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Case report

A case of diffuse large B-cell lymphoma with interstitial pneumonia

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HIGHLIGHTS

- The case raises awareness about atypical clinical manifestations that may be overlooked as the cause of interstitial pneumonia (IP), despite its increasing prevalence yearly
- Patients with hematological tumors undergoing chemotherapy should pay close attention to changes in respiratory symptoms during treatment to prevent complications
- Patients with hematological tumors require prompt treatment when a new syndrome occurs during regular chemotherapy

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ABSTRACT

This report involves a 54-year-old female patient diagnosed with diffuse large B-cell lymphoma who developed interstitial pneumonia (IP) during treatment. The patient presented to the ward with enlarged lymph nodes in the neck and was treated with the standard regimen, which included rituximab, cyclophosphamide, doxorubicin liposomes, vincristine, and prednisone (R-CDOP regimen). After 3 cycles, the treatment was assessed as effective. However, following the 4th cycle, the patient experience shortness of breath after physical activity. A repeat lung computer tomography indicated IP, which completely recovered after receiving "full coverage" treatment. Subsequently, the patient underwent 2 cycles of cyclophosphamide, doxorubicin liposomes, vincristine, and prednisone (CDOP), followed by local radiotherapy. Currently, the patient is now being followed up with regular reviews.

Introduction

Diffuse large B-cell lymphoma (DLBCL), which accounts for approximately one-third of non-Hodgkin's lymphomas (NHL), is a hematological malignancy (HM).[1] The first-line treatment regimen for DLBCL includes rituximab in combination with cyclophosphamide, adriamycin, vincristine, prednisone (R-CHOP) or cyclophosphamide, doxorubicin liposomes, vincristine, and prednisone (R-CDOP). This report presents a case of a patient who developed interstitial pneumonia (IP) after receiving standard treatment. The patient recovered with aggressive treatment and is currently in the review follow-up phase.

Patients with DLBCL are susceptible to the development of IP during chemotherapy. The causative factors for this condition are often complex and involve individualized disease-related and pharmacological factors. The onset of IP and initial symptoms are atypical, displaying an insidious nature. During treatment, it is crucial to focus on changes in respiratory symptoms, and the differential diagnosis should consider possible complications, such as lung infection, interstitial lung lesions, pulmonary

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embolism, pneumothorax, and tumor lung involvement. If new pulmonary complications develop during regular chemotherapy, aggressive targeted treatment is required to restore lung function. This step is necessary to create favorable conditions for completing chemotherapy and controlling tumor progression.

The results of a univariate analysis reported in the literature[2] showed a higher incidence of IP in individuals aged ≥60 years, those with stage III-IV disease, elevated lactic dehydrogenase (LDH), International Prognostic Index (IPI) score of 3–5, and those receiving the R-CDOP regimen. In addition, Qian et al.[3] found that male smokers and those with B symptoms might also be at an increased risk of developing IP.

Case presentation

The patient, a 54-year-old female, was admitted to our hospital due to cervical lymph node enlargement for 1 month, which had aggravated over the past 2 days. In February 2022, the patient accidentally touched a left neck mass. After 12 days of antibiotic treatment, the mass on the left side of the neck gradually reduced in size. However, in March 2022, the neck mass increased in size again and touched the left inguinal mass. There is no significant effect of antibiotics intervention for two days. Consequently, she was admitted to the Geriatrics Department of the Second Medical Center of the Chinese People's Liberation Army General Hospital for further examination and treatment. Upon admission, the patient was eating and sleeping well, with no significant weight loss or diarrhea. Her medical history included a bilateral mastectomy in 2009, ablation of thyroid cysts in 2019, and Laparoscopic resection of a mucinous cystadenoma of the right ovary in 2020.

The patient's Eastern Cooperative Oncology Group performance status (ECOG PS) was 0–1 points, and no significant anemia was detected. Enlarged lymph nodes, approximately 3 cm in size were observed in the left neck. No palpable superficial lymph nodes, liver, or spleen were found. Clear breath sounds were heard in both lungs without any obvious dry or wet rales. The abdominal examination revealed no significant abnormalities; blood tests did not show any significant abnormalities either.

A positron emission tomography/computed tomography (PET/CT) examination conducted on March 24, 2022, showed a soft tissue density shadow measuring (size: 12 × 11 mm, standard uptake value [SUV] max: 16.1) in the left oropharyngeal region, along with multiple hypermetabolic lymph nodes (size: 30 × 24 mm, SUV max: 34.9) in the left neck, indicating the possibility of malignancy. No other obvious abnormalities were observed. Laryngoscopy revealed new biological swelling on the left side of the tongue root. Magnetic resonance imaging (MRI) of the neck demonstrated a nodule on the left tongue root and multiple enlarged lymph nodes in the left carotid sheath space. On March 29, 2022, a biopsy of the hypoechoic mass in the left neck region II was performed under the guidance of color Doppler ultrasound. The pathological examination revealed DLBCL of non-germinal center-of-cell origin. Immunohistochemical results showed: Common acute lymphoblastic leukemia antigen-10(CD10) (−), antilymphocyte globulin (CD3) (T cell+), paired box-5 (PAX-5) (+), Common acute lymphoblastic leukemia antigen–20(CD20) (+), B-cell lymphoma-6(Bc1-6) (+), multiple myeloma oncogene-1 (MUM-1) (+), nucleus related antigen (Ki-67) (+75%), B-cell lymphoma-2(Bc1-2) (weak+), V-myc avian myelocytomatosis viral oncogene homolog (C-myc) (+), synapsin (Syn) (−), Common acute lymphoblastic leukemia antigen-19 (CD19) (+), CyclinD1 (−), Calcitonin (−), thyroid transcription factor-1 (TTF-1) (−), Common acute lymphoblastic leukemia antigen-5 (CD5) (T cell+), p63 (−), programmed cell death-ligand 1 (PD-L1) (−), and creatine kinase (CK) (−). Molecular pathology examination results indicated: EBV- encoded ribonucleic acid (EBER) (−). The biopsy of the tongue root under laryngoscopy revealed squamous epithelial mucosal tissue and atypical lymphocyte infiltration in the lamina propria, and the clinical diagnosis is DLBCL, non-germinal center cell origin stage II A.

Subsequently, the patient received the R-CDOP regimen between April 1 and May 13, 2022. Polyethylene glycol granulocyte colony-stimulating factor (PEG-G-CSF) was administered after each treatment cycle to support treatment. PET/CT scan after 3 cycles of treatment showed that the treatment was effective. Compared with PET/CT examination on March 24, 2022, the metabolism of soft tissue in the left oropharyngeal region was significantly reduced, In addition, the enlarged lymph nodes in the left neck were significantly smaller than before, with a substantial decrease in metabolism, considering complete-metabolic-remission (CMR), score: 2. The metabolism of the small lymph nodes in the right neck was slightly lower than before.

On June 11, 2022, after completing the planned 4 cycles of treatment, the patient developed a fever the following day. The maximum temperature reached 38.5 °C and lasted for approximately half a day. Subsequently, the patient experienced a significant decrease in appetite, and food consumption dropped to one-third of the previous amount. On June 24, 2022, a reexamination of the lung CT showed a diffuse increase in lung density in both lungs, and the interstitial structure was blurred, especially in both the upper lungs and the middle lobe of the right lung. The bronchus of the left lower lung anterior basal segment exhibited irregularities, and the adjacent lung parenchyma appeared partially blurred. The possibility of IP injury was considered after multidisciplinary consultation, in addition to drug-induced pneumocystis carinii pneumonia (PCP) or cytomegalovirus pneumonia (CMV). We treated the patients with hormones, anti-infection drugs (meropenem + sulfamethoxazole + ganciclovir + caspofungin), globulin supplementation, and symptomatic support. The detection of fungal D-glucan, EB virus DNA, cytomegalovirus DNA, antibody, and blood next-generation sequencing (NGS) improved, and the results of etiology were all negative. On June 28, 2022, a reexamination of the lung CT indicated a noticeable reduction in the original lesions compared to the previous examination. As a result, the anti-infective drugs were gradually discontinued, hormone levels were reduced, and the pulmonary interstitial changes completely subsided by the reexamination of lung CT on July 8 [Figure 1]. However, despite multidisciplinary consultation, infectious diseases could not be completely ruled out due to the possibility of drug-related interstitial lung injury. On July 8 and July 29, 2022, the patient received the 5th and 6th cycles of the CDOP regimen. Subsequently, On September 5, 2022, radiotherapy was performed on the cervical lymph nodes, and the follow-up stage began.

Discussion

IP is a potentially fatal complication that can arise in lymphoma patients receiving chemotherapy. The early clinical manifestations of IP may be atypical, and as the disease progresses, it can lead to pulmonary interstitial fibrosis, resulting in symptoms such as dyspnea, respiratory failure, and even death.[2] The reported incidence of IP in various studies varies greatly, ranging from 0.03% to 29.0%.[2–4]

In a recent domestic study conducted by Zhu Jun et al.,[5] data from 2212 patients collected between 2009 and 2014 revealed an incidence of IP was 32.4% (76/1925) in NHL (P = 0.210). Accordingly, a meta--analysis[6] encompassing 12 studies and analyzing 3423 NHL patients found that among the three available patient-related risk factors (age, sex, and smoking habit), six disease-related risk factors (pathological type, Ann Arbor stage, IPI score, lactate dehydrogenase level, serum β2-microglobulin, B symptoms), and three drug-related risk factors (doxorubicin liposome replacing doxorubicin, combined with rituximab, and granulocyte colony-stimulating factor used in the treatment), only drug-related risk factors were found to be significantly related to IP development. The average incidence rates of IP in the CHOP, R-CHOP, and R-CDOP schemes were 1.0%, 7.0%, and 22.0%, respectively. In addition, the statistical data of Sichuan Cancer Hospital[7] showed that the total incidence of IP was 4.9% (27/556), and the incidence of IP in CHOP, R-CHOP, and R-CDOP groups was 1.1% (2/186), 5.2% (10/191) and 8.4% (15/179), respectively (P = 0.005), demonstrating statistically differences. However, it is important to note that each study report represents a single-arm study, with variations in the clinical characteristics and risk stratification of the enrolled patients. The dosage of liposomal doxorubicin also varies in cases of IP.

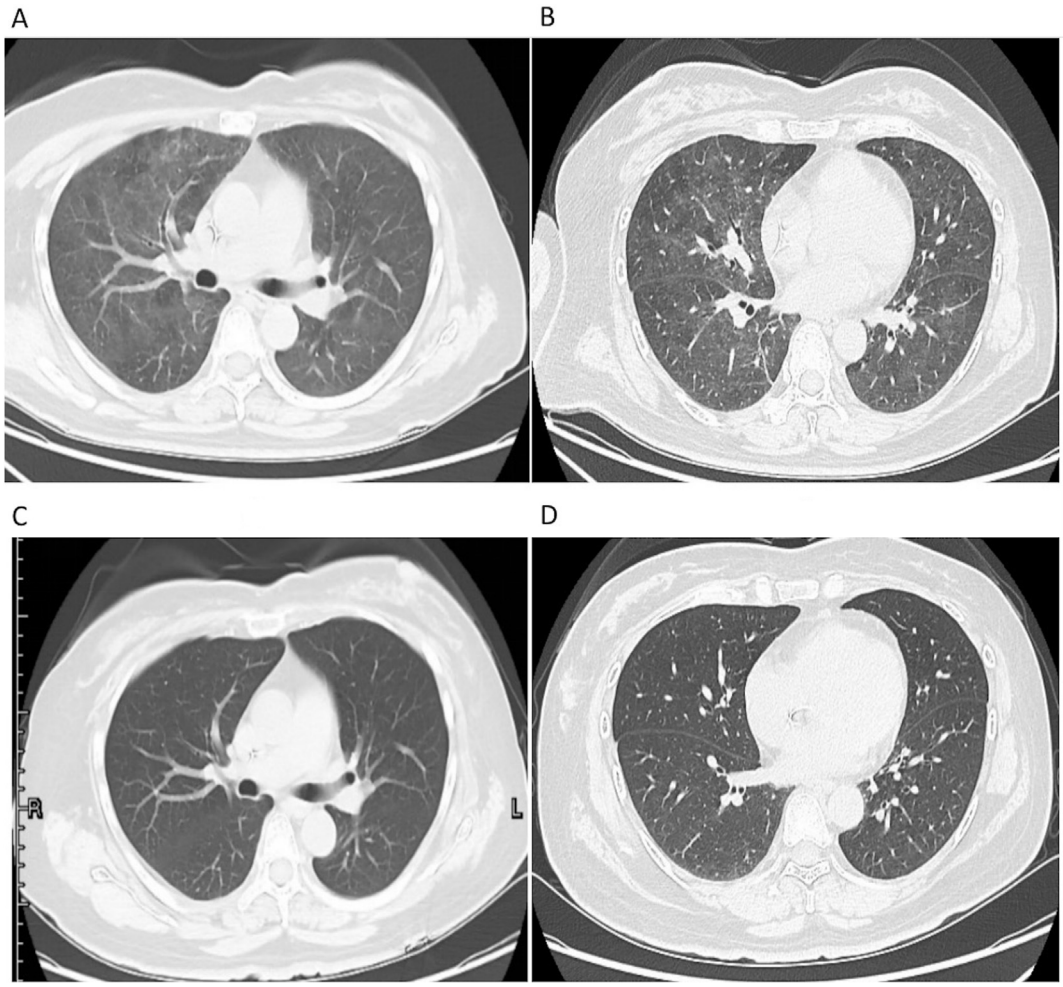

Figure 1. The lung-CT comparison before and after "full coverage" treatment. (A) and (B) show the period of IP, while (C) and (D) show the complete recovery of the lungs after treatment and the disappearance of inflammatory changes. IP: Interstitial pneumonia.

Literature reports have shown that rituximab can cause IP. Wang Qian et al.,[3] statistics showed that the incidence of IP in the R-CHOP group was 14.8%, which was significantly higher than the 2.4% incidence in the CHOP group. Other studies have also reported incidences ranging from 3.7% to 16.7%.[8] In 2019, Ruijin Hospital[2] treated patients with DLBCL using R-CHOP and R-CDOP regimens. The incidences of IP with these two regimens were 2.60% and 28.95%, respectively, and the difference was statistically significant ($P < 0.010$).

A study on the survival period of patients with DLBCLa and IP, based on statistical data from Sichuan Cancer Hospital,[7] showed that patients with IP had a 3-year progression-free survival (PFS) and overall survival (OS) rates of 74.1% and 46.9%, respectively. Another study[9] reported that among 816 patients with HM, 61 were diagnosed with IP. The survival rate of HM patients with IP was significantly lower than that of patients without IP, with 5 years OS ($P = 0.027$). However, no significant difference in OS was observed between patients with infectious and noninfectious IP ($P = 0.323$).

In this case, IP appeared after four cycles of the R-CDOP regimen, consistent with literature findings that it often occurs after the third and fourth courses of chemotherapy.[10] The Initial clinical symptoms were atypical, with no obvious cough, expectoration, dyspnea, and other respiratory symptoms commonly associated with IP. This may be attributed to the patient youthful age and good physical strength. After hormone shock, anti-infection, and globulin supplementation treatment, a review of the lung CT scan showed the complete disappearance of visible interstitial changes. Subsequently, the patient received an additional 2 cycles of the CDOP regimen, resulting in a significant reduction in lesion metabolism, indicating the continued effectiveness of the treatment. Considering the overall benefit to the patient and the need to avoid damage to bone marrow, kidney, liver, and kidney function associated with continued systemic treatment. It is recommended to complete the full course of systemic treatment and then switch to local treatment. Elderly patients undergoing antitumor treatment face numerous risks. In cases where there are atypical clinical manifestations, it is crucial to improve examination to minimize the chance of missing diagnoses, misdiagnoses, and serious treatment-related complications that could lead to poor prognosis.

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Authors contribution

Ge Song conducted the case arrangements and wrote the article. Changxi Zhou, Shuxia Wang, and Tianqi Tao contributed to the diagnosis and treatment of the disease. Xuan Wu, Bo Yang, and Weiping Guan were involved in the study design and helped draft the manuscript. Ping Zhu and Xuechun Lu conceived, helped design, and coordinated the study. All the authors have read and approved the final draft of the manuscript.

Ethics statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and national responsible committees

on human experimentation and the *Helsinki Declaration* of 1964 and its later amendments or equivalents. Informed consent was obtained from all patients included in the study.

Data availability statement

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Conflict of interest

None.

Acknowledgments

None.

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