Dual immune checkpoint inhibitor cardonilumab induces immune myocarditis in a patient with cancer-related myocardial metastasis: A case report

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Abstract. Cadonilimab is a bispecific immune checkpoint inhibitor (ICI) targeting both programmed death 1 and cytotoxic T-lymphocyte activator 4, thus blocking both immune checkpoint pathways. Cadonilimab exerts several antitumor effects and is used to treat various types of cancer, including gastric, liver, lung, cervical and pancreatic cancer, and esophageal squamous cell carcinoma. However, ICIs are also associated with the onset of several immune-related adverse events (irAEs), including immune-mediated pneumonia, immune-mediated colitis and myocarditis. Among them, myocarditis is a rare but potentially life-threatening side effect. The current study describes the case of a 49-year-old patient with lung cancer and myocardial metastasis, who developed myocarditis and heart failure following therapy with cadonilimab. After three cycles of cadonilimab treatment for 2 months, the patient experienced persistent wheezing and a paroxysmal cough, prompting hospitalization. Multidisciplinary assessment and laboratory findings supported a diagnosis of immune-related myocarditis. Following treatment with low-dose diuretics and intravenous methylprednisolone (adjusted dose), and management of anemia, the patient recovered well and was discharged on hospital day 21. This case study highlights the importance of vigilance for severe cardiovascular complications associated with dual ICI cadonilimab immunotherapy. Therefore, close outpatient monitoring is critical during treatment with cadonilimab, with particular attention awarded to the overall condition of the patients. Special consideration should be given to risk factors, such as cardiac metastasis and impaired lung function, which could predispose patients to irAEs associated with immunotherapy, and more particularly with myocarditis. Based on the current experience, the present study offers practical recommendations for the prevention of cadonilimab-induced myocarditis to improve patient outcomes.

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Abbreviations: ICI, immune checkpoint inhibitors; irAEs, immune-related adverse events; CTLA-4, cytotoxic T-lymphocyte activator 4; PD-1, programmed death 1; PD-L1, programmed death ligand 1; NSCLC, non-small cell lung cancer

Key words: cadonilimab, cancer, immune checkpoint inhibitor, myocarditis, immune-related adverse event

Introduction

Immune checkpoint inhibitors (ICIs) are antibodies that block negative regulators of T-cell immune responses, particularly programmed death 1 (PD-1) and cytotoxic T-lymphocyte activator 4 (CTLA-4). Although ICIs are increasingly recommended as standard therapies for the treatment of several types of cancer, such as lung, esophageal and colorectal cancer, their immune-enhancing effects can result in a wide range of immune-related adverse events (irAEs), including cardiovascular toxicity (1). Notably, it has been reported that combination ICI therapy targeting both PD-1 and CTLA-4 is considered as a major risk factor for the development of ICI-related myocarditis. Cadonilimab, a bispecific tumor immunotherapy drug, can simultaneously target PD-1 and CTLA-4 (2). Although cadonilimab exhibits a more favorable safety profile compared with the conventional PD-1/CTLA-4 combination therapy, myocarditis is still listed as a potential adverse effect in its prescribing information. Cadonilimab, as a novel dual ICI, has limited post-marketing experience in the field of lung cancer. To the best of our knowledge, the present study represents the first documented case of immune-mediated myocarditis induced by this agent in patients with malignant lung tumors, which renders this case particularly distinctive. The present study aims to share these clinical experiences to facilitate medical practice. Notably, this case also exhibited concurrent cardiac metastasis, a convergence of multiple rare events creating an exceptional clinical scenario. Whether cardiac metastasis potentiates the risk of immune-mediated myocarditis remains speculative and warrants further investigation for validation.

Case report

The present study reports the case of a 49-year-old male previously diagnosed with TNM stage IIIA lung cancer (pT3N2M0) (3), accompanied by multiple lymph node metastases in the mediastinum and bilateral lungs. The patient, who had undergone a radical lung cancer resection in June 2018, was admitted to Shandong Provincial Hospital (Shandong, China) in November 2023 due to persistent dyspnea and paroxysmal cough following 2 cycles of cadonilimab (625 mg administered via intravenous infusion every 3 weeks). The patient had no notable family or social history, and no prior history of heart disease. A right upper lobectomy was performed in June 2018, and the postoperative pathological examination confirmed non-small cell lung cancer (NSCLC), while the immunohistochemical results revealed programmed death ligand 1 (PD-L1) positivity (Fig. 1). The surgical intervention, postoperative pathological diagnosis and subsequent immunohistochemical analyses were all conducted at Shandong Provincial Hospital. The patient was postoperatively treated with a chemotherapy regimen that included pemetrexed and lobaplatin. The patient underwent postoperative adjuvant chemotherapy consisting of pemetrexed (800 mg) and lobaplatin (100 mg) administered via intravenous infusion. The treatment regimen comprised 3 cycles, with each cycle repeated every 21 days. During treatment, a follow-up chest computed tomography (CT) scan revealed a right-sided pleural effusion (Fig. 2), thus prompting a change of the treatment protocol. Therefore, the treatment was changed to pemetrexed and carboplatin chemotherapy combined with pembrolizumab and Endostar. The treatment protocol comprised one cycle of pemetrexed (800 mg) and carboplatin (500 mg) chemotherapy combined with pembrolizumab (200 mg intravenously every 3 weeks for 7 cycles) plus recombinant human endostatin (30 mg/day via continuous intravenous infusion pump for 7 days). In October 2019, the patient exhibited decreased cortisol levels: 13.61 nmol/l at 8:00 am (reference range, >166 nmol/l) and 11.83 nmol/l at 4:00 pm (reference range, >73.8 nmol/l). Therefore, following consultation with the Department of Endocrinology, immunotherapy was discontinued, and hydrocortisone replacement therapy was initiated with hydrocortisone at a dosage of 30 mg daily (20 mg at 8:00 am and 10 mg at 2:00 pm). Under the guidance of the Department of Endocrinology, the patient was transitioned to routine outpatient follow-up management at a frequency of once per month.

In January 2021, a CT scan showed nodular thickening of the left interlobar pleura and partial enlargement of multiple lymph nodes in the mediastinum and hilum of both lungs, suggestive of metastatic disease (Fig. 3). Due to the patient's prior development of grade III pituitary dysfunction following immunotherapy, it was decided that immunotherapy with ICIs should not be restarted. Between January 2021 and May 2021, the patient completed six treatment cycles consisting of paclitaxel (400 mg), carboplatin (500 mg) and bevacizumab (400 mg) administered intravenously every 3 weeks, while maintaining the original hydrocortisone replacement regimen. Following contraindication evaluation, three additional cycles were administered in March, April and May 2023 using a modified protocol of nab-paclitaxel (450 mg) and bevacizumab (500 mg) delivered via intravenous infusion at 3-week intervals.

In September 2023, cardiac magnetic resonance imaging (MRI) revealed localized thickening of the left and right ventricular myocardium, with diffuse abnormal signal intensity and contrast enhancement, accompanied by a significant amount of pericardial effusion. These findings were suggestive of metastatic disease (Fig. 4), and the patient was considered to exhibit progressive disease. Due to the considerable challenges in obtaining myocardial biopsy specimens from the metastatic lesions, the diagnosis was primarily based on imaging findings. Pelvic MRI performed at an external hospital revealed signs of metastasis in the soft tissues of the gluteal muscles and the right acetabulum. A biopsy of the gluteal soft-tissue mass was subsequently performed at Shandong Provincial Hospital, with pathological examination confirming squamous cell carcinoma (Fig. 5). Given the patient's prior resistance to single-agent ICI therapy and in accordance with the patient's own preferences, cadonilimab was chosen as the second-line treatment regimen. Following risk assessment and according to the patient's wishes, treatment with the PD-1/CTLA-4 bispecific antibody cadonilimab in combination with single-agent chemotherapy and anti-angiogenic therapy was initiated in September 2023. The patient was hospitalized for treatment during the same month. The treatment protocol consisted of gemcitabine (1.6 g) combined with anlotinib (8 mg) and cadonilimab (625 mg) administered via intravenous infusion every 3 weeks.

At 2 months post-cadonilimab treatment initiation, in November 2023, the patient experienced persistent dyspnea, a paroxysmal cough and expectoration of small amounts of white mucoid sputum. Laboratory tests showed elevated high-sensitivity cardiac troponin T (HS-TnT) levels at 287.00 pg/ml (reference range, <14 pg/ml). The patient's pro-B-type natriuretic peptide (pro-BNP) levels were elevated at 2,543.00 pg/ml (reference range, <125 pg/ml) (Fig. 6). Based on the patient's treatment history with cadonilimab, reported irAEs and imaging findings, immune-related pneumonia, potentially combined with immune myocarditis, was suspected.

On the following days, the patient's cardiac biomarkers continued to fluctuate with an upward trend. Transthoracic echocardiogram revealed a left ventricular ejection fraction of 53%. Serological testing did not indicate the presence of myocarditis-related viral infections. Considering the temporal association with cadonilimab initiation, a multidisciplinary team consultation supported a preliminary diagnosis of secondary immune cadonilimab-induced myocarditis.

The patient continued to experience symptoms of shortness of breath, paroxysmal cough and the production of small amounts of white mucoid sputum. Given the rapid progression commonly associated with irAEs, the patient received 160 mg methylprednisolone daily. Subsequently, the patient showed significant clinical improvement, with reduced coughing and dyspnea, and only an occasional dry cough. Laboratory tests revealed elevated C-reactive protein (CRP) and human serum amyloid A levels at 128.30 mg/l (reference range, <10 mg/l) and 279.73 mg/l (reference range, <10 mg/l), respectively. Procalcitonin and interleukin-6 (IL-6) levels were also measured, with the results showing mildly elevated procalcitonin levels at 0.26 ng/ml (reference range, <0.05 ng/ml). Considering the improvement in the patient's symptoms and the decrease in HS-TnT levels to 287.00 pg/ml (reference range, <14 pg/ml), the preliminary diagnosis of immune-related pneumonia and

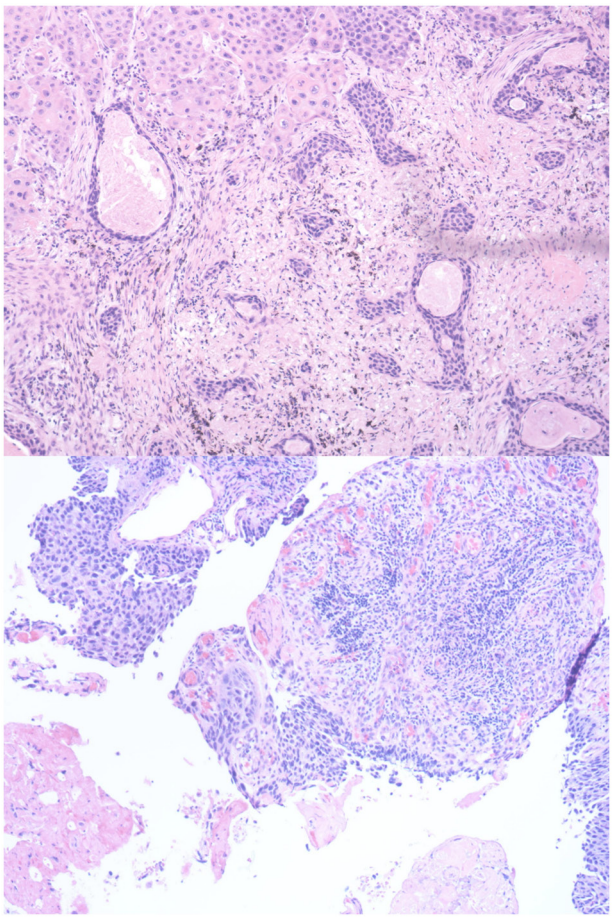

Figure 1. Pathological and immunohistochemical staining. Upper panel: Pathological section of the pulmonary lesion (hematoxylin and eosin staining; x20 magnification). Lower panel: Immunohistochemical analysis of programmed death ligand 1 expression (x20 magnification).

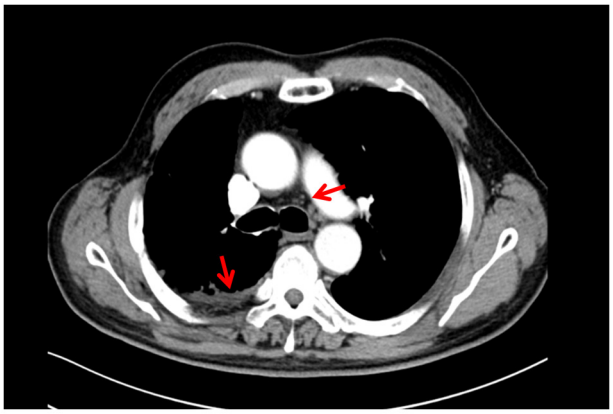

Figure 2. Postoperative chest computed tomography scan of the primary lesion. The red arrow on the left indicates pleural effusion, while the red arrow on the right denotes mediastinal lymphadenopathy.

immune myocarditis was established. Therefore, the dose of methylprednisolone was increased to 200 mg/day.

Another 2 days later, the patient experienced a worsening cough, persistent chest tightness and dyspnea. Continuous oxygen therapy was therefore administered via nasal cannula. A respiratory rate of 22-25 breaths/min (reference range,

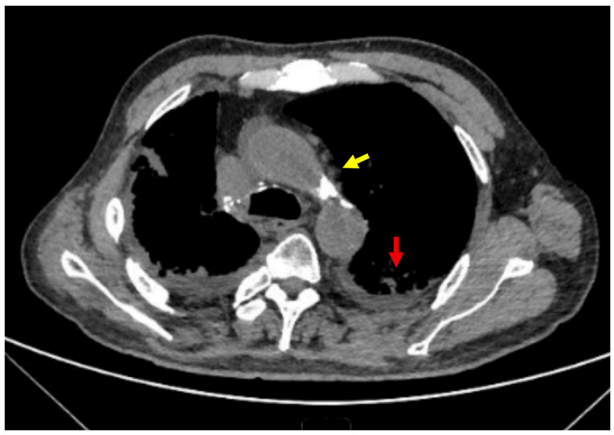

Figure 3. Chest computed tomography findings from January 2021. The red arrow indicates nodular pleural thickening in the left lung. The yellow arrow indicates multiple enlarged lymph nodes in the mediastinum and bilateral hilar regions.

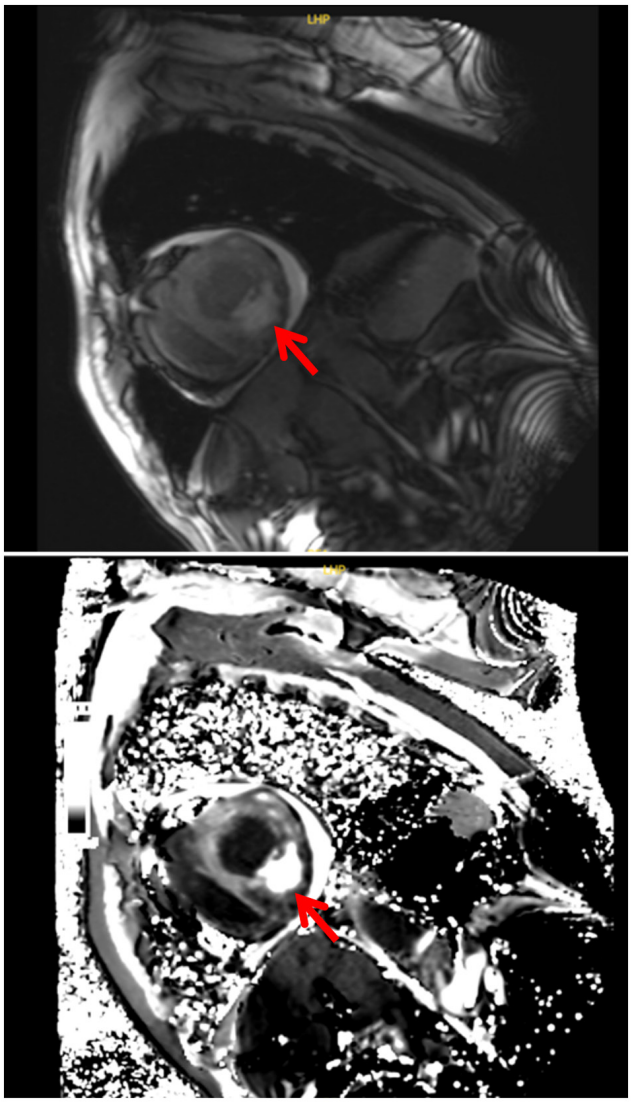

Figure 4. Magnetic resonance imaging showing myocardial metastasis. The upper image demonstrates tumor and pericardial effusion on T2-weighted imaging, while the lower image shows apparent diffusion coefficient mapping. The red arrows indicate areas of focal myocardial thickening with diffuse abnormal signal intensity and contrast enhancement, suggestive of metastatic lesions.

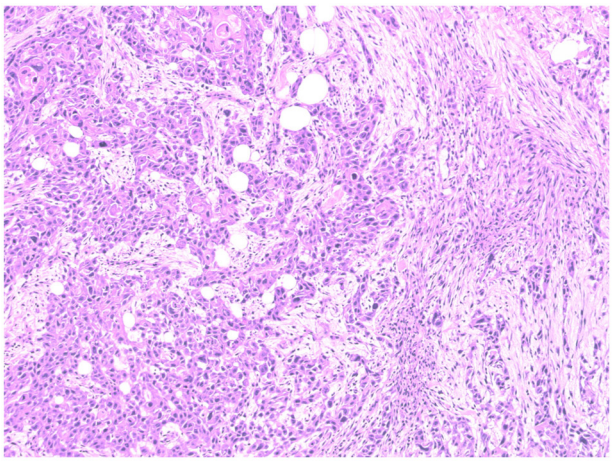

Figure 5. Histopathological image of the gluteal soft-tissue mass (H&E staining; x20 magnification).

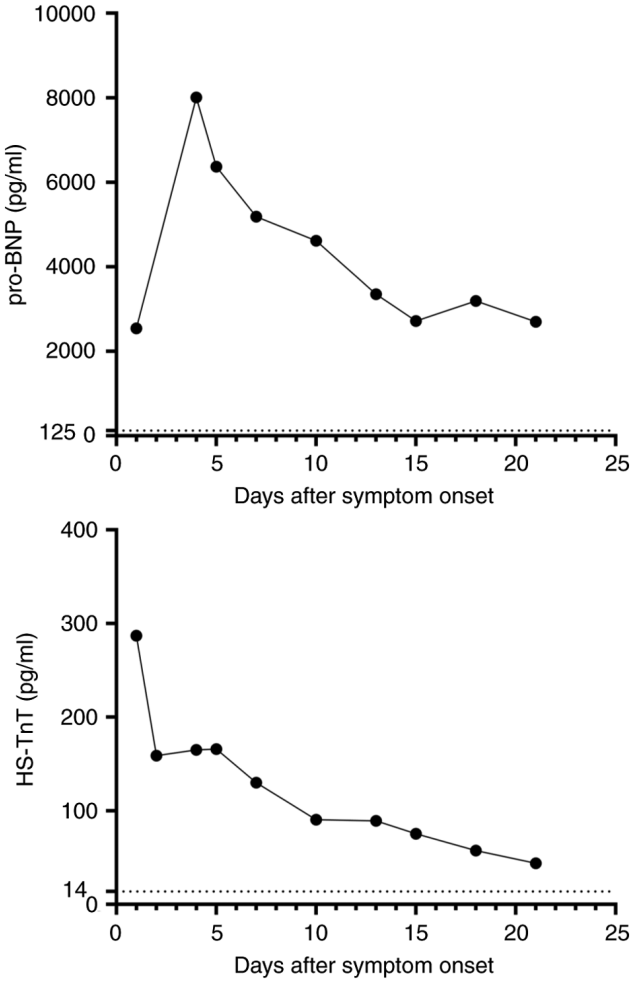

Figure 6. Timeline of three cardiac biomarkers during hospitalization. The levels of pro-BNPand HS-TnT are shown. Dotted lines represent the upper normal range. Pro-BNP, pro-B-type natriuretic peptide; HS-TnT, high-sensitivity cardiac troponin T.

16-20 breaths/min), a heart rate of 86 beats/min (reference range, 60-100 beats/min) and elevated CRP levels at 24.45 mg/l (reference range, <10 mg/l) were recorded. Despite improvement in infection markers, pro-BNP levels were significantly increased at 8,010 pg/ml (reference range, <125 pg/ml.), while the bilateral lung rales were reduced. Considering the overall clinical picture, the exacerbation of dyspnea was primarily attributed to newly developed heart failure. Due to the severity of the patient's dyspnea, continuous oxygen therapy was required. Additionally, diuretic therapy with furosemide (20 mg daily) was initiated and maintained for 3 days until clinical symptom resolution. A cardiology consultation was obtained, and based on the consequent recommendations, a low-dose diuretic regimen was initiated, comprising hydrochlorothiazide (12.5 mg administered orally once daily), spironolactone (10 mg administered orally once daily) and coenzyme Q10 (10 mg administered orally three times daily). Electrocardiography revealed a possible atrial ectopic rhythm, with ST-T abnormalities in the anterior wall, suggesting myocardial ischemia (Fig. 7). A follow-up chest CT scan showed significant improvement in the bilateral pneumonia compared with the that in previous scans.

After 3 days of furosemide diuretic therapy, the patient's respiratory-related symptoms were significantly improved. The diagnosis of heart failure was ultimately confirmed based on symptomatic relief and the corresponding reduction in NT-proBNP levels to 6,371 pg/ml (reference range, <125 pg/ml) following diuretic therapy. No significant changes in HS-TnT levels were reported. According to the recommendations from the cardiology consultation, the dose of methylprednisolone was increased to 280 mg, while the oral administration of furosemide and spironolactone was continued. Ongoing monitoring of pro-BNP levels and cardiac biomarkers was advised, along with regular assessment of albumin and electrolyte levels. On the same day, routine cardiac ultrasound revealed a solid myocardial mass, suggestive of tumor metastasis.

After 5 days of furosemide diuretic therapy, the patient reported resolution of chest tightness and dyspnea, with only an occasional cough and minor production of white mucoid sputum. Laboratory examinations demonstrated elevated pro-BNP levels at 5,185.00 pg/ml (reference range, <25 pg/ml), and HS-TnT levels at 130.00 pg/ml (reference range, <14 pg/ml). The patient exhibited decreased serum calcium and potassium levels. Despite the aforementioned abnormal laboratory results, the clinical condition of the patient continued to improve, with pro-BNP levels showing a downward trend, thus allowing the continuation of diuretic therapy. However, since diuretic therapy led to hypoalbuminemia, the patient received artificial albumin. Given the persistently increased HS-TnT levels, the management plan included continuation of 280 mg of methylprednisolone once daily for 3 more days.

After 8 days of furosemide diuretic therapy, the patient was clinically stable, with no fever, notable coughing, sputum production or symptoms of chest tightness and dyspnea. Potassium levels increased from 2.72 to 4.12 mmol/l (reference range, 3.5-5.3 mmol/l) and albumin levels increased from 26.8 to 31.1 g/l (reference range, 40-55 g/l), and therefore the intravenous administration of artificial albumin was discontinued, while oral potassium citrate granules were continued for potassium replacement. The serum levels of HS-TnT and pro-BNP continued to decline, and the dose of methylprednisolone was reduced to 200 mg. The other treatment regimens remained unchanged.

At 12 days after the initial onset of the persistent dyspnea and paroxysmal cough, the patient's immune myocarditis and

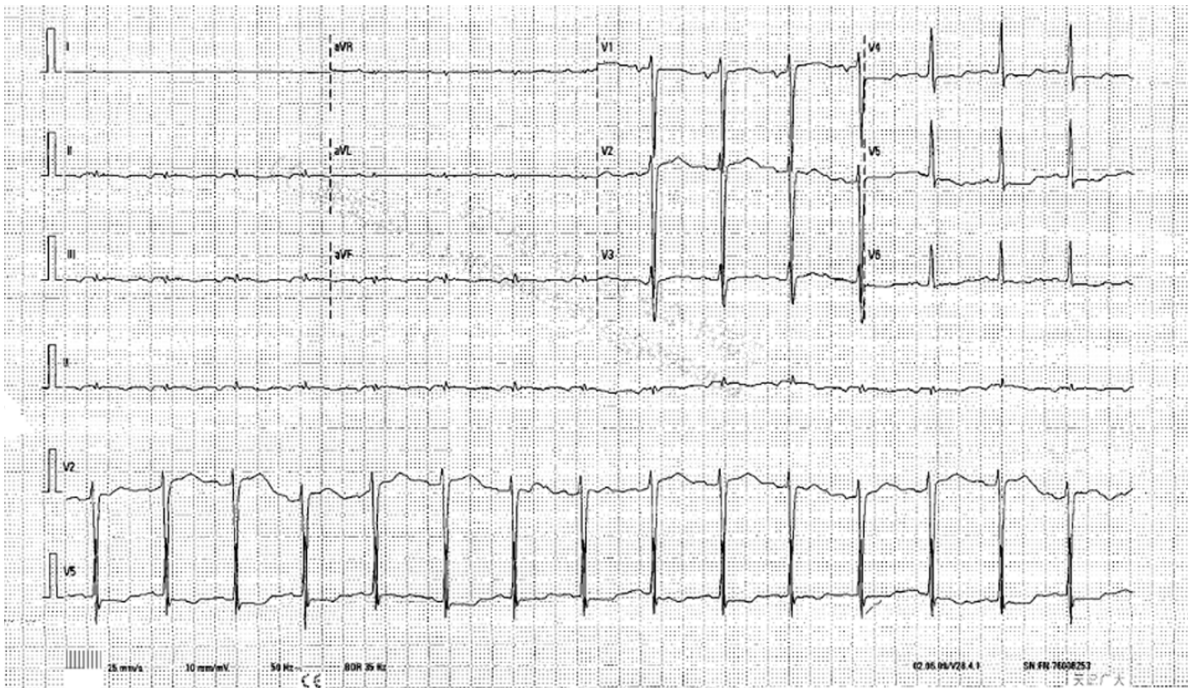

Figure 7. Electrocardiogram suggestive of possible ectopic atrial rhythm.

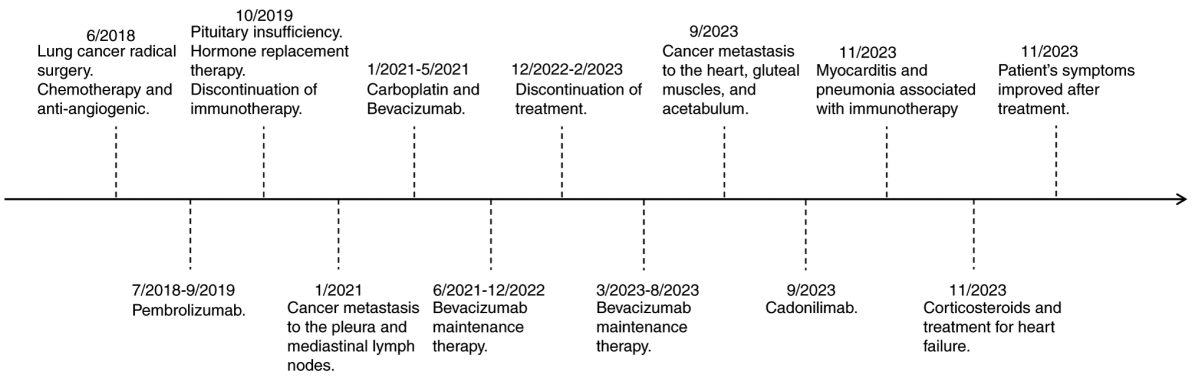

Figure 8. Chronology of key events.

pneumonia were under control, and the clinical condition was stable. Following a multidisciplinary discussion with the Department of Cardiology, it was decided that no further adjustment to the corticosteroid therapy was necessitated. Anti-inflammatory and diuretic treatment was continued.

At 14 days after the initial onset of the persistent dyspnea and paroxysmal cough, the patient reported a recurrence of significant dyspnea. The levels of HS-TnT had increased to 75.50 pg/ml. Further laboratory examinations revealed pro-BNP levels at 2,719.00 pg/ml (Fig. 6). Despite the aforementioned symptoms, a follow-up examination indicated improvement in cardiac function, and therefore the dose of methylprednisolone was reduced to 160 mg once daily.

At 17 days after the initial onset of the persistent dyspnea and paroxysmal cough, evaluation of the cardiac biomarkers showed HS-TnT levels at 57.50 pg/ml (reference range, <14 pg/ml) and pro-BNP levels at 3,191.00 pg/ml (reference range, <125 pg/ml) (Fig. 6). Due to persistent hypoalbuminemia, hypocalcemia and hypokalemia, oral potassium and calcium supplementation was continued, while the dose of methylprednisolone was further reduced to 120 mg once daily.

20 days after the initial onset of persistent dyspnea and paroxysmal cough, significant improvement in the levels of the three cardiac biomarkers was observed, with HS-TnT and pro-BNP levels at 43.90 pg/mland 2,701.00 pg/ml, respectively (Fig. 6). Since the clinical condition of the patient remained stable, with largely controlled immune myocarditis and pneumonia, and no indications for further antitumor therapy, the patient was discharged with instructions for regular home monitoring (Fig. 8). Regarding steroid therapy, the patient received 80 mg prednisone once daily for 1 week, followed by a weekly reduction of 20 mg until discontinuation after 4 weeks.

Discussion

The present study reports the case of a patient with lung cancer who developed irAEs, including both pneumonitis and myocarditis induced by the bispecific ICI cadonilimab, concurrently

with cardiac metastasis, a relatively uncommon clinical manifestation. The patient successfully recovered following treatment with glucocorticoids and diuretics for heart failure, combined with symptomatic management. Currently, to the best of our knowledge, there are no other reports on cadonilimab-induced immune myocarditis. In recent years, immunotherapy has fundamentally changed the treatment strategy for NSCLC (4). The use of PD-1/PD-L1 inhibitors combined with anti-CTLA-4 antibodies as first-line therapy has significantly improved survival outcomes in patients with advanced NSCLC compared with platinum-based chemotherapy alone (5). Cadonilimab is a PD-1/CTLA-4 bispecific tumor immunotherapy drug that can simultaneously bind to PD-1 and CTLA-4, thus inhibiting both immune checkpoint pathways. A clinical trial indicated that in patients with metastatic NSCLC, cadonilimab showed notable efficacy as a second-line monotherapy after the failure of platinum-based double chemotherapy and initial immunotherapy, with outcomes similar to those of other ICIs used after first-line chemotherapy (2). Furthermore, a reported case of immunotherapy-resistant advanced lung adenocarcinoma demonstrated favorable therapeutic efficacy with cadonilimab combined with chemotherapy (6).

However, in particular cases, the therapeutic benefits of ICIs can be offset by the development of severe irAEs. For instance, myocarditis is a rare but serious side effect of ICIs, characterized by a high mortality rate of 39.7% (1). Compared with combination ICI therapy, cadonilimab exhibits a more favorable safety profile. However, the prescribing information of the drug still indicates a potential risk of inducing immune myocarditis. ICIs targeting CTLA-4 or PD-1/PD-L1 are associated with the development of several irAEs, including immune-mediated pneumonia, immune-mediated colitis and myocarditis. A previous study demonstrated that PD-1/CTLA-4 combination therapy-related mortality was typically attributed to colitis (32/86 of reported cases; mortality rate, 37%) and myocarditis (22/88 of reported cases; mortality rate, 25%), with myocarditis showing the highest fatality rate (52/131 of reported cases; mortality rate, 39.7%) (7). The majority of cases of myocarditis and related mortality occur early after the initiation of ICI therapy (8). The median time to onset of myocarditis is ~27 days (range, 5-155 days) (1). Combination ICI therapy is a major risk factor for ICI-related myocarditis, with a higher incidence of myocarditis being reported in patients receiving combination therapy compared with that in patients treated with CTLA-4 or PD-1/PD-L1 monotherapy (8). Cumulative evidence has demonstrated that combined CTLA-4 and PD-1 inhibition represents the primary risk factor for immune checkpoint inhibitor-induced myocarditis. Both CTLA-4 and PD-1 can inhibit T-cell activation. However, they act through different cellular and molecular mechanisms (9). Therefore, the increased incidence of myocarditis observed with combination therapy could be attributed to the additive immunomodulating effects of targeting both biological pathways or from the functional interactions between CTLA-4 and PD-1 that exacerbate the development of myocarditis (10). The management of ICI-induced myocarditis typically involves high-dose corticosteroids, which have been shown to reduce the risk of major adverse cardiac events (11). In the current case, high-dose methylprednisolone treatment was administered, resulting in a favorable clinical recovery.

The patient exhibited elevated IL-6 levels 1 day after the onset of myocarditis symptoms. A single-center retrospective cohort study indicated that IL-6 and tumor necrosis factor-α were the most commonly elevated cytokines in ICI-related myocarditis, thus supporting the diagnostic potential of these markers (12). Emerging evidence has highlighted the presence of shared antigens or high-frequency T-cell receptor sequences among the myocardium, skeletal muscle and tumor tissues (13), thus suggesting that cadonilimab could target myocardial cells while exerting its antitumor effects. The loss of CTLA-4/PD-1 axis function could also result in the development of autoimmune myocarditis and dilated cardiomyopathy, indicating that these molecules could serve a key role in preventing autoimmunity (9). Furthermore, PD-L1 gene deletion and anti-PD-L1 treatment could promote the progression of transient myocarditis into a fatal form, thus implying that PD-1/PD-L1 and CTLA-4 could play a crucial role in limiting T cell-mediated autoimmune myocarditis (9,10).

In patients with ICI-related myocarditis, expansion of cytotoxic $CD8^+$ T effector cells, and more particularly CD45RA cells (Temra $CD8^+$ cells), has been reported. Transcriptomic analyses of these Temra $CD8^+$ clones demonstrated a highly activated and cytotoxic phenotype (9). It was therefore speculated that following treatment with ICIs, activated T cells could not only recognize tumor antigens, but also shared myocardial antigens, thereby triggering myocarditis (14). Furthermore, it has been also reported that cadonilimab can effectively induce the secretion of IL-2 and IFN-γ, which may contribute to myocardial damage. Notably, high doses of IL-2 have been associated with severe cardiac toxicity. In a study on IL-2-induced cardiac toxicity, among 57 patients receiving high-dose IL-2 therapy, 2 cases (3.5%) developed IL-2-induced myocarditis (15). In the present case, following multidisciplinary consultation and considering the patient's condition, a high-dose corticosteroid regimen was chosen, resulting in a favorable recovery. However, in more severe cases of immune myocarditis, high-dose corticosteroids alone may not effectively reverse disease deterioration, thus requiring more effective therapeutic approaches. A study establishing a murine ICI-induced myocarditis model demonstrated that depletion of $CD8^+$ T cells or macrophages, combined with IFN-γ signaling blockade, significantly reduced cardiac infiltration of C-X-C motif chemokine ligand-expressing ($CXCL9^+$ and $CXCL10^+$) macrophages, thereby attenuating myocarditis progression. This therapeutic approach may confer translational implications for future myocarditis management. ICI-related myocarditis is associated with the expansion of a specific population of inflammatory IFN-γ-induced macrophages, thus suggesting that IFN-γ blockade could be a potential therapeutic approach for this condition (16). In a previous study, treatment with CTLA4-immunoglobulin (CTLA4-Ig) successfully rescued mice with lethal myocarditis developed in $Ctla4^{+/-}$ $Pdcd1^{-/-}$ mice. The severity of myocarditis was found to be gene dosage-dependent, thus suggesting that restoring CTLA4 and/or PD-1 signaling could be sufficient to prevent disease progression. Abatacept, a recombinant CTLA4-Ig, could significantly reduce mortality in $Ctla4^{+/-}$ $Pdcd1^{-/-}$ mice (17). Therefore, CTLA4-Ig could hold therapeutic potential in treating severe refractory ICI-related myocarditis. Additionally, a case report on a patient with corticosteroid-refractory ICI-related myocarditis showed that treatment with abatacept resulted in favorable clinical

outcomes (18). In addition, in another case of severe fulminant myocarditis induced by nivolumab, an ICI, extracorporeal membrane oxygenation was also an effective therapeutic option in life-threatening situations (19). The present case report serves as an important reminder for clinicians. Particular vigilance is needed when administering ICIs to patients with cardiac metastasis, since they can be at enhanced risk for developing irAEs, such as myocarditis.

In conclusion, ICIs have the potential to induce severe irAEs. More particularly, with ICIs, such as cadonilimab, early recognition and timely treatment are crucial for improving clinical outcomes. Close monitoring of the patient's early response to immunotherapy is essential, along with awareness of potential risk factors, such as cardiac metastases. In terms of treatment, high-dose corticosteroids are considered as the cornerstone of treatment of several irAEs, including myocarditis. Based on our clinical experience, we recommend that treatment plans should be developed through multidisciplinary consultations to ensure prompt management of irAEs.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

TL, ZY, QL and RZ were responsible for analyzing patient data and treatment administration. TL, BZ, ZK and PZ contributed to advising on patient treatment and obtaining medical images. TL wrote the manuscript. All authors have read and approved the final version of the manuscript. TL, ZY, QL, RZ, BZ, ZK and PZ confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

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

Competing interests

The authors declare that they have no competing interests.

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