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Case Report

Internal Medicine Section

Probable Nivolumab-induced Myocarditis Presenting as Fulminant Heart Failure in an Elderly Patient with Advanced Hodgkin's Lymphoma: A Case Report

HARISRITHA PALADAGU[1], STEVE THOMAS[2]

ABSTRACT

Immune checkpoint inhibitors have revolutionised the management and treatment of various malignancies, including advanced-stage Hodgkin's lymphoma. Here is a case of a 76-year-old female patient who presented with a history of fatigue, generalised weakness and pedal oedema for the past two months. The patient was initially found to have severe pancytopenia. On further evaluation, the patient was diagnosed with Stage IV Hodgkin's lymphoma. The patient was initiated on chemotherapy with a Nivolumab-containing regimen. After two weeks, the patient developed breathlessness, hypoxia and pulmonary oedema. Cardiac evaluation revealed global left ventricular hypokinesia with an ejection fraction of 35% on echocardiography, and serial biomarkers were found to be elevated. Despite maximum care and management, the patient died of cardiogenic shock. Nivolumab, though rare, has been found to cause myocarditis. This highlights the need for vigilant use of Immune checkpoint inhibitors, considering the risk of serious complications, particularly among elderly patients.

Keywords: Cardiogenic shock, Cardiotoxicity, Immune checkpoint inhibitors, Immune-related adverse events, Programmed death-1 inhibitor

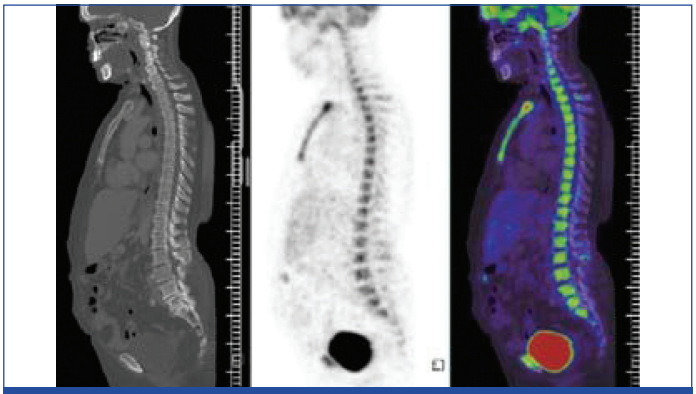
CASE REPORT

A 76-year-old female reported with complaints of fatigue, generalised weakness and pedal oedema for the past two months. The patient was apparently asymptomatic until two months ago, following which she presented with complaints of fatigue and generalised weakness, initially on exertion, gradually progressing to fatigue while performing less than ordinary activities associated with gradually progressive pedal oedema. There were no associated complaints of chest pain, palpitations, syncope or decreased urinary output. There was no prior documented history of ischaemic heart disease, hypertension, or diabetes. There was no history of smoking (active and passive) or alcohol consumption. There was no family history of malignancy.

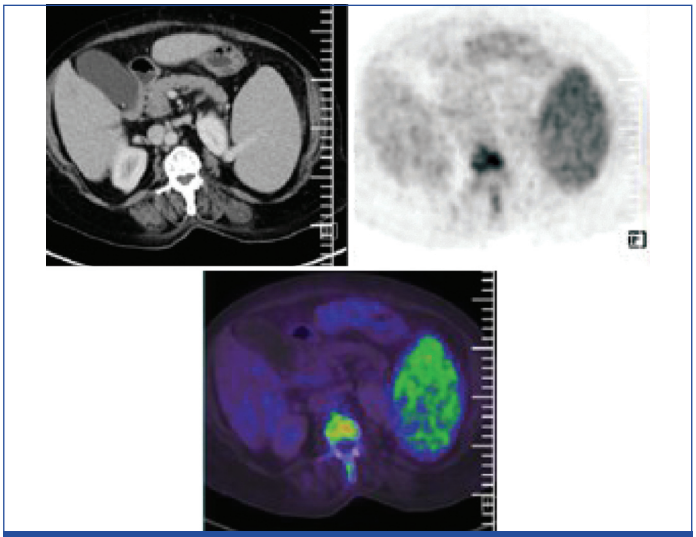
On examination, blood pressure was 110/70 mmHg, pulse rate was 76 beats per minute with regular rhythm and normal volume, and SpO2 was 98% with room air. Pallor and bilateral pitting pedal oedema were noted. There were no signs of icterus, cyanosis, clubbing or lymphadenopathy. Cardiovascular and respiratory examinations were unremarkable. On abdominal examination, the patient had no palpable organomegaly.

Initial laboratory investigations revealed pancytopenia (haemoglobin: 6.2 g/dL, total leukocyte count: 680/µL, neutrophils: 31%, lymphocytes: 60% and platelet count: 57,000/µL). The peripheral smear showed normocytic, normochromic red blood cells with elliptocytes and tear-drop cells. Bone marrow aspiration and biopsy revealed features consistent with Hodgkin's lymphoma with CD30 positivity. A whole-body PET-CT scan demonstrated widespread metabolically active disease with SUV maximum 9.1 taken at the level of the body of the left iliac bone, findings with small volume lymph nodes having fluorodeoxyglucose uptake above and below the diaphragm consistent with stage IV Hodgkin's lymphoma [Table/Fig-1-3].

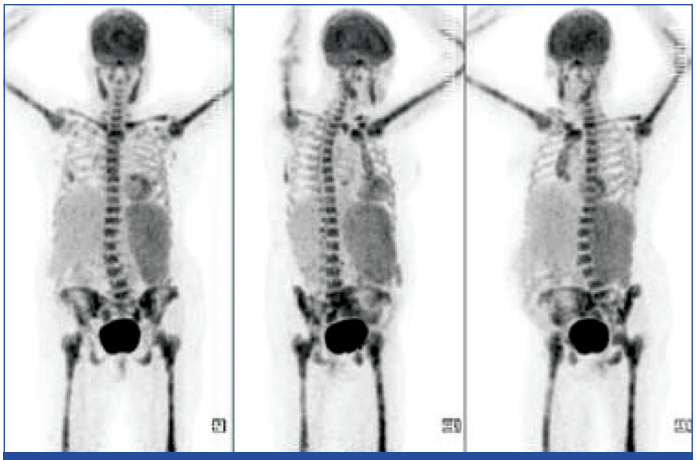
ECG demonstrated normal sinus rhythm with a heart rate of 71 beats/minute and a QT interval of 423 ms. Two-dimensional echocardiography revealed a left ventricular ejection fraction of 60%



[Table/Fig-1]: An 18F-FDG PET CT image showing diffuse increased fluorodeoxyglucose uptake along the vertebral column, consistent with bone marrow involvement.



[Table/Fig-2]: The 18F-FDG PET CT image representing fluorodeoxyglucose-avid splenomegaly with diffusely increased tracer uptake compared to background activity.



[Table/Fig-3]: The 18F-FDG PET/CT image demonstrating diffuse increased Fluorodeoxyglucose uptake throughout the axial and appendicular skeleton.

with mild concentric left ventricular hypertrophy with no associated regional wall motion abnormality. Baseline Troponin I done before initiating the chemotherapy regimen (comprising nivolumab, vinblastine, doxorubicin, and dacarbazine) was 0.01 ng/mL.

The patient was initiated on chemotherapy on December 9, 2025, comprising nivolumab (140 mg diluted in 100 mL normal saline, administered following premedication with intravenous methylprednisolone 125 mg, intravenous pheniramine maleate, and oral paracetamol 650 mg), intravenous vinblastine 9 mg, intravenous doxorubicin (35 mg diluted in 100 mL normal saline and infused over 15 minutes), and intravenous dacarbazine (560 mg diluted in 250 mL of 5% dextrose and infused over one hour).

Approximately two weeks after initiation of therapy, she developed an acute onset of breathlessness and hypoxia. On readmission (around December 21, 2025), the patient was tachypnoeic and hypoxic, requiring oxygen support. Clinical examination revealed features suggestive of acute pulmonary oedema with bilateral crepitations. Chest X-ray showed diffuse bilateral fluffy opacities with minimal bilateral pleural effusion, and ultrasound abdomen showed hepatomegaly suggestive of systemic congestion.

Electrocardiogram showed sinus tachycardia 125 beats per minute, QT interval 430 ms without significant ST-T changes. Cardiac biomarkers at admission were elevated, with troponin levels of 3.24 ng/mL and B-type Natriuretic Peptide (BNP) levels of 3000 pg/mL. Two-dimensional transthoracic echocardiography revealed global left ventricular hypokinesia with a left ventricular ejection fraction of 35%, consistent with moderate systolic dysfunction. Repeat cardiac biomarker assessment after six hours demonstrated a rising trend, with troponin levels increasing to 4.40 ng/mL and BNP levels to 3500 pg/mL.

These findings suggested an acute onset of cardiac dysfunction with heart failure. Blood and urine cultures were negative, ruling out sepsis-related cardiac dysfunction. The differential diagnoses considered included immune checkpoint inhibitor-associated myocarditis, anthracycline-induced cardiotoxicity, acute coronary syndrome, and stress-induced (Takotsubo) cardiomyopathy. However, the acute onset of symptoms within two weeks of initiation, along with elevated cardiac biomarkers, favored immune-mediated cardiotoxicity [1-3]. Anthracycline toxicity was considered; however, it is less common and typically associated with higher cumulative doses, making it a less likely primary aetiology in this case.

A definitive diagnosis could not be established due to the absence of cardiac MRI or endomyocardial biopsy, which remains a limitation of this report.

The patient was managed with oxygen support, intravenous diuretics, and close haemodynamic monitoring. Due to worsening respiratory distress and persistent tachycardia, she required intensive care admission, mechanical ventilation and inotrope support. High-dose intravenous methylprednisolone (1 g/day for 3 days) was initiated in view of suspected immune check point inhibitor-associated myocarditis, with a plan to taper steroids subsequently.

During hospitalisation, the patient developed haematuria. Urine culture showed no growth. Antiplatelets and anti-coagulation were withheld despite which the patient continued to have haematuria. However, a detailed urogenital evaluation could not be performed due to the patient's rapidly deteriorating clinical condition. Immune-related cystitis was considered as a differential in this clinical context. Despite aggressive management, the patient developed refractory cardiogenic shock and succumbed to illness.

DISCUSSION

The regimen comprising doxorubicin, bleomycin, vinblastine, and dacarbazine has historically been considered the standard of care for classical Hodgkin lymphoma. However, bleomycin-related pulmonary fibrosis and morbidity remain significant concerns. In recent years, immune checkpoint inhibitors such as nivolumab have shown promising efficacy and improved tolerability. Emerging evidence supports the use of nivolumab-containing regimens as a viable alternative, especially in patients with advanced Hodgkin lymphoma [4]. In this case, the choice of nivolumab-based regimen was guided by these considerations.

Immune checkpoint inhibitors, including nivolumab, have revolutionised cancer therapy but are associated with immune-related adverse events affecting multiple organs. Cardiovascular toxicity, though rare, is increasingly recognised, with myocarditis being the most severe manifestation [1]. Immune checkpoint inhibitor-associated myocarditis has an incidence of approximately 0.5-1% but carries a high mortality rate of up to 50% [1,5]. The mechanism involves T-cell-mediated myocardial inflammation due to loss of immune tolerance [5,6].

Symptoms typically occur early, often within the first few weeks of therapy initiation, consistent with the present case [2]. Electrocardiographic abnormalities such as conduction disturbances, atrioventricular block and arrhythmias, which are commonly reported in immune checkpoint inhibitor-associated myocarditis, may precede overt ventricular dysfunction. Cardiac biomarkers, particularly troponin, are highly sensitive and may be elevated even in subclinical disease, making them useful for early detection and monitoring [1,2,5].

Immune checkpoint inhibitor-associated myocarditis, although uncommon, has been increasingly reported in the literature with a similar pattern of early onset and early clinical deterioration [7,8]. Several studies describe fulminant myocarditis occurring shortly after initiation of nivolumab therapy, often progressing to cardiogenic shock despite aggressive management. In a multicentre study by Mahmood SS et al., fatal myocarditis developed within weeks of therapy initiation, progressing rapidly to cardiogenic shock and death [1]. Similarly, a case report by Bharathidasan K et al., described fatal myocarditis secondary to nivolumab, highlighting the aggressive clinical course and potential for rapid decompensation [9]. Furthermore, emerging evidence suggests that immune checkpoint inhibitor-related myocarditis represents a severe and potentially fatal form of cardiotoxicity with variable presentation but consistently high mortality [1]. In comparison, this patient developed symptoms within two weeks of initiation of nivolumab and progressed rapidly to fulminant heart failure and cardiogenic shock. This clinical course closely mirrors previously reported cases, reinforcing the need for early recognition and intervention.

Guidelines from the European Society of Cardiology (ESC) and American Society of Clinical Oncology (ASCO) recommend immediate discontinuation of immune checkpoint inhibitors, early initiation of high-dose corticosteroids and multidisciplinary management [2,3,10].

In steroid-refractory cases, additional immunosuppressive agents such as mycophenolate mofetil, intravenous immunoglobulin, or abatacept may be considered, although evidence remains limited and largely based on case series [2,3,10].

In this case, the temporal association, elevated cardiac biomarkers, and new-onset Left Ventricular (LV) dysfunction strongly suggest Immune Checkpoint Inhibitor (ICI)-induced myocarditis. Although anthracycline-induced cardiotoxicity is an important differential, it usually correlates with cumulative dose exposure. Early toxicity is rare but possible [1]. Blood and urine cultures were negative, tropical panel was negative, ruling out sepsis-related cardiac dysfunction. Acute coronary syndrome was considered unlikely, as echocardiography demonstrated global hypokinesia, in contrast to segmental regional wall motion abnormalities typically seen in ischaemic myocardial injury [1]. Stress-induced cardiomyopathy was considered unlikely due to the absence of a typical apical ballooning pattern on echocardiography [1].

The absence of confirmatory investigations such as cardiac MRI or biopsy limits diagnostic certainty; however, real-world clinical scenarios often rely on exclusion of alternative aetiologies. This case highlights the importance of baseline cardiac evaluation before initiating ICI therapy, early recognition of cardiac symptoms, evaluation and prompt initiation of immunosuppression. Early onset of cardiac dysfunction following nivolumab therapy in this patient highlights the need for heightened clinical vigilance during the initial treatment cycles.

CONCLUSION(S)

Nivolumab-associated myocarditis is uncommon but can progress rapidly and may be fatal. New symptoms such as breathlessness, hypoxia, arrhythmia following ICI therapy should lead to urgent evaluations that include ECG, troponin/BNP and echocardiography with consideration for cardiac MRI and early immunosuppression if myocarditis is suspected. Assessing baseline risks and early monitoring may be especially crucial for older patients receiving combination therapy.

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PARTICULARS OF CONTRIBUTORS:
1. 3rd Year General Medicine Postgraduate Student, Department of General Medicine, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.
2. Consultant, Department of Hematology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Harisritha Paladagu,
Flat No. 404, Tower 1a, Prince Highlands Apartments, Iyyapanthangal,
Chennai-600056, Tamil Nadu, India.
E-mail: iisrithaii@gmail.com

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