

Diffuse myocardial infiltration in secondary cardiac lymphoma: A case report

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Abstract. Cardiac lymphomas are rare, with a high proportion developing as secondary lymphomas. The symptoms of secondary heart lymphoma are often nonspecific and may not be detected promptly, leading to a poor prognosis. This case report describes the case of a 53-year-old male patient diagnosed with diffuse large B-cell lymphoma originating in the thymus. Prior to treatment, ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) confirmed the diagnosis of diffuse lymphoma invasion in the heart. After chemotherapy, the cardiac lesions largely regressed. Cardiac magnetic resonance imaging, echocardiography and PET/CT revealed post-chemotherapy tumor necrosis and fibrosis in the myocardium, resulting in the formation of a left ventricular aneurysm. This case report discusses the diagnosis and treatment of secondary cardiac lymphoma, focusing on diffuse myocardial infiltration as the primary manifestation.

Introduction

The incidence of malignant tumors in the heart is low (1) and secondary tumors are more common (2). Cardiac lymphoma, which includes both primary and secondary tumors, refers to a lymphoma that invades the heart and pericardium. Secondary cardiac lymphoma is more prevalent than its primary counterpart, accounting for 20% of all secondary cardiac tumors,

with mortality rates of ~8.5-25% (2). It is most common in men, particularly for patients with immunosuppression, with a median age of 60 years (3,4). It is more frequently associated with non-Hodgkin's lymphoma of B-cell origin, particularly diffuse large B-cell lymphoma (DLBCL) (5), and typically presents as a right-sided heart mass (6).

The diagnosis of secondary cardiac lymphoma is challenging due to the lack of symptoms and numerous secondary cardiac lymphomas are identified at autopsy. In the few symptomatic patients, clinical manifestations are frequently nonspecific. These may include characteristic features such as superior vena cava syndrome, respiratory distress (dyspnea), constitutional symptoms and thoracic pain (7-9). In addition, patients who undergo current combination chemotherapy regimens have good prognoses. However, secondary cardiac lymphoma outcomes remain poor due to delayed diagnoses caused by the lack of symptoms (6). Thus, an understanding of the manifestations of secondary cardiac lymphoma may lead to early diagnosis and improved survival rates for these patients. The present case report describes the clinical presentation and treatment of a 53-year-old male patient diagnosed with secondary DLBCL of the heart. The primary imaging feature before treatment was diffuse lymphoma infiltration in the myocardium, resulting in cardiac enlargement. Following chemotherapy, the cardiac tumor resolved and myocardial necrosis occurred, leading to the formation of a left ventricular aneurysm. Throughout the diagnosis and treatment process, multimodal imaging was used to diagnose and monitor the patient's cardiac condition.

Case report

A 53-year-old male presented at Mianyang Central Hospital (Mianyang, China) in May 2023 with pain and swelling behind their sternum for ~20 days. The patient denied having had any fever or weight loss but reported fatigue and dyspnea. The patient's initial blood pressure was normal at 104/79 mmHg and the heart rate was 107 beats per minute (normal range, 60-100 beats per minute). The patient had no history of lymphoma. The clinical examination results were unremarkable. Enhanced chest computed tomography (CT) revealed a mediastinal mass, enlargement of the heart with predominant enlargement of the left ventricle, thickening of the pericardial

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wall and a small amount of fluid accumulation in the pericardial cavity (Fig. 1A and B). Minor bilateral pleural effusion was also observed. Electrocardiography indicated T-wave inversion in leads I, II, aVL and V2-V6, and the persistent T-wave inversions may reflect chronic structural remodeling of the left ventricle.

Due to the risk associated with cardiac puncture, the patient refused to undergo cardiac biopsy. Subsequently, the patient underwent pathological biopsy of the mediastinal mass with a punch needle. Subsequently, hematoxylin and eosin staining and immunohistochemical staining were performed according to standard protocols (10). Hematoxylin and eosin staining showed proliferative lesions in lymphoid tissue, disappearance of follicular structures and significant cellular pleomorphism (Fig. 1C). The immunohistochemical staining was positive for CD20 (cat. no. kit-0001), CD79 α (cat. no. RMA-0552), Bcl-2 (~90%; cat. no. RMA-0660), multiple myeloma oncogene 1 (cat. no. RMA-0310), paired box gene 5 (cat. no. MAB-0706) and Kiel-67 (~80%; cat. no. RMA-0731); scattered positive for CD3 (cat. no. MAB-0740) and Bcl-6 (cat. no. MAB-0746); negative for CD5 (cat. no. MAB-0827), CD23 (cat. no. MAB-0504), cellular myelocytomatosis oncogene (cat. no. RMA-0552), CD10 (cat. no. MAB-0668), pan-cytokeratin (cat. no. kit-0009) and terminal deoxynucleotidyl transferase (cat. no. RMA-0651) (Fig. 1D and E). The ready-to-use antibodies used for immunohistochemical staining were obtained from Maxim Biotechnology Co., Ltd. The mediastinal mass was diagnosed as a DLBCL of thymic origin according to the National Comprehensive Cancer Network guideline (11). ^{18}F -fluorodeoxyglucose positron emission tomography/CT (^{18}F -FDG PET/CT) revealed global cardiac enlargement and a diffuse increase in cardiac glucose metabolism (Fig. 2A and B). In addition, it demonstrated mediastinal invasion and involvement of the upper and lower mediastinal lymph nodes, pancreas and bone (Fig. 2A, C and D). Magnetic resonance imaging (MRI) demonstrated an increased T2 and diffusion-weighted imaging (DWI) signal within the heart (Fig. 3A and B). Cardiac ultrasonography revealed widespread thickening of the myocardial wall with an ejection fraction (EF) of 64% and a stroke volume (SV) of 92 ml (Fig. 3C). Multimodal imaging suggested cardiac invasion. After ruling out contraindications, chemotherapy was initiated with the first-line regimen R-CHOP (Rituximab 600 mg on day 0, cyclophosphamide 1 g on day 1, doxorubicin 60 mg on day 1, vincristine 2 mg on day 1 and prednisone 100 mg on days 1-5). At 5 days after the initial chemotherapy cycle, the patient exhibited a significant improvement in fatigue and dyspnea.

During chemotherapy, ultrasonography indicated a gradual improvement in heart size, with no adverse cardiac events. After completing six cycles of chemotherapy at 5 months, the patient showed no discomfort. ^{18}F -FDG PET/CT revealed a reduction in heart volume, ventricular wall thinning, increased glucose metabolism in certain areas of the left ventricular wall and complete remission of the remaining lymphoma lesions (Fig. 4A and B). Cardiac ultrasonography showed an aneurysm in the left ventricular apex with associated wall thrombus formation, an EF of 30% and an SV of 42 ml (Fig. 4C). Cardiac MRI (CMR) demonstrated extensive enhancement of the ventricular wall, indicating possible residual myocardial fibrosis or lymphoma (Fig. 4D). Except for the myocardial

abnormalities, all other lesions in the patient had resolved completely. Further antitumor treatments were not pursued due to the uncertainty of whether myocardial abnormalities represented residual lymphoma and the potential for chemotherapy or local radiotherapy to exacerbate myocardial necrosis and cause heart rupture (4). Enhanced CT was performed every 3 months after the completion of chemotherapy. At the time of writing this study (12 months post-chemotherapy), the patient's general condition was stable, with no evidence of tumor progression. The timeline of clinical treatment and the state of the disease are shown in Table I.

Discussion

Secondary cardiac lymphoma is more prevalent in the right side of the heart and is characterized by invasive, intramural and pericardial growth patterns. It may present as solitary or multiple masses. The patient with secondary cardiac lymphoma described in this case report exhibited extensive lymphoma infiltration in the ventricular wall, manifesting as infiltrative hypertrophic cardiomyopathy that extended to the mediastinal spaces. This condition is relatively rare, with only a few case studies reporting similar manifestations (3,12-14), leading to diagnostic challenges. Cardiac ultrasonography is the preferred imaging method for cardiac lymphoma invasion screening and can detect cardiac masses and abnormal myocardial echoes (15). CT can delineate the morphology, location and extent of the cardiac or mediastinal masses (16). In the present case, ultrasonography and CT scans only identified abnormal cardiac morphology without a definitive diagnosis of secondary cardiac lymphoma. CMR offers superior temporal and spatial resolutions. However, compared with myocarditis, cardiac lymphoma lacks specific MRI signals and enhancement characteristics (17). DWI and apparent diffusion coefficient (ADC) sequences are important for determining tumor malignancy. However, their application to the heart is limited owing to poor display effects, and CMR typically does not include DWI and ADC scans. In the present case, partial cardiac images were obtained during upper abdominal MRI examination. Owing to significant myocardial thickening, the DWI sequence revealed diffusion limitations in the myocardial tissue, enhancing the accuracy of the myocardial property diagnosis. For patients with substantial myocardial thickening, DWI and ADC sequences may be used to ascertain the nature of myocardial abnormalities. ^{18}F -FDG PET/CT is the preferred examination method for most lymphoma types and is indispensable for pretreatment staging, posttreatment restaging and efficacy evaluation. It can also detect asymptomatic lymphomas with cardiac invasion (3,17). In the present case, no cardiac or mediastinal space invasion by the lymphoma was identified on CT or cardiac ultrasonography prior to treatment. ^{18}F -FDG PET/CT clearly delineated the extent of lymphoma invasion in the mediastinum and heart and was used to compare changes in cardiac morphology and glucose metabolism post-chemotherapy, providing an accurate assessment of the efficacy of chemotherapy.

Currently, there are no systematic guidelines for the diagnosis and treatment of secondary cardiac lymphomas. The two fundamental treatment principles are early chemotherapy and the prevention of complications (18). As the sole effective

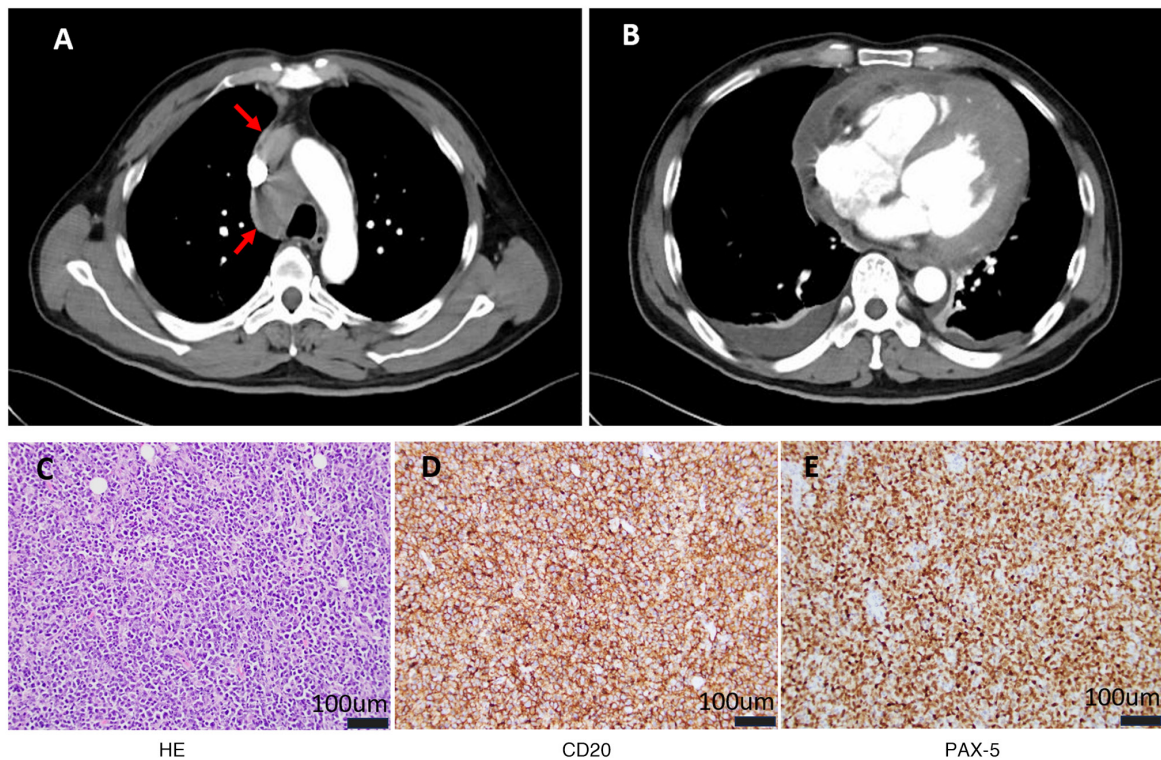


Figure 1. Chest enhanced CT and pathological images before treatment. (A) Masses in superior mediastinum (red arrow). (B) Enlargement of the heart with a predominant enlargement of the left ventricle, thickening of the pericardial wall and a small amount of fluid accumulation in the pericardial cavity. (C) Hematoxylin and eosin staining image shows proliferative lesions in lymphoid tissue, disappearance of follicular structures and significant cellular pleomorphism. (D and E) Immunohistochemical staining images positive for (D) CD20 and (E) paired box gene-5 (magnification, x200; scale bars, 100 μ m).

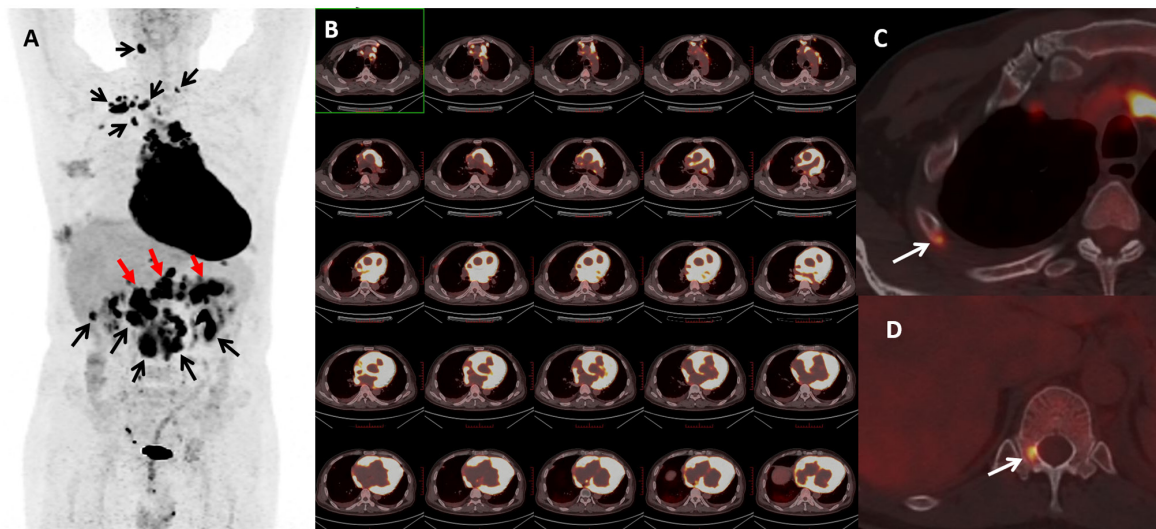


Figure 2. PET/CT imaging prior to treatment. (A) PET maximum intensity projection: Multiple high-glucose metabolism lymph nodes above and below the diaphragm (black arrows; SUVmax: 13.5) and multiple high-glucose metabolic lesions in the pancreas (red arrows; SUVmax: 15.5). (B) PET/CT fusion axial images of the mediastinum: Global and diffused accumulation of high-glucose metabolic lesions in the mediastinum and heart (SUVmax: 14.9), with the involvement of both ventricles, interventricular septum and atria. (C and D) PET/CT fusion axial images: Localized increased glucose metabolism in (C) the right third rib axilla and (D) 10th thoracic vertebrae (white arrows; SUVmax: 9.3). PET/CT, positron emission tomography/computed tomography; SUVmax, maximum standardized uptake value.

treatment, chemotherapy often aims for remission and, in rare cases, may be associated with fatal events during its initiation (16). In accordance with the National Comprehensive Cancer Network guidelines (11), the R-CHOP regimen represents the standard first-line therapeutic approach for diffuse

large B-cell lymphoma. Based on these evidence-based recommendations, R-CHOP was initiated as the primary treatment modality for the patient of the present study. The R-CHOP regimen administered in this case led to significant improvements in cardiac-related symptoms within five days

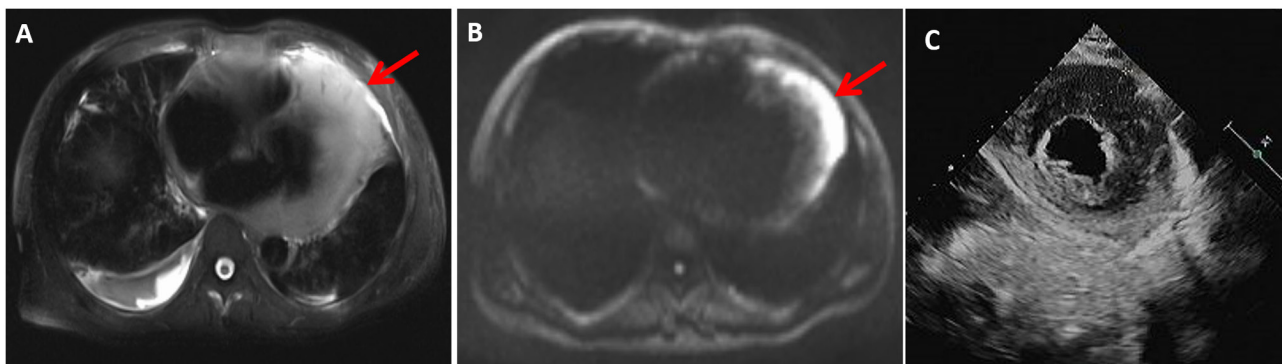


Figure 3. Imaging examination before treatment. (A) MRI T2-weighted imaging axial image: Significant thickening of the left ventricular wall and increased T2 signal (red arrow). (B) MRI DWI axial image: Increased DWI signal in the left ventricular wall, indicating diffusion limitation (red arrow). (C) Short axis echocardiography: Widespread thickening of the heart wall. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging.

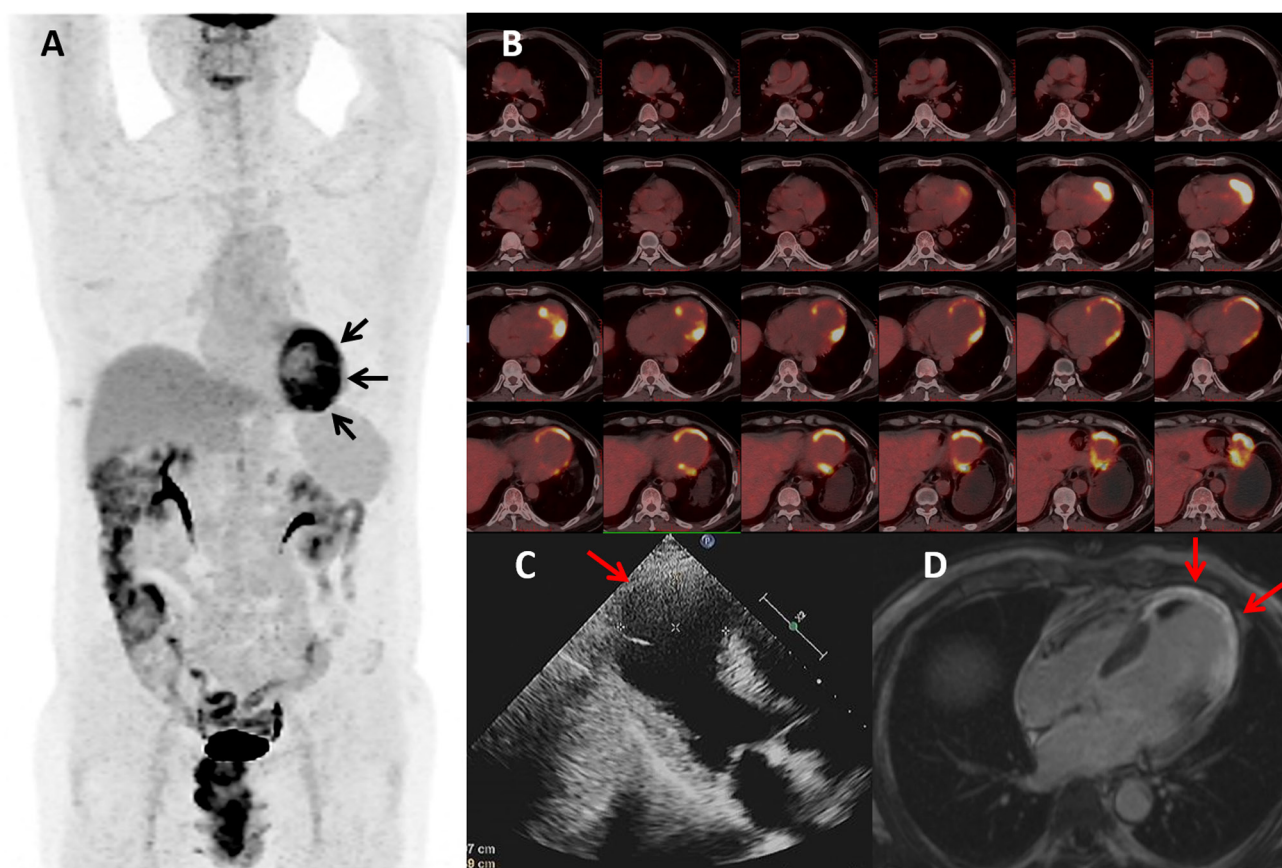


Figure 4. Imaging examination after treatment. (A) PET maximum intensity projection: A reduction in heart volume, elevated glucose metabolism in the left ventricular wall (black arrow), along with complete remission of the remaining lymphoma lesions. (B) PET/computed tomography fusion axial images of the mediastinum: Increased glucose metabolism in certain areas of the left ventricular wall (maximum standardized uptake value: 12.4). (C) Left ventricular long axis echocardiography: An aneurysm (red arrow; length, ~49.7 mm; width, ~23.8 mm) of the left ventricular apex with associated wall thrombus formation. (D) Cardiac magnetic resonance imaging delay enhancement image: Extensive enhancement of the ventricular wall (red arrow), indicating possible residual myocardial fibrosis or lymphoma. PET, positron emission tomography.

after the first chemotherapy cycle, suggesting that the chemotherapeutic agents were effective against cardiac lesions and further confirming that the cardiac abnormalities were due to lymphoma invasion. After completing six cycles of chemotherapy, multimodal imaging techniques showed that, apart from a few suspected lymphoma lesions remaining in the left ventricular wall, the remaining lymphoma lesions had resolved completely. The real-time dynamic imaging capabilities of

cardiac ultrasonography revealed the presence of a ventricular aneurysm. Although the CMR cardiac movie sequence can also be used to visualize the heartbeat, the hypertrophy of the patient's heart and the presence of an apical ventricular aneurysm limited full visualization during the scan. Although the EF and SV measured using ultrasound significantly decreased after treatment, the patient did not exhibit any symptoms. To date, no tumor recurrence has been observed during follow-up

Table I. Timeline of clinical treatment and the state of the disease.

Time-point	Presentation/event
20 days prior to admission	Pain and swelling behind the sternum.
Day 1; May 2023	Enhanced chest CT revealed a mediastinal mass, enlargement of the heart, thickening of the pericardial wall and a small amount of fluid accumulation in the pericardial cavity.
Days 5 to 15	The patient underwent pathological biopsy of the mediastinal mass and it was diagnosed as a diffuse large B-cell lymphoma of thymic origin.
Day 20	Multimodal imaging suggested cardiac invasion.
Day 23	After ruling out contraindications, chemotherapy was initiated, with the first-line regimen chosen as R-CHOP.
5 months	After completing six cycles of chemotherapy, multimodal imaging suggested that, except for the myocardial abnormalities, all other lesions achieved complete remission. The cardiac ultrasound showed an aneurysm of the left ventricular apex with associated wall thrombus formation.
Till 17 months	CT reexamination indicated no evidence of tumor progression.

R-CHOP comprised Rituximab 600 mg on day 0, cyclophosphamide 1 g on day 1, doxorubicin 60 mg on day 1, vincristine 2 mg on day 1 and prednisone 100 mg on days 1-5. CT, computed tomography.

Table II. Treatment outcomes of other similar cases.

Author/s, year	Article type	Number of cases	Pathological type	Chemotherapy regimen	PFS, months	OS, months	(Refs.)
Soens <i>et al</i> , 2012	Case report	1	DLBCL	-	1	1	(19)
Li <i>et al</i> , 2017	Case series	6	DLBCL	CHOP/R-CHOP	3-12	6-28+	(20)
Yang <i>et al</i> , 2023	Case report	1	DLBCL	CHOP, CAR-T/NK	7	18	(21)

DLBCL, diffuse large B-cell lymphoma; PFS, progression-free survival; OS, overall survival; CHOP, cyclophosphamide + doxorubicin + vincristine + prednisone; R-CHOP, Rituximab + cyclophosphamide + doxorubicin + vincristine + prednisone; CAR-T, chimeric antigen receptor T-cell; CAR-NK, chimeric antigen receptor natural killer cells.

after treatment. The patient's progression-free survival and overall survival so far were longer than 17 months.

To the best of our knowledge, only three published studies have systematically investigated cardiac involvement in DLBCL, each demonstrating distinct clinical trajectories. Soens *et al* (19) reported on a 59-year-old male presenting with acute cardiac tamponade manifesting as severe dyspnea. Despite undergoing pericardial fenestration, the patient developed fatal biventricular failure due to extensive lymphomatous myocardial infiltration within one month of intervention. Notably, the diagnosis of secondary cardiac DLBCL was only confirmed at autopsy, underscoring the diagnostic challenges associated with this condition. Li *et al* (20) conducted a retrospective analysis of 10 histologically confirmed cardiac lymphoma cases, revealing that 6 patients (60%) exhibited secondary cardiac involvement of DLBCL. Their therapeutic protocol primarily incorporated CHOP/R-CHOP chemotherapy regimens, with 3 patients (30%) receiving supplemental thoracic radiotherapy. The observed survival outcomes, with progression-free survival ranging from 3 to 12 months and

overall survival extending from 6 to >28 months, emphasize the heterogeneous, yet generally poor prognosis associated with cardiac DLBCL. In a more recent and comprehensive report, Yang *et al* (21) detailed the clinical course of a 59-year-old male patient with DLBCL confirmed through combined histopathological examination of mediastinal and peripancreatic masses, further validated by fluorescence *in situ* hybridization analysis. This case was particularly notable for its extensive treatment protocol, which sequentially incorporated R-CHOP chemotherapy, anti-CD19 chimeric antigen receptor T-cell immunotherapy, chimeric antigen receptor natural killer cell immunotherapy and ultimately allogeneic hematopoietic stem cell transplantation. Despite this aggressive multimodal approach, disease progression ensued, culminating in an OS of 18 months. The therapeutic paradigms outlined in these studies exhibit substantial concordance with the treatment strategy applied in the present study. Collectively, these clinical observations, coupled with the existing literature, strongly suggest that early detection and timely intervention are pivotal factors influencing therapeutic efficacy in cardiac DLBCL. This

conclusion is particularly salient given the typically aggressive disease course and diagnostic complexities associated with cardiac involvement in DLBCL (Table II) (19-21).

This case report has several limitations that warrant consideration. Primarily, the absence of a post-treatment ¹⁸F-FDG PET/CT scan precluded the assessment of metabolic activity changes in the lesions. In addition, the current follow-up duration remains insufficient to comprehensively evaluate the long-term therapeutic outcomes and potential disease progression.

The diagnosis of secondary cardiac lymphoma with diffuse myocardial infiltration is challenging. The use of multimodal imaging examinations is essential to enhance the diagnostic accuracy. Physicians should promptly initiate chemotherapy and monitor patients for potential cardiac complications throughout the treatment. Posttreatment multimodal imaging techniques remain crucial for assessing myocardial morphology, metabolic alterations, necrosis and fibrosis to effectively manage the adverse outcomes associated with chemotherapy.

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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

BL treated the patient. DH and LX acquired data. DH, CW and BL performed the literature search and data analysis. DH drafted the manuscript. CH and XD designed the study and revised the manuscript. All authors contributed to the manuscript and have read and approved the submitted version. DH and BL confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Biomedical Ethics Committee of Mianyang Central Hospital (Mianyang, China; approval no. S20230350-01) and conducted according to the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patient consent for publication

The patient provided written informed consent for the publication of his data and the medical images.

Competing interests

The authors declare that they have no competing interests.

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