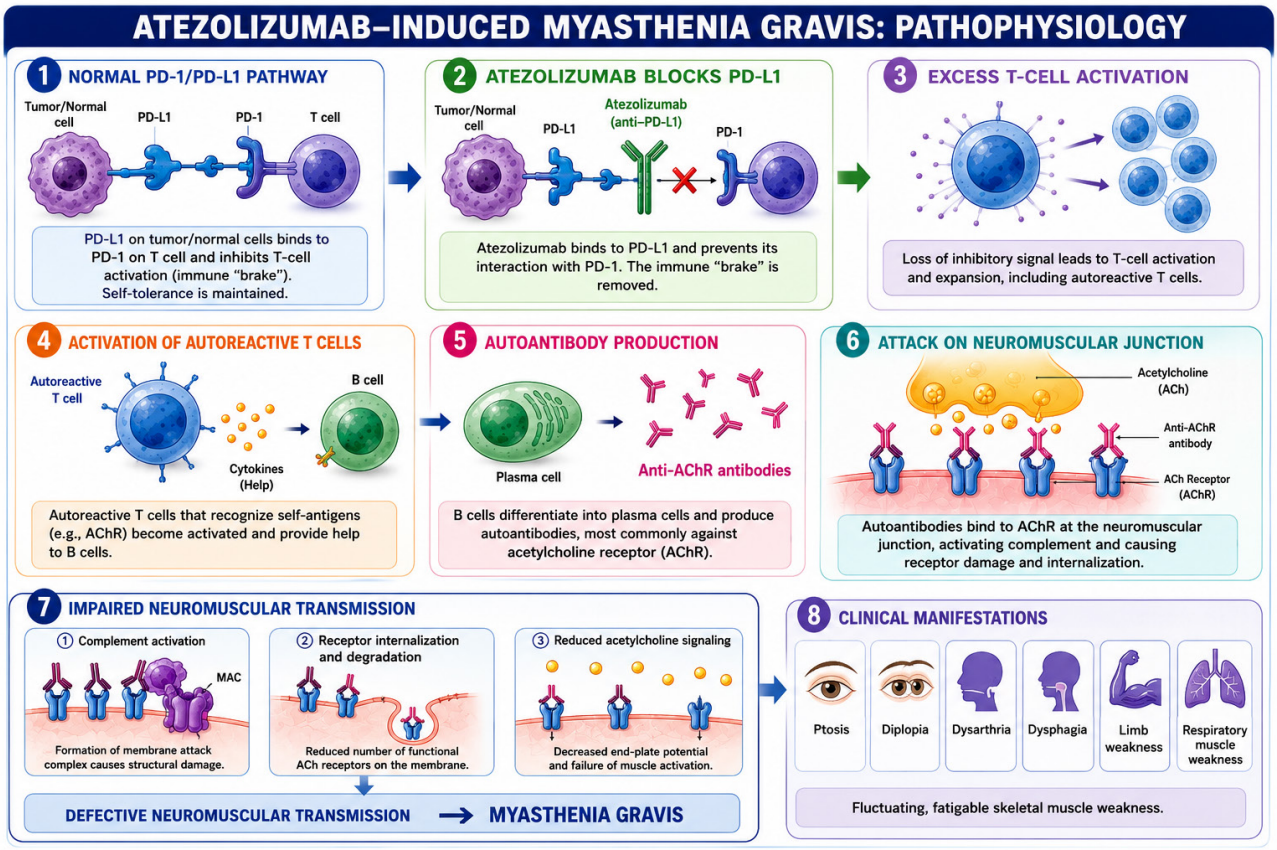
Atezolizumab and bevacizumab were discontinued, and the patient was treated with IVIG for 5 days, corticosteroids, and pyridostigmine 60 mg three times daily. Owing to persistent ventilator dependence, tracheostomy was performed. A second course of IVIG was administered because of inadequate clinical response. Despite aggressive therapy, the patient remained ventilator dependent. His subsequent course was complicated by sepsis, myocarditis, and demyelinating motor-sensory axonal polyradiculoneuropathy. Following discussions with the patient and family regarding prognosis and goals of care, he was transferred to a transition care facility with portable ventilator support, where he later succumbed to his illness.

DISCUSSION

ICI-induced MG is an uncommon but potentially fatal neurological irAE. Although neurological toxicities occur in less than 5% of patients receiving ICIs, MG represents one of the most severe manifestations because of its association with respiratory failure, myocarditis, and increased mortality[3].

The largest systematic review by Safa et al.[3] analysed 65 patients with ICI-associated MG and demonstrated a median symptom onset of approximately 4 weeks after initiation of immunotherapy. Respiratory failure occurred in nearly half of the patients, while mortality approached 30%, substantially higher than that observed in idiopathic MG[3]. Subsequent reviews have confirmed these findings and highlighted the aggressive clinical course of ICI-induced MG compared with classical autoimmune MG[5].

In our patient, symptoms developed approximately 2 weeks after the first cycle of atezolizumab and bevacizumab, strengthening the temporal association with ICI therapy. This early onset is consistent with previous



| ***Figure 4.*** *Proposed pathophysiology of atezolizumab-induced myasthenia gravis.*

reports suggesting that most cases occur within the first 4–8 weeks of treatment, frequently after the first or second treatment cycle[3,5].

Several clinical characteristics distinguish ICI-induced MG from classical MG. Disease progression is often rapid, with many patients presenting with bulbar symptoms and respiratory compromise at diagnosis. Concurrent myositis and myocarditis occur significantly more frequently than in idiopathic MG and are recognized markers of poor prognosis[3,4].

The pathophysiological mechanism underlying atezolizumab-induced MG is illustrated in *Figure 4*. Blockade of the PD-L1 pathway removes inhibitory signals regulating T-cell activation, resulting in loss of self-tolerance and expansion of autoreactive T lymphocytes. These autoreactive cells stimulate B-cell differentiation and production of antibodies directed against acetylcholine receptors at the neuromuscular junction. Subsequent complement activation, receptor internalization, and receptor degradation impair neuromuscular transmission, producing the characteristic manifestations of MG[6].

This proposed mechanism is consistent with current understanding of ICI-associated autoimmunity.

Although nivolumab and pembrolizumab account for the majority of reported cases, atezolizumab-associated MG has increasingly been described in the literature. Published reports suggest a clinical phenotype similar to that observed with PD-1 inhibitors, characterized by rapidly progressive weakness, bulbar dysfunction, and respiratory failure. Several fatal cases have also been reported, particularly in patients with overlap myocarditis and inflammatory myopathy[7,8].

A review of reported cases demonstrates several recurring clinical features. Ocular symptoms, particularly ptosis and diplopia, frequently represent the earliest manifestations. Bulbar dysfunction including dysphagia and dysarthria is common. Elevated creatine kinase levels may indicate concomitant myositis, while elevated troponin levels should prompt urgent evaluation for myocarditis. Mortality is highest among patients with overlap MG–myositis–myocarditis syndrome[4].

Our patient had several adverse prognostic indicators reported in the literature, including advanced age, respiratory failure requiring prolonged mechanical ventilation, myocarditis, and additional immune-mediated neurological involvement in the form of demyelinating motor-sensory axonal polyradiculoneuropathy. An unusual aspect of this case was the development of profound hypercapnic respiratory failure during ventilator weaning despite otherwise unremarkable cardiopulmonary investigations. Recognition of bilateral ptosis and subsequent neuromuscular junction testing were critical in establishing the diagnosis.

Current management guidelines recommend immediate discontinuation of the offending ICI and prompt initiation of immunosuppressive therapy. For patients with bulbar involvement, respiratory compromise, or rapidly progressive weakness, IVIG or plasma exchange

should be instituted early, as outcomes appear superior to corticosteroid therapy alone[7,9]. Despite receiving two courses of IVIG in addition to corticosteroids and pyridostigmine, our patient remained ventilator dependent and ultimately developed progressive multisystem immune-related complications. *Table 1* outlines the key differences between classical MG and ICI-induced MG. Furthermore, to contextualize our case, *Table 2* summarizes previously

Characteristic	Classical myasthenia gravis	ICI-Induced myasthenia gravis
Typical onset	Gradual	Acute and rapidly progressive
Time to presentation	Variable	Usually within 4–8 weeks of ICI initiation
Ocular symptoms	Common	Common, often the initial manifestation
Bulbar involvement	Variable	Frequent
Respiratory failure at presentation	Less common	Common
Overlap with myositis	Rare	Frequent
Overlap with myocarditis	Rare	Frequent
CK elevation	Usually absent	Frequently elevated
Troponin elevation	Uncommon	Suggestive of overlap myocarditis
Mortality	Low with appropriate treatment	Significantly higher (particularly with overlap syndromes)
Standard treatment	Pyridostigmine, steroids, immunosuppression	Immediate ICI discontinuation, IVIG/plasma exchange, corticosteroids, multidisciplinary care

Table 1. *Comparison of classical myasthenia gravis and immune checkpoint inhibitor-induced myasthenia gravis. (adapted from published systematic reviews and clinical practice guidelines[3-7]).*
Abbreviations: ICI, Immune checkpoint inhibitors; CK, creatine kinase; IVIG, intravenous immunoglobulin.

Reference	Underlying malignancy	Time to onset	Clinical features	Associated irAEs	Treatment	Outcome
Thakolwiboon et al.[10]	Advanced urothelial carcinoma	Shortly after initiation of atezolizumab	Generalized weakness, dysarthria, dysphagia, respiratory involvement	Immune-mediated myasthenia gravis	Pyridostigmine, corticosteroids, IVIG	Clinical improvement reported
Kobayashi et al.[8]	Hepatocellular carcinoma	After atezolizumab therapy	Myasthenia gravis with severe muscle weakness	Concurrent myositis	Corticosteroids, plasma exchange, IVIG	Fatal
Samar et al.[9]	Hepatocellular carcinoma	During atezolizumab treatment	Myasthenia gravis/ myasthenia-like syndrome with neuromuscular manifestations	Neuromuscular immune-related toxicity	Immunosuppressive therapy and supportive management	Fatal
Present case	Metastatic hepatocellular carcinoma	2 weeks after first cycle of atezolizumab-bevacizumab	Fatigability, dysphagia, bilateral ptosis, hypercapnic respiratory failure	Myocarditis and demyelinating motor-sensory axonal polyradiculoneuropathy	IVIG (2 courses), corticosteroids, pyridostigmine	Fatal

Table 2. *Selected published reports of atezolizumab-associated myasthenia gravis.*
Abbreviations: irAEs, immune-related adverse events; IVIG, intravenous immunoglobulin.

published cases of atezolizumab-associated MG, with emphasis on clinical presentation, associated irAEs, therapeutic interventions, and patient outcomes.

This case adds to the limited literature describing atezolizumab-associated MG and highlights the potential for rapid progression to life-threatening respiratory failure. Clinicians should maintain a high index of suspicion for neuromuscular junction disorders in patients receiving ICIs who develop unexplained dyspnoea, dysphagia, ptosis, or ventilator weaning failure.

CONCLUSION

Atezolizumab-induced MG is a rare but highly morbid neurological irAE. Early symptoms such as ptosis, dysphagia, fatigability, and unexplained hypercapnic respiratory failure should prompt urgent evaluation for neuromuscular junction dysfunction. Given the high incidence of respiratory compromise and overlap syndromes, early discontinuation of ICI therapy and prompt initiation of IVIG or plasma exchange are essential to improve outcomes. Increased awareness among oncologists, intensivists, and neurologists is crucial for early diagnosis and timely intervention.

REFERENCES

1. National Comprehensive Cancer Network. Management of immunotherapy-related toxicities. NCCN Clinical Practice Guidelines in Oncology. Version 2025.
2. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012;12(4):252-64. doi: 10.1038/nrc3239.
3. Safa H, Johnson DH, Trinh VA, Rodgers TE, Lin H, Suarez-Almazor ME, et al. Immune checkpoint inhibitor related myasthenia gravis: single center experience and systematic review of the literature. J Immunother Cancer. 2019;7(1):319. doi: 10.1186/s40425-019-0774-y.
4. Touat M, Maisonobe T, Knauss S, Ben Hadj Salem O, Hervier B, Auré K, et al. Immune checkpoint inhibitor-related myositis and myocarditis in patients with cancer. Neurology. 2018;91(10):e985-e994. doi: 10.1212/WNL.0000000000006124 Erratum in: Neurology. 2019;93(6):280. doi: 10.1212/WNL.0000000000007380.
5. Huang YT, Chen YP, Lin WC, Su WC, Sun YT. Immune Checkpoint Inhibitor-Induced Myasthenia Gravis. Front Neurol. 2020;11:634. doi: 10.3389/fneur.2020.00634.
6. Makarious D, Horwood K, Coward JIG. Myasthenia gravis: An emerging toxicity of immune checkpoint inhibitors. Eur J Cancer. 2017;82:128-136. doi: 10.1016/j.ejca.2017.05.041.
7. Schneider BJ, Naidoo J, Santomasso BD, Lacchetti C, Adkins S, Anadkat M, et al. Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. J Clin Oncol. 2021;39(36):4073-4126. doi: 10.1200/JCO.21.01440. Erratum in: J Clin Oncol. 2022;40(3):315. doi: 10.1200/JCO.21.02786.
8. Kobayashi Y, Nagamatsu K, Shimizu Y, Nakayama A, Sekijima Y. Atezolizumab-induced myasthenia gravis and myositis: a fatal case report and review of the literature. Int Cancer Conf J. 2025;14(4):428-432. doi: 10.1007/s13691-025-00791-w.
9. Samar MR, Naviwala MSS, Abdy FR, Shahzadi M. Atezolizumab-induced neuromuscular syndrome mimicking myasthenia gravis in a patient with hepatocellular carcinoma - an area of concern. Ecancermedicalscience. 2025;19:1949. doi: 10.3332/ecancer.2025.1949.
10. Thakolwiboon S, Karukote A, Wilms H. De Novo Myasthenia Gravis Induced by Atezolizumab in a Patient with Urothelial Carcinoma. Cureus. 2019;11(6):e5002. doi: 10.7759/cureus.5002.