

## Case Report

# Primary cardiac malignant lymphoma: a case report and literature review

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**Abstract:** Primary cardiac lymphoma (PCL) is a rare hematological malignancy with involvement of the heart and/or pericardium. It belongs to the extra-nodal non-Hodgkin's lymphoma (NHL). The most common histological type is diffuse large B cell lymphoma. It generally carries a poor prognosis due either to a delay in the diagnosis or to infiltration of heart structures. Here, we described a 68-year-old male patient who was diagnosed with PCL and accompanied with severe wound infection. The patient receives PR after 6 cycles of R-CHOP regimen, and the wound infection was healing after treated with broad-spectrum antibiotics. We summarize the literatures, and briefly describe the manifestations, diagnosis, treatments and prognosis of PCL. Echocardiography, CT, MRI and PET-CT are used to evaluate the tumor, and our case is the very first case-report of primary cardiac lymphoma with PET-CT scan evaluation before and after chemotherapy. PCL is a rare disease, which be diagnosed and treated in time may improve its prognosis, however, its biological and clinical characteristics are still unknown. The goals of this article are to raise awareness of this disease, show the difficulties of diagnosing and also put emphasizes on the role of chemotherapy in its treatment, so that PCL can be diagnosed and treated in time.

**Keywords:** Primary cardiac lymphoma, large B cell lymphoma, chemotherapy

### Introduction

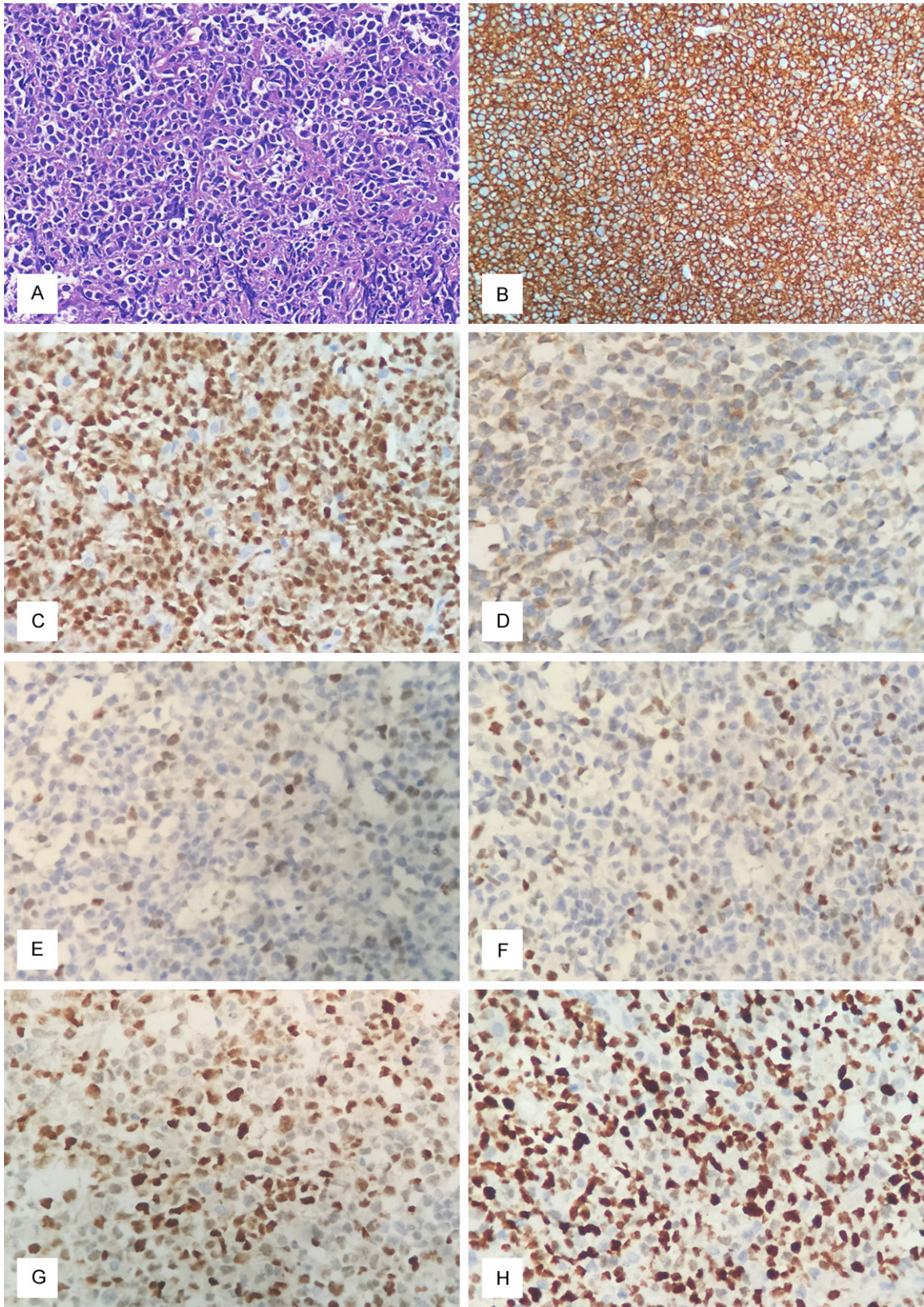
Primary cardiac tumor is a rare disease, with an incidence ranging from 0.001% to 0.03%, 80% of them are benign tumors [1]. PCL constitutes about 1.3%-2% of all heart tumors, and 5% of primary malignant tumors of heart [1, 2]. The clinical manifestations may be variable attributed to the location of the tumor, that is why it is so difficult in diagnosing. Different patients react differently to the treatment, and symptoms progress rapidly even with timely treatments, all of the above make a poor prognosis of PCL. In fact, primary lymphomas of the heart is so rare that their clinical and biological behavior is largely unknown. Here, we reported a rare case of PCL with severe wound infection after an open-heart biopsy, and reviewed the literatures.

### Case report

A 68-year-old previously healthy male was admitted to a local hospital because of chest

pain, shortness of breath and intense fatigue which had lasted for half a month. Diagnosis of a cardiac tumor was made with the help of echocardiography, which confirmed the presence of a mass in the right atrium. With a presumptive diagnosis of a cardiac tumor, an open chest operation was performed, during which a biopsy of the tumor was taken. Fast pathological examination of the frozen tissue suggested the diagnosis of lymphoma, also because the mass was tightly adhered to the surrounding tissue, so doctors finished the surgery without resecting the mass completely. Postoperative pathological examination showed a diffuse large B cell lymphoma. A detailed histological exam of the tumor revealed that the cells was CD20(+), CD3(-), pax-5(+), CD5(-), CD10(-), bcl-2(+), bcl-6(+), MUM1(+), Ki-67(+80%), P53(-), C-Myc(+20%), and molecular pathological exam showed EBER(-) (**Figure 1**). IGH and IGK gene rearrangement test showed IGH Fr2A+Fr2B was positive, and IGH Fr3A, IGK was negative. Positron emission tomography-computed to-

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**Figure 1.** Histomorphology of the right atrial mass. A: Differentiation with severe cytologic atypia (H&E; original magnification,  $\times 200$ ); B: Cell membrane expression of CD20 (original magnification,  $\times 200$ ); C: Nuclear expression

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of PAX-5 (original magnification,  $\times 200$ ); D: Cell membrane expression of bcl-2 (original magnification,  $\times 200$ ); E: Nuclear expression of bcl-6 (original magnification,  $\times 200$ ); F: Nuclear expression of c-myc more than 20% (original magnification,  $\times 200$ ); G: Nuclear expression of MUM-1 (original magnification,  $\times 200$ ); H: Nuclear expression of ki-67 more than 80% (original magnification,  $\times 200$ ). (It's a frozen tissue of right atrium, a tiny tissue full of tumor cell and very few normal cardiomyocytes, which made histological exam extremely difficult).

mography (PET-CT) scan revealed post thoracotomy changing; tumor infiltration of the heart, mediastinal and abdominal lymph nodes, left kidney, and jejunum; pericardial and pleural effusion on both sides (**Figure 2A**). After surgery, the patient developed severe wound infection with liquid exuding from the incision. With the general condition getting worse, the patient was transferred to our department.

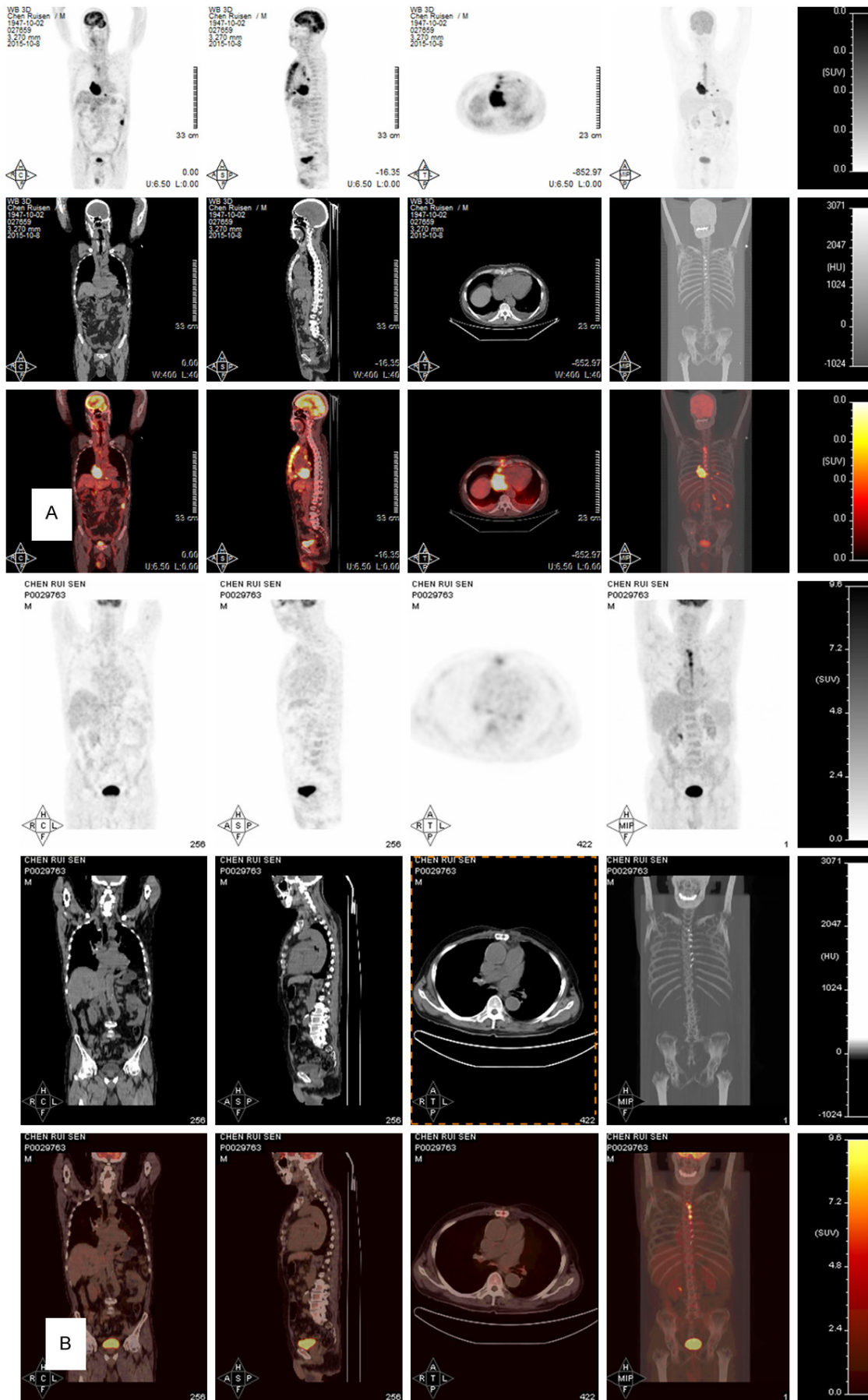
On admission, the patient had no complaints of fever above  $38^{\circ}\text{C}$ , night sweating or loss of more than 10% of body weight over a period of six months or less (B symptoms). Physical examination revealed a severely infected sternal incision with pus exuding continuously from the wound, and sinuses can be found (**Figure 3**). Exudate culture proved staphylococcus aureus infection. A bone marrow biopsy was obtained to evaluate for involvement by lymphoma, the result was negative. A transthoracic echocardiography (TTE) showed a massive tumor occupying almost all of the right atrium, about  $6.2\text{ cm}\times 4.8\text{ cm}$  in size, and the foramen ovale was reopening with bidirectional current shunt, slight pericardial effusion (**Figure 4A, 4B**). Electrocardiogram (ECG) revealed atrial flutter with 3:1 atrioventricular conduction, T wave change. The final diagnosis of this patient is non-Hodgkin's lymphoma (primary cardiac lymphoma, diffuse large B cell, staging IV A, IPI 4), and arrhythmia (atrial flutter). Therefore, we disinfected the incision twice a day, daptomycin was used to control the infection, which was insensitive to vancomycin. In the other hand, the patient received systemic chemotherapy with a dose-reduced R-CHOP regimen (mini R-CHOP: rituximab  $375\text{ mg}/\text{m}^2\text{ d0}$ , cyclophosphamide  $375\text{ mg}/\text{m}^2\text{ d1}$ , epirubicin  $35\text{ mg}/\text{m}^2\text{ d1}$ , vindesine  $1\text{ mg}/\text{m}^2\text{ d1}$  and prednisone  $40\text{ mg}/\text{m}^2\text{ d1-d5}$ ). After the first cycle of R-CHOP regimen, patient's general condition was improved, all symptoms were relieved, and the wound was also recovering. Because of the good response, we continued the R-CHOP regimen, and increase the dose to standard level (rituximab  $375\text{ mg}/\text{m}^2\text{ d0}$ , cyclophosphamide

$750\text{ mg}/\text{m}^2\text{ d1}$ , epirubicin  $70\text{ mg}/\text{m}^2\text{ d1}$ , vindesine  $1.4\text{ mg}/\text{m}^2\text{ d1}$  and prednisone  $60\text{ mg}/\text{m}^2\text{ d1-d5}$ ). After four cycles of R-CHOP regimen, another PET-CT scan was performed to evaluate the efficacy of chemotherapy, the result was encouraging, tumor tissue was significantly reduced (**Figure 2B**), both CT scan and echocardiography also showed significantly shrink of the tumor (**Figure 4C**). Up to now, the patient had finished 2 cycles of chemotherapy with mini R-CHOP, 4 cycles of R-CHOP, and evaluated as PR.

### Discussion

There is no unified diagnostic criteria for PCL, but two definitions are commonly accepted: Zahzria et al. consider that PCL can be diagnosed when the tumor involves the pericardial space and myocardium [3], while Curtsinger et al. state that PCL can only be diagnosed when there is an absence of the lymphoma outside pericardial sac [4]. The primitive occurrence of PCL is very low, it composes only 0.5% of all extra-nodal lymphomas [5]. A series of cases have been reported that this disease occurs more frequently in male patients and typically in the elderly, the median age of the patients is 63-67 years, male to female ratio is 2(3):1 [5-7]. PCL is often located in the right atrium and right ventricle, but less in left atrium and left ventricle [7]. More than 80% of PCL is diffuse large B cell non-Hodgkin's lymphoma, few T cell lymphoma [8]. PCL patients show various and non-specific symptoms, depending on the location and the size of the mass, such as shortness of breath or dyspnea, chest pain or angina, palpitation or arrhythmia, weakness or fatigue, weight loss, fever or night sweats [9, 10]. The most common presentations are heart failure and pericardial effusion [11]. In our case, the patient is also an old male, complained about chest pain, shortness of breath and fatigue, the tumor is located in the right atrium, and pathological examination proved diffuse large B cell non-Hodgkin's lymphoma of the heart, ECG revealed arrhythmia, which were all corresponded with the literatures.

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**Figure 2.** PET-CT scan result. A: PET-CT scan before chemotherapy revealed: post thoracotomy changing; tumor infiltration of the heart, mediastinal and abdominal lymph nodes, left kidney, and jejunum; pericardial and pleural effusion on both sides. B: PET-CT scan after 4 cycles chemotherapy of R-CHOP regimen.



**Figure 3.** A severely infected sternal incision with pus exuding continuously from the wound, sinuses can be found around it.

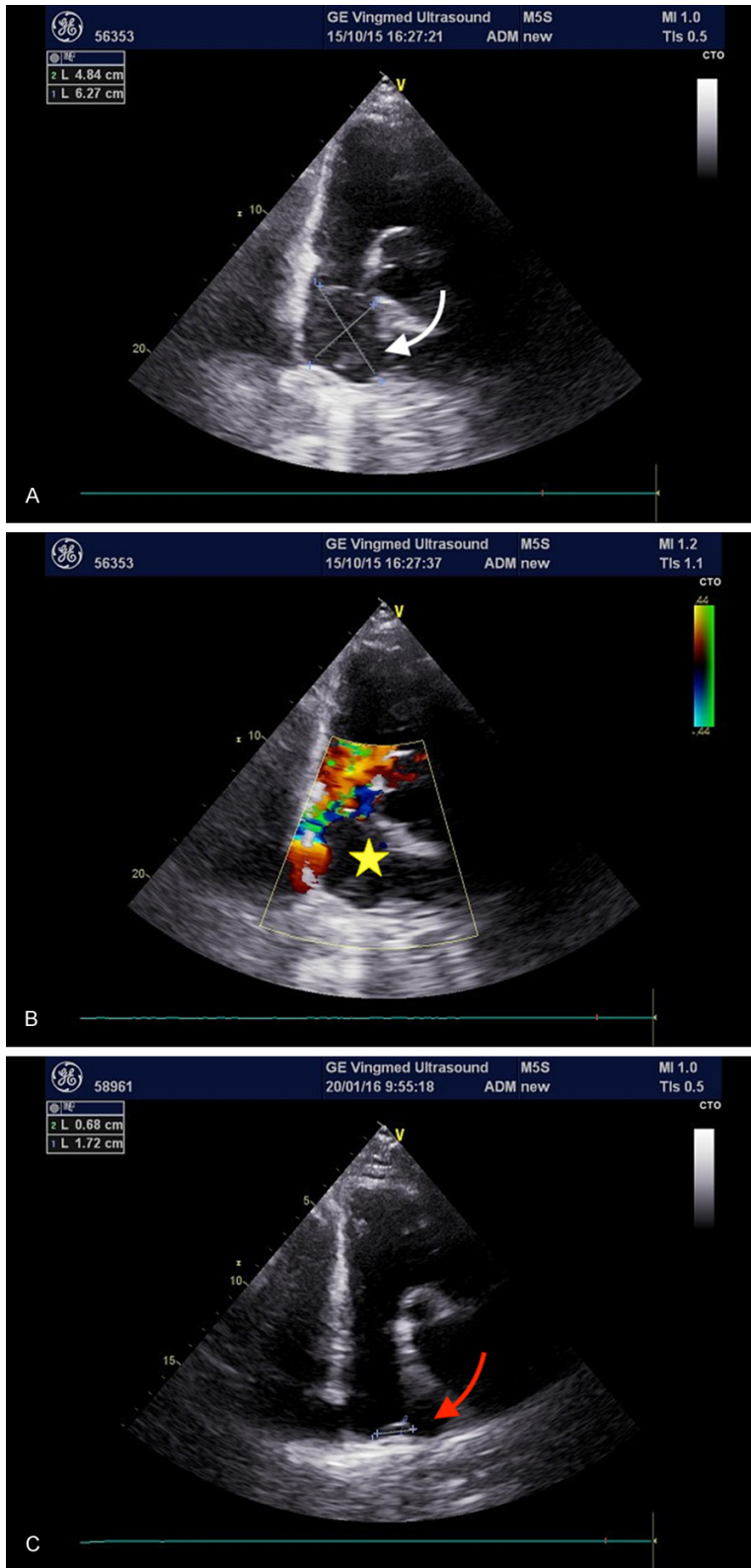
To diagnose PCL is particularly difficult due to its nonspecific clinical manifestations. Imaging techniques combined with invasive procedures are commonly used. ECG may show atrioventricular bundle branch blocks, atrial fibrillation, low voltages, or negative T waves [12]. Echocardiography (both transesophageal, as well as transthoracic) is a good noninvasive examination that can detect the presence of the tumor and also the exist pericardial effusion [13]. Fortunately, our patient had echocardiography in time, it not only showed the location and size of the tumor, detected the foramen ovale reopen, but also seen as a helpful noninvasive examination for evaluating the efficacy of treatment. However, most B-ultrasonic doctors are lack of experience on PCL, which may cause echocardiography less accurate as CT. That's why we strongly recommended echocardiography should be performed by experienced B-ultrasonic doctors. CT scan and magnetic resonance imaging (MRI) are the mainly used

imaging techniques to detect cardiac tumors, observe their locations and relationship with surrounding tissues. Recently, PET-CT scan is also used to evaluate the metastasis and staging of the disease [14]. To the best of our knowledge, our case is the very first case-report of primary cardiac lymphoma with PET-CT scan evaluation before and after chemotherapy. Histologic and immunochemical examinations of the involved tissue, as well as cytogenetic studies are always required to confirm diagnosis. In order to exclude the involvement of the bone marrow, a bone marrow biopsy and aspiration is indicated.

Treatment approaches include combinations of: chemotherapy, radiotherapy, tumor mass resection, and autologous stem cell transplant. Chemotherapy is the most effective treatment of PCL [15]. Chin et al. reported that when treating with chemotherapy alone 61% of patients have a remission, while surgery alone has no effect to the outcome, because it is difficult to resect the tumor completely [16]. Anthracycline-containing regimens, primarily CHOP plus rituximab have been commonly performed and with good response [17, 18]. Risks of chemotherapy include cardiac rupture when rapid tumor regression occurs, massive pulmonary emboli, refractory heart failure, or cardiac arrhythmias [10]. Radiotherapy has been reported in some patients, alone or combined with chemotherapy, with apparent further improvement in survival [2, 12]. High-dose chemotherapy, followed by autologous stem cell transplant also has been applied in few cases [7, 17]. Because the severe infection, we chose mini R-CHOP regimen. Since the patient achieved a good response with R-CHOP regimen, two weeks later we continued one cycle of mini R-CHOP, after that standard dose R-CHOP were performed every three weeks.

The prognosis of PCL is so poor that most patients die within a few weeks following the diagnosis. Survival is mainly affected by 4 factors: immune status, left ventricular involvement, presence of extra-cardiac disease, and arrhythmia [6]. The longest survival was reported by Groton et al. for a patient treated with

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**Figure 4.** Transthoracic echocardiography (TTE) result. A: TTE before treatment revealed: a large mass in the right atrium (white arrow). B: Foramen ovale was reopening with bidirectional current shunt. C: After 5 cycles of combination chemotherapy, the right atrial mass markedly decreased (red arrow).

surgical resection and adjuvant chemotherapy survived for more than 13 years [19]. Rolla et al. reported the median survival time of 66 PCL patients is 7 months [10]. A retrospective analysis of Anghel et al. stated 27 patients who were given chemotherapy alone, after a median follow-up of 7 months (range 0.07-144) only 5 were alive and free of disease [7]. Almost all of the literatures are case reports, which makes the analysis of outcome very difficult. Our patient received PR after 6 cycles of R-CHOP regimen, and we will continuously follow up the long-term survival of the patient.

Primary cardiac lymphoma is an extremely rare condition with various non-specific symptoms, but a high mortality rate. A prompt and proper diagnosis may affect the prognosis. It is necessary for doctors to use proper treatments as early as possible in order to achieve better outcomes for the PCL patients, R-CHOP regimen is commonly performed and with good response. However, their biological and clinical characteristics are still unknown, more cases should be discussed.

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### Disclosure of conflict of interest

None.

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