

A case of PD-1 inhibitor-induced myasthenia gravis and acute coronary syndrome: a case report

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Case Report

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Abstract

Background

This case report describes a patient who developed PD-1 inhibitor-induced myasthenia gravis (MG) and acute coronary syndrome (ACS). This condition is clinically uncommon and presents substantial management challenges, warranting attention from clinicians.

Case presentation

A 65-year-old man with hepatocellular carcinoma developed PD-1 inhibitor-induced MG and non-ST-segment elevation myocardial infarction (NSTEMI), presenting with diplopia, ptosis, limb weakness, elevated hs-TnT, and ST-segment depression. Although the myasthenic symptoms gradually improved after immunosuppressive therapy, the hs-TnT levels never normalized. Strikingly, seven months after the initial event, the patient suffered an acute ST-segment elevation myocardial infarction (STEMI) requiring percutaneous coronary intervention for total occlusion of the left anterior descending artery.

Conclusion

This course delivers an important clinical alert for patients with PD-1 inhibitor-induced MG and ACS: persistently elevated hs-TnT following neurological symptom resolution may signal ongoing coronary pathology and portend a high risk of future major adverse cardiac events, underscoring the imperative for dedicated, long-term cardiac surveillance in this population.

1 Introduction

Liver cancer is a malignant tumor occurring in liver cells and intrahepatic bile duct epithelial cells¹. In recent years, immune checkpoint inhibitors (ICIs), including programmed cell death protein 1 (PD-1), programmed death-ligand 1 (PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), have gradually become standard treatments for advanced liver cancer². By enhancing immune cell function against tumors, ICIs may also disrupt immune tolerance, leading to immune-related adverse events (irAEs)³. While irAEs predominantly affect the skin, endocrine system, and gastrointestinal tract⁴, neurological and cardiovascular irAEs, though less common, are associated with rapid progression and high mortality^{5,6}. ICI-induced cardiovascular events, including myocarditis (19.1%) and myocardial infarction (6.5%), have been reported in 1%–4.2% of patients^{6,7}. Myasthenia gravis (MG) is the most common neurological irAE, occurring in approximately 26.8% of cases, often with myocarditis or myositis⁸. Concurrent MG and acute coronary syndrome (ACS) following PD-1 inhibitor therapy is relatively uncommon⁹.

Here, we report the case of a patient with hepatocellular carcinoma (HCC) who developed MG and ACS following anti-PD-1 therapy, aiming to improve clinicians' understanding of the diagnosis, management, and prognosis of such rare adverse events.

2 Case presentation

A 65-year-old man had no previous history of hypertension, diabetes, kidney disease, heart disease, or hyperlipidemia. He had a 30-year smoking history and had quit smoking 2 years prior. In May 2023, he was diagnosed with HCC at our hospital and underwent right hemihepatectomy and cholecystectomy on May 18, 2023. On June 25, 2023, he received TACE with fluorouracil, epirubicin hydrochloride, sodium folinate and loperatin. This was followed by the first course of tislelizumab immunotherapy and targeted therapy with lenvatinib mesylate the next day.

13 days after the first course of tislelizumab (July 8, 2023), the patient presented with bilateral ptosis, diplopia and limb weakness. On July 13, 2023, the patient was admitted to the neurology department. Neurological examination revealed bilateral ptosis, more pronounced in the right eye, and the muscle strength of the upper limbs was graded 4 according to the Medical Research Council (MRC) scale, while that of the lower limbs was MRC grade 3. Tendon reflexes in all four limbs were normal and the Jolly test was positive.

On the second day of admission (July 14, 2023), the patient developed dyspnea and required mechanical ventilation. At the same time, repetitive nerve stimulation (RNS) showed a positive decrement response to low-frequency stimulation of the left trapezius and right orbicularis oculi muscles (Table 1). In addition, electromyography (EMG) revealed peripheral neuropathy of the right tibial nerve (motor fiber involvement with demyelinating changes) and reduced amplitude of bilateral facial nerves. Anti-acetylcholine receptor (AChR) antibodies were detected as positive, with a titer exceeding 20 nmol/L (reference value, <0.45 nmol/L). A chest CT scan revealed no evidence of a mediastinal mass. Therefore, based on the International Consensus Guidance for the Management of MG, the final diagnosis was MG with Osserman Type III, which caused by PD-1 inhibitors. The patient's MG clinical scores were as follows: Quantitative Myasthenia Gravis Score (QMGS) 19 points and Activities of Daily Living (ADL) 14 points. Intravenous immunoglobulin (IVIG) therapy (2g/kg total dose, 0.4g/kg/day from July 14 to July 18, 2023) and Mestinon were promptly initiated. Concurrently, the laboratory data demonstrated a progressive increase in high-sensitivity troponin T (hs-TnT) levels, rising from 0.41 µg/L at admission to 0.710 µg/L (reference value, 0-0.014 µg/L) on the third day of admission. Creatine kinase (CK) decreased from 2592 U/L to 1239 U/L (reference value, 50-310 U/L), CK-MB decreased from 139 U/L to 101 U/L (reference value, 0-24 U/L), and BNP level was normal (10.9 ng/L; reference value, 0-67.6 ng/L). The Electrocardiogram (ECG) showed ST-segment depression in leads I, aVL, II, III, avF, and V3-V6, along with sinus tachycardia and complete right bundle branch block. The echocardiogram showed decreased left ventricular diastolic function, with a left ventricular ejection fraction (LVEF) of 63%. The patient did not experience chest pain. However, the cardiologist determined that non-ST-segment elevation myocardial infarction (NSTEMI) could not be ruled out and initiated treatment with clopidogrel and low-molecular-weight heparin to manage cardiovascular risk.

Table 1
The results of percentage decrease in amplitude of repeated electric shock wave in this case

Name	1 Hz	2 Hz	3 Hz	5 Hz	10 Hz
left abductor digiti minimi	-2%	-1%	0	2%	-5%
left orbicularis oculi muscle	6%	1%	7%	8%	-1%
right orbicularis oculi muscle	9%	13%	16%	12%	10%
left orbicularis oris muscle	2%	3%	3%	2%	/
left trapezius muscle	7%	8%	17%	13%	/
left deltoid muscle	/	2%	6%	-2%	/

On the sixth day of admission (July 18, 2023), the patient developed dysphagia and dysarthria. His ADL score was 21 points. And he was subsequently started on high-dose methylprednisolone (1000 mg daily for 4 days, then tapered to 500 mg for 2 days, and then to 250 mg for 2 days), in addition to maintenance Mestinon. After 8 days of treatment, there was significant improvement in the symptoms of limb weakness and dyspnea, and his ADL score decreased to 17 points. He was subsequently transitioned from mechanical ventilation to high-flow nasal oxygen therapy. The medication regimen was then adjusted to oral prednisone acetate. During this period, hs-TnT remained elevated at 0.698 µg/L.

Over the following 7 days, the patient's clinical symptoms continued to improve gradually and hs-TnT level declined to 0.24µg/L. However, on the 21st day of admission (August 2, 2023), the patient's condition deteriorated abruptly, presenting with respiratory failure and a subsequent lapse into a coma. The patient was immediately placed on mechanical ventilation and regained consciousness shortly thereafter. Plasma exchange (PE) was initiated while maintaining Mestinon, and after completing 8 rounds of PE (a total of 3350 mL of plasma), the patient showed significant improvement, with the ability to rotate both eyeballs upward and downward, and marked alleviation of blepharoptosis and limb weakness compared to before; subsequently, the ventilator was successfully removed. After treatment, the patient's QMGS was 8 points and his ADL score was 4 points. The final diagnosis was considered to be MG and NSTEMI caused by PD-1 inhibitor.

After one and a half months of admission (August 30, 2023), the patient was discharged with slight eyelid ptosis, no limb weakness and no shortness of breath. Hs-TnT level remained mildly elevated at 0.148 ng/mL. The patient was advised to continue immunosuppressive therapy and to maintain periodic monitoring of cardiac enzyme levels post-discharge (Fig. 1).

On January 24, 2024, routine surveillance imaging revealed a new solitary HCC nodule (1.7 × 1.6 cm) in hepatic segment S3. The patient underwent surgical resection of the nodule on February 7, 2024, and postoperative pathology confirmed hepatocellular carcinoma. This was followed by two sessions of

adjuvant TACE on March 1 and April 1, 2024. Since March 2024, the patient has been maintained on lenvatinib mesylate (a multi-target TKI, without ICI).

7 months after discharge (April 9, 2024), the patient experienced sudden-onset chest pain and was admitted to the emergency department. The hs-TnT level was elevated (0.557 µg/L) again, and the ECG showed ST-segment elevation consistent with acute myocardial infarction. He immediately underwent coronary angiography, which revealed 100% stenosis at the proximal end of the left anterior descending branch (LAD). No abnormalities were observed in the right coronary artery (RCA). Percutaneous coronary intervention (PCI) was performed, with two stents placed in tandem at the proximal end of the LAD. The patient's chest pain improved significantly after PCI.

21 months after discharge (May 14, 2025), the patient was admitted for chest tightness. The hs-TnT level was within normal limits (0.014 µg/L). Coronary angiography revealed 80–85% stenosis in the mid-segment of the RCA. One stent was implanted in the RCA.

As of the latest follow-up (June 5, 2025), the patient's condition is stable, with a QMGs of 1 point. He has not experienced any further episodes of chest pain. A timeline of the patient's clinical course can be found in Fig. 2.

3 Discussions

PD-1 is an inhibitory receptor on immune cells that maintains immune balance by limiting T cell activation³. Tumor cells can exploit this pathway by expressing PD-L1, thereby suppressing T cell function and promoting immune evasion^{10,11}. PD-1 inhibitors block this interaction, restoring T cell-mediated tumor killing¹². However, overactivated T cells may also attack normal tissues, leading to the development of irAEs¹³. In our case, the patient developed PD-1 inhibitor-induced MG and ACS, a presentation distinct from previously reported overlapping syndromes. This highlights the need for further investigation to optimize management strategies.

3.1 The Features and Mechanisms of PD-1 Inhibitor-Induced MG with or without ACS.

Most cases of immune-related MG (ir-MG) are associated with the use of PD-1 inhibitors¹⁴. Compared with classic MG, ir-MG more often leads to respiratory failure and higher mortality, while diagnosis can be difficult as repetitive nerve stimulation and anti-AChR antibodies are less frequently positive¹⁵. Ir-MG is strongly associated with myositis, though our patient showed neither muscle pain nor EMG evidence of myogenic damage, indicating isolated MG and underscoring the broad spectrum of immune-related adverse events¹⁶.

The mechanism of PD-1 inhibitor-induced MG likely involves autoreactive T-cell activation, proinflammatory cytokine release, and enhanced T-cell–B-cell interactions promoting autoantibody

production^{5,17}. The overlap of MG and ACS remains unclear but may involve: (1) antigen cross-reactivity, where tumor antigens resemble those of neuromuscular junctions, cardiomyocytes, or vascular walls, leading to tissue injury^{5,18}. (2) systemic immune overactivation, with heightened T-cell activity and cytokine production triggering diffuse damage to both neuromuscular junctions and the cardiovascular system¹⁹.

3.2 Delayed and persistent hs-TnT elevation may represent a distinctive feature in some cases of PD-1 inhibitor-associated ACS.

ACS is the most common type of non-myocarditis MACE, accounting for approximately 36.3% of cases, with a median onset of 23.5 days after ICI initiation⁹. In conventional ACS, hs-TnT typically peaks within 24–48 hours and normalizes within 10–14 days²⁰. In contrast, in our patient, hs-TnT peaked only on the fourth day of hospitalization and remained mildly elevated for more than eight months, suggesting a mechanism possibly distinct from the classic pathogenesis of conventional ACS caused by plaque rupture or erosion²¹.

Several mechanisms may account for this phenomenon. First, PD-1 inhibitors may induce or accelerate inflammation within unstable coronary plaques²², leading to prolonged erosion or microthrombus formation and thus a delayed troponin peak. Second, ICI-associated coronary vasospasm cannot be excluded as a contributor to myocardial injury²³. These diffuse vascular pathologies could lead to ongoing myocyte damage and repair, resulting in persistent low-level troponin elevation. This case suggests that delayed and persistent hs-TnT elevation may be a feature of PD-1 inhibitor-associated ACS. However, further studies are needed to confirm this observation and clarify the mechanisms.

3.3 High-sensitivity cardiac troponin (hs-cTn) may serve as a potential predictor of long-term outcomes in survivors of PD-1 inhibitor-associated ACS.

Current guidelines recommend that patients receiving ICIs undergo baseline cardiac troponin (cTn) or high-sensitivity cardiac troponin (hs-cTn) testing, with high-risk patients requiring regular monitoring during the first 4–6 weeks of treatment²⁴. Several studies have shown that dynamic monitoring of hs-cTn can predict cardiovascular events following ICI therapy, and elevated TnT levels at discharge are significantly associated with an increased risk of subsequent cardiovascular events^{25,26}. However, large-scale evidence linking persistently elevated hs-cTn with long-term outcomes in survivors of ICI-related ACS remains lacking, creating challenges for clinical management²⁷.

Our patient demonstrated persistently elevated hs-TnT for several months after the initial ACS and subsequently developed multiple severe coronary events within just 22 months. This suggests that sustained hs-TnT elevation may serve as a biomarker of adverse outcomes in survivors of ICI-related ACS, possibly reflecting ongoing vascular inflammation and unstable plaques. For these patients, beyond conventional secondary prevention, closer risk stratification with frequent coronary imaging and potentially enhanced anti-inflammatory therapy may be warranted.

In summary, PD-1 inhibitors may induce rare MG and ACS. Early recognition and prompt management are essential to improve patient outcomes. Delayed and persistent elevation of hs-TnT is a possible feature of PD-1 Inhibitor-Induced ACS. For survivors of ICI-related cardiovascular adverse events, regular hs-cTn monitoring may help identify individuals at high risk of subsequent cardiovascular disease.

Declarations

Ethical standards and consent to participate

The studies involving humans were approved by Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article. Clinical trial number: not applicable.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

BP contributed to the study conception, reviewed the literature, drafted the manuscript and drew the figures. CD, ZZ, YZ and OH critically revised the article. GC, GW, YZ and MZ analysed and checked the patient's data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Figures

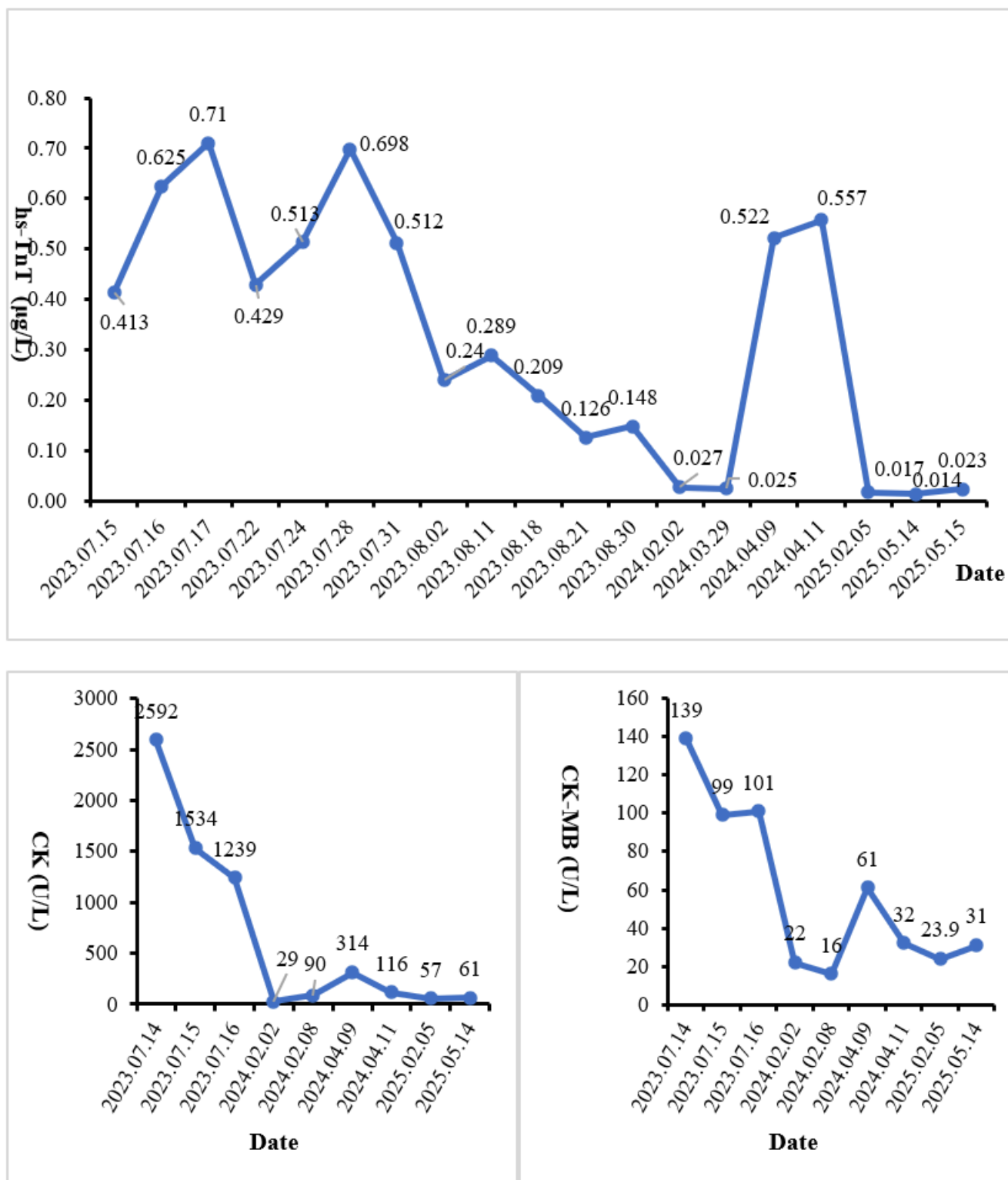


Figure 1

Changes in cardiac enzyme levels during the course of the disease.

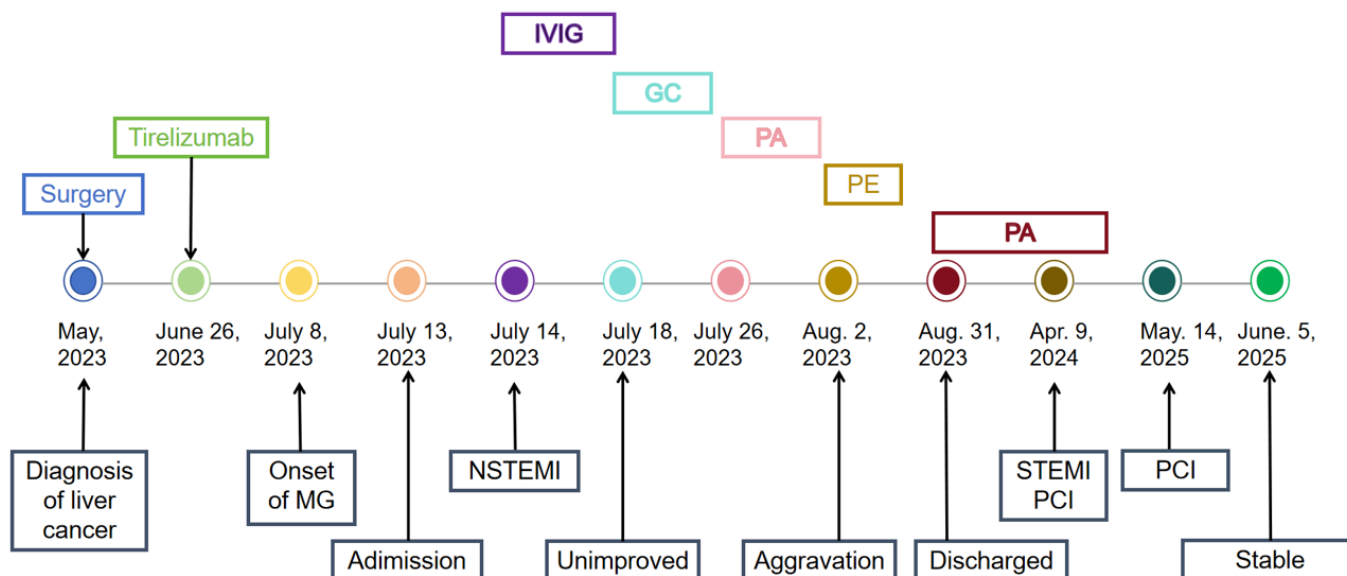


Figure 2

Clinical course in this case. IVIG=intravenous immunoglobulin; PA=prednisone acetate; GC=glucocorticoid; PE=plasma exchange; NSTEMI=non-ST-segment elevation myocardial infarction; STEMI=ST-segment elevation myocardial infarction; PCI=percutaneous coronary intervention.