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Case Report

Immune-related Myocarditis, Guillain–Barré Syndrome, and Myasthenia Gravis Exacerbation after Pembrolizumab Therapy in a Patient with Recurrent B3 Thymoma: A Case Report

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Abstract

Thymic epithelial tumors, including thymoma and thymic carcinoma, are rare malignancies for which platinum-based chemotherapy is the standard first-line treatment. Second-line options include chemotherapy, targeted therapy, immune checkpoint inhibitors (ICIs), or combination regimens. While thymoma has been strongly associated with paraneoplastic autoimmune disorders, previous clinical trials have demonstrated an increased risk of severe immune-related adverse events, such as myocarditis when treating thymoma patients with ICIs. Herein, we report a case of recurrent B3 thymoma in a patient who developed myocarditis, overlapping Guillain–Barré syndrome, and myasthenia gravis exacerbation after receiving a single dose of 100 mg pembrolizumab therapy. The patient recovered after steroid pulse therapy, intravenous immunoglobulin administration, and plasma exchange.

Keywords: B3 thymoma, case report, Guillain–Barré syndrome, immune-related adverse events, myasthenia gravis, myocarditis

Introduction

In a phase II study conducted by Cho *et al*., pembrolizumab demonstrated a moderate anticancer effect in treating refractory or relapsed thymic epithelial tumors (TETs).[1] However, severe immune-related adverse events (irAEs) developed in five of the seven thymoma patients (71.4%) and three of the 26 thymic carcinoma patients (11.5%). This aligns with the well-documented predisposition to autoimmune disorders among patients with thymoma compared to those with thymic carcinoma. Another phase II study, the PECATI trial, evaluated the combination of pembrolizumab and lenvatinib in 43 patients

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with TETs, including seven with B3 thymoma and 36 with thymic carcinoma.[2] The results showed that the incidence of severe irAEs seemed to be much lower when pembrolizumab was used to treat B3 thymoma or thymic carcinoma. Only two of the 43 patients (4.7%) developed severe irAEs, with one developing myocarditis and the other pneumonitis.

Managing severe irAEs is challenging. Here, we describe a patient with recurrent B3 thymoma who developed myocarditis, overlapping Guillain–Barré syndrome, and myasthenia gravis (MG) exacerbation after receiving a single dose of 100 mg pembrolizumab. The patient subsequently recovered after steroid pulse therapy, intravenous immunoglobulin (IVIG) administration, and plasma exchange.

Case Report

This case was a 50-year-old woman with a history of recurrent metastatic B3 thymoma. She has been diagnosed with metastatic B3 thymoma invading the pericardium, great vessels, and left pleura in 2015, with the initial presentation of drooping eyelids and diplopia. A diagnosis of MG was made, and she was treated with cyclophosphamide, doxorubicin, and cisplatin, followed by concurrent chemoradiotherapy (CCRT) (50 Gy) to the involved fields plus etoposide and cisplatin. A partial response was achieved, and the symptoms of MG completely resolved. In 2018, she developed pleural recurrence, which was treated successfully with repeated CCRT (40 Gy plus etoposide). In 2025, recurrence was detected again, and she chose to receive pembrolizumab 100 mg every 3 weeks as the salvage therapy, since she preferred a chemotherapy-free regimen due to concerns about side effects.

One week after her first pembrolizumab infusion, she developed a 3-day history of nonradiating, tight, dull chest pain unresponsive to rest. Serial measurements demonstrated elevated troponin-I concentrations (range, 2.8–6.2 ng/mL; reference, 0–0.04 ng/mL). Electrocardiography (ECG) revealed ST-T segment changes, and coronary angiography showed no evidence of obstructive coronary artery disease.

However, the symptoms persisted, and follow-up ECG demonstrated wide-complex tachycardia with diffuse ST-T abnormalities [Figure 1a]. Laboratory measurements revealed markedly elevated troponin-T (967.6 ng/mL; reference, <14 ng/mL). Adenosine was administered to differentiate the origin of the wide QRS complex, and the lack of response suggested a ventricular origin. She then received amiodarone loading and two synchronized electrical cardioversions (100 J, 150 J), resulting in a reduction in the ventricular rate to 107 beats per minute with right bundle branch block pattern [Figure 1b]. Echocardiography showed a reduced left ventricular ejection fraction of 47.6% without obvious regional wall motion abnormalities.

A few hours after initial stabilization, she became unresponsive and developed acute hypercapnic respiratory failure, requiring endotracheal intubation. Her vital capacity was severely reduced (650 mL; normal 3.0–3.5 L). Repeat coronary angiography showed patent vessels, and an endomyocardial biopsy revealed subacute myocarditis with scattered CD20-positive B cells, diffuse CD3-positive T cells, CD68-positive macrophages, and diffuse PD-1 positivity [Figure 2]. Infectious and autoimmune workup was negative except for mildly elevated acetylcholine receptor antibodies (1.771 nmol/L; reference <0.2 nmol/L). A neurological examination showed ptosis and generalized weakness, suggestive of MG exacerbation.

Given the clinical presentation (chest pain, diplopia, ptosis, cardiogenic shock, ventricular arrhythmia), exclusion of alternative etiologies (no evidence of acute coronary syndrome or acute infectious myocarditis), elevated troponin-T level, and the microscopic presentation of an myocardial biopsy (overt inflammatory cell infiltrates within the myocardial tissues), a diagnosis of immune checkpoint inhibitor (ICI)-associated myocarditis was established according to the diagnostic criteria listed in the 2022 European Society of Cardiology (ESC) cardio-oncology guidelines.[3] Three of the minor criteria were met: clinical syndrome (e.g. fatigue, myalgias, chest pain, diplopia, ptosis, dyspnea, orthopnea, edema, palpitations, syncope, muscle weakness, cardiogenic shock); ventricular arrhythmia or new conduction system disease; other irAEs (notably myositis, myopathy, MG).[3] High-dose pulse steroid therapy with intravenous methylprednisolone 500 mg/day was initiated. However, the response was unsatisfactory after two doses of 500 mg methylprednisolone, and the troponin-T level dropped by <30%. Due to the poor response to steroid treatment, IVIG at 0.4 g/kg/day was given for 5 days as salvage treatment. Three days after starting IVIG, substantial improvements in ptosis and muscle strength were noted. However, the muscle power did not recover fully, and subsequent nerve conduction studies demonstrated features of acute polyradiculoneuropathy. A clinical diagnosis of

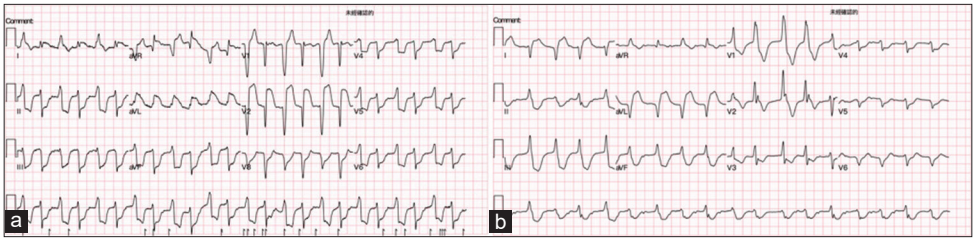

Figure 1: Wide QRS complex recorded on electrocardiography. (a) Initial electrocardiogram obtained in the emergency department, demonstrating wide QRS complex tachyarrhythmia. (b) Electrocardiogram following two synchronized electrical cardioversions, revealing a wide QRS rhythm with right bundle branch block morphology

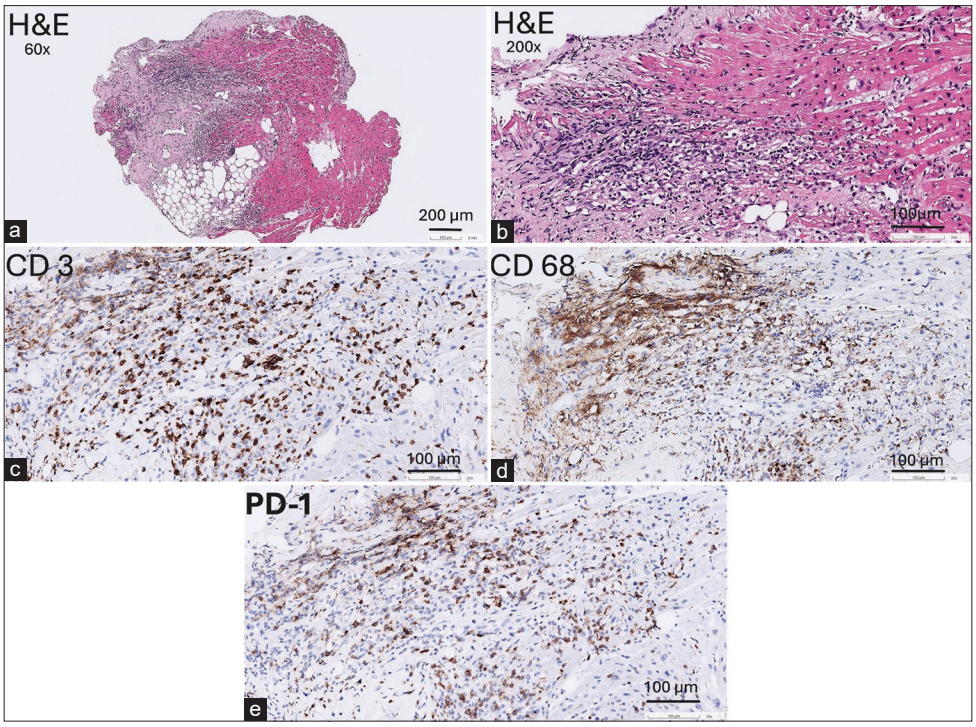

Figure 2: Microscopic findings of the endomyocardial biopsy. (a) Endomyocardial tissue, low-power filed (H and E, ×60). (b) The high-power field of the endomyocardial tissue demonstrated focal epimyocarditis with vascular thickening. Interstitial and focal perivascular lymphocyte infiltrates and myocyte injury/necrosis were seen; giant cell formation was not observed (H and E, ×200). (c) Diffuse infiltration of CD3-positive T lymphocytes. (d) Diffuse infiltration of CD68-positive macrophages. (e) Positive staining for programmed cell death protein 1 (PD-1) within the inflammatory infiltrate

Guillain–Barré syndrome (GBS) was made, for which she underwent ten sessions of therapeutic plasma exchange.

Over the following months, her muscle strength gradually improved, and she was successfully weaned from mechanical ventilation 6 months after presentation. Figure 3 demonstrates the chronological changes in troponin-T level and the treatments the patient received.

Discussion

ICI-associated myocarditis occurs in approximately 0.1%–1% of treated patients but is associated with a high mortality rate of 25%–50%.[4,5] In TETs, the incidence is notably higher. In one phase II trial, three of seven patients (43%) with thymoma developed grade 4 myocarditis after pembrolizumab infusion, compared to none of 26 patients with thymic carcinoma. All affected thymoma cases were B2 or B2/B3 subtypes.[1] Another phase II study reported grade 4 myocarditis in 2 of 40 patients (5%) with thymic carcinoma treated with pembrolizumab.[6] These findings suggest that treating B2 thymoma with pembrolizumab should be done with extreme caution, as the incidence of severe myocarditis is unacceptably high. Conversely, a separate phase II trial enrolling 46 patients (seven with B3 thymoma, 36 with thymic carcinoma) demonstrated an acceptable safety profile for pembrolizumab plus lenvatinib, with two cases of severe irAEs (one pneumonitis and one myocarditis).[2]

The diagnosis of ICI-associated myocarditis, as outlined in the 2022 ESC cardio-oncology guidelines, is summarized in Table 1. The diagnosis requires an elevated troponin level plus either one major or two minor criteria, following the exclusion of acute coronary syndrome and infectious myocarditis.[3]

Endomyocardial biopsy is typically confirmatory, with the Dallas criteria requiring the presence of both inflammatory infiltrates and myocardial necrosis on histopathology. Immunohistochemical staining for markers including CD3, CD4, CD8, and CD68 can facilitate the identification of infiltrating immune cell populations, whereas diffuse PD-L1 expression supports an ICI–related mechanism of myocardial injury. Our patient presented with characteristic chest pain, ventricular arrhythmia with new conduction system abnormalities (right bundle branch block), reduced left ventricular systolic function, and exacerbation of MG — fulfilling four minor diagnostic criteria. Collectively, these findings strongly supported a diagnosis of ICI-associated myocarditis.

The management of ICI-associated myocarditis includes high-dose corticosteroids (prednisone 1–2 mg/kg/day[5,7] or methylprednisolone 1000 mg/day pulse followed by 1 mg/kg daily),[6] with escalation to additional immunosuppressive agents (mycophenolate, infliximab, and antithymocyte globulin) for refractory cases. Agents targeting costimulatory pathways (abatacept) or CD52 blockade (alemtuzumab) may be considered in specific cases.[8]

In this case, the patient had a suboptimal response to corticosteroids but improved rapidly following IVIG. This case highlights the risk of severe, multisystemic irAEs, including

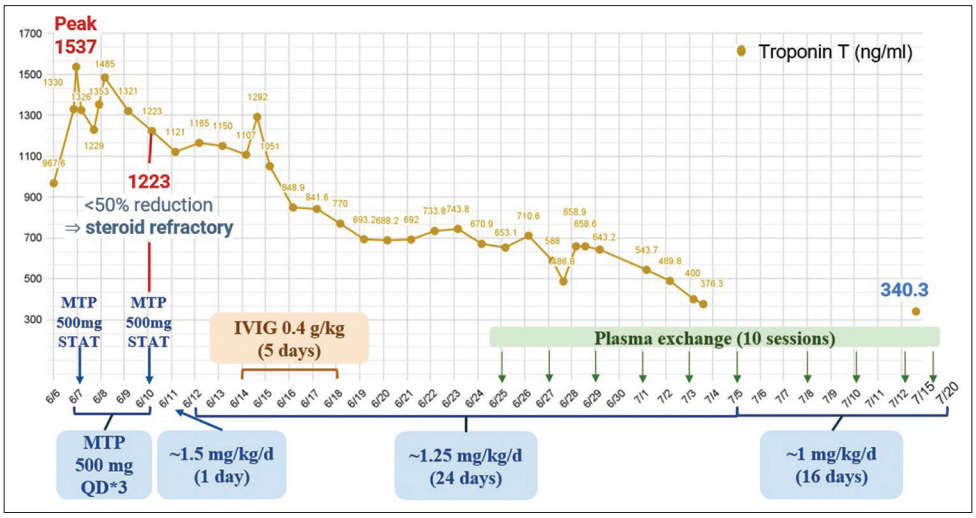

Figure 3: Timeline of treatment interventions and corresponding changes in troponin-T levels. IVIG: Intravenous immunoglobulin

Table 1: Clinical diagnosis criteria for immune checkpoint inhibitor myocarditis

Major criterion
CMR diagnostic for acute myocarditis (modified Lake Louise criteria)
Minor criteria
Clinical syndrome (e.g., fatigue, myalgias, chest pain, diplopia, ptosis, dyspnea, orthopnea, edema, palpitations, syncope, muscle weakness, cardiogenic shock)
Ventricular arrhythmia or new conduction system disease
Decline in left ventricular systolic function, with or without regional wall motion abnormality
Other irAEs (notably myositis, myopathy, MG)
Suggestive CMR findings

CMR: Cardiac magnetic resonance imaging, irAEs: Immune-related adverse events, MG: Myasthenia gravis

myocarditis, GBS, and MG exacerbation, in patients with B3 thymoma receiving ICI therapy. Although pembrolizumab has demonstrated efficacy in B3 thymoma and thymic carcinoma, the significant risk of grade 3/4 irAEs underscores the importance of vigilant monitoring and prompt multidisciplinary intervention.

We report a complex case of ICI-associated myocarditis with concurrent GBS and exacerbation of MG occurring shortly after a single pembrolizumab infusion in a patient with recurrent B3 thymoma. This case underscores the importance of heightened clinical vigilance, timely recognition, and prompt, multidisciplinary management of severe irAEs. Early intervention was critical for the patient's recovery, and highlights the need for careful risk–benefit assessment before initiating treatment and close monitoring in this high-risk population.

Declaration of patient consent

This study was performed in accordance with and conforming to the Declaration of Helsinki. The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Author contributions

YJY: clinical care provision, literature review, and manuscript preparation. HWH: clinical care provision. CNC: clinical care provision. WLM: clinical care provision, manuscript co-writing, and revision. All authors have reviewed and approved the final manuscript and agree to be personally accountable for their respective contributions.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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