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One case of intervariable diffuse large B cell lymphoma mixed with pulmonary tuberculosis

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Abstract: *This study reports a rare case of diffuse large B-cell lymphoma (DLBCL) complicated with active pulmonary tuberculosis. The patient, after undergoing R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy, developed respiratory distress and cough, eventually diagnosed as pulmonary tuberculosis. Clinical analysis reveals that lymphoma patients are at increased risk of reactivating latent tuberculosis infection (LTBI) due to immunosuppression caused by the disease itself and immunosuppressive treatments. This case underscores the importance of latent TB screening in lymphoma patients during treatment to prevent opportunistic infections. Moreover, the study discusses the challenges of implementing simultaneous anti-tuberculosis and anti-tumor therapies, providing valuable insights for clinicians to optimize diagnosis and treatment strategies.*

Keywords: *Diffuse large B-cell lymphoma; tuberculosis; latent tuberculosis infection*

1. Introduction

Tuberculosis (tuberculosis, TB) is a chronic infectious disease that threatens human health. According to the World Health Organization, there were 10.6 million new TB cases worldwide in 2022, of which 55 percent were male, 33 percent were female, 12 percent were children, and 1.3 million deaths[1]. About one-quarter of the global population is infected with Mycobacterium tuberculosis[2] . From 5% to 10% of individuals with latent TB infection (latent tuberculosis infection, LTBI) will eventually develop active TB[3].In the LTBI population, most develop active TB, such as concurrent HIV infection, cancer, immunosuppression therapy, or development of kidney transplantation, diabetes[4].

Lymphoma is a malignant tumor arising from lymph nodes or lymphoid tissues, including Hodgkins lymphoma (HL) and non-Hodgkins lymphoma (non-Hodgkins lymphoma, NHL)[5].Diffuse large B-cell lymphoma (Diffuse Large B-cell Lymphoma, DLBCL) is one of the highest incidence types of non-Hodgkins lymphoma (NHL), accounting for approximately one-third of lymphoma cases worldwide, and is highly heterogeneous and aggressive[6,7].Cases of lymphoma patients developing active tuberculosis during chemotherapy are rare, and the mechanism of chemotherapy on tuberculosis infection in lymphoma patients remains unclear. A case of intervariable diffuse large B cell lymphoma with pulmonary tuberculosis was reported as follows.

2. Case presentation

The patient, a 68-year-old male, was admitted to our hospital on 20 October 2023 due to "dyspnea and cough for 10 days after the 5th chemotherapy for lymphoma". In May 2023, the patient was diagnosed as "Intervariable diffuse large B cell lymphoma stage A" due to the neck mass pathology. June 10th18F-FDG PET / CT indicated multiple systemic enlargement, hypermetabolic lymph nodes, and multiple metabolic increase in the liver, and multiple solid and calcified stones in both lungs. Regular chemotherapy was given to R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) on September 1818F-FDG PET / CT lesions decreased and metabolism. During the fifth recuperation after chemotherapy, he developed dyspnea, cough, sputum, and white and thick sputum.

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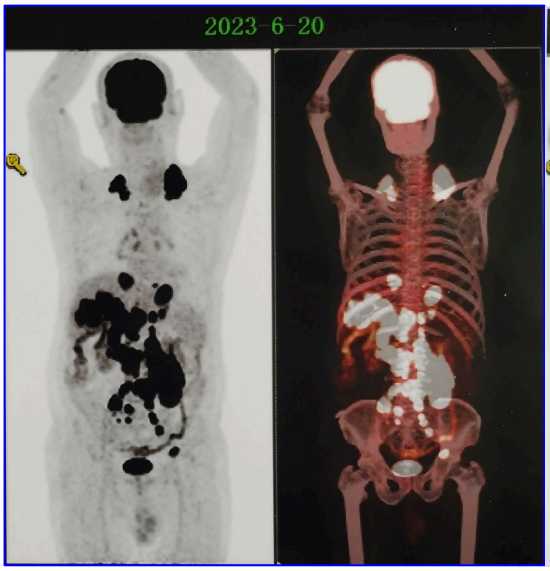
He immediately went to the hospital and was transferred by bronchoscopy to our hospital with acid-fast bacteria (+). T: Hospital examination: 37.0℃, SPO 2:77%, R: 28 times / min, BP: 139 / 76 mmHg, conscious, cyanosis. Respiratory sound in both lungs was thick, unheard dry and wet rales, heart rate 88 times / min, rhythm, unheard noise, Gene-xpert examination: MTB detection, rifampin sensitive. Fungal D-glucan: Fungal D-glucan detection 181.81. Arterial blood gas analysis: arterial blood carbon dioxide partial pressure was 23 mmHg, pH (37℃) 7.54, and oxygen partial pressure (37℃) 79 mmHg. Chest CT: multiple patchy, flaky high density foci in both lungs, multiple enlarged lymph nodes with calcification in mediastinum, and bilateral pleural thickening and adhesion. Admission diagnosis: 1. Secondary tuberculosis right upper, middle and lower left smear (+) initial treatment, 2 severe pneumonia with type I respiratory failure, and 3 variable diffuse large B cell lymphoma stage A. After admission, relevant examination indicated high fungal-D titer, and out-of-hospital lavage indicated: Candida albicans detection, anti-knot therapy and fungal treatment, anti-tuberculosis treatment regimen for isoniazid (H), rifampicin (R), and moxifloxacin (moxifloxacin), ethambutol (E), antifungal treatment. However, "voriconazole" was discontinued. The patient had lymphoma with severe hypoproteinemia, and was treated with human blood albumin infusion, anti-tuberculosis, anti-infection, anti-fungal, liver-preservation and other symptomatic supportive treatment. Chest CT review one month after discharge, compared with the hospital on November 24,2023, some chest CT lesions were slightly absorbed and reduced than before. The patient is currently in good condition, with slight palpitation and chest tightness after activities, no special discomfort, no fever, chills, no cough, sputum, breathing difficulties, etc., spirit, diet and sleep.



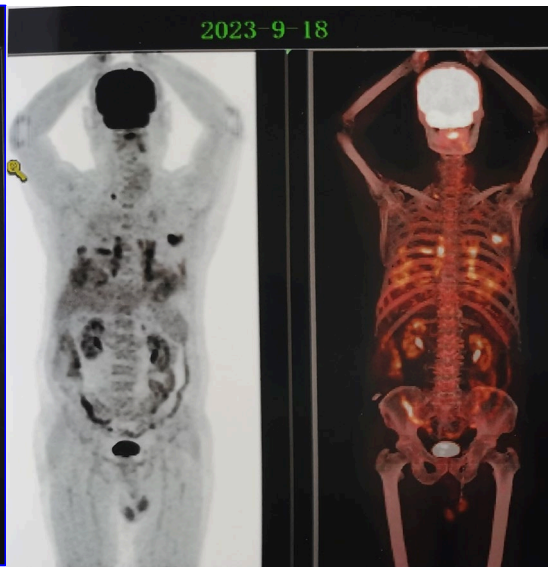
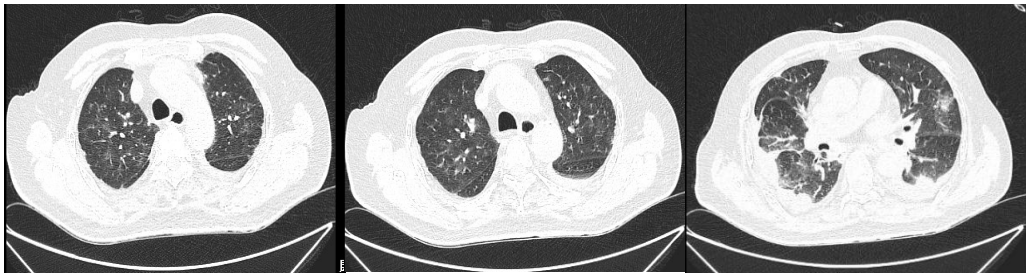


Figure 1 June 2018F-FDG PET / CT *Figure 2 on September 1818F-FDG PET / CT*

Figure 1, June 2018F-FDG PET / CT suggested multiple systemic enlargement, hypermetabolic lymph nodes, and multiple metabolic increase in the liver. Figure 2, on September 1818F-FDG PET / CT twice compared before reduction and decreased metabolism; in complete remission after lymphoma treatment.



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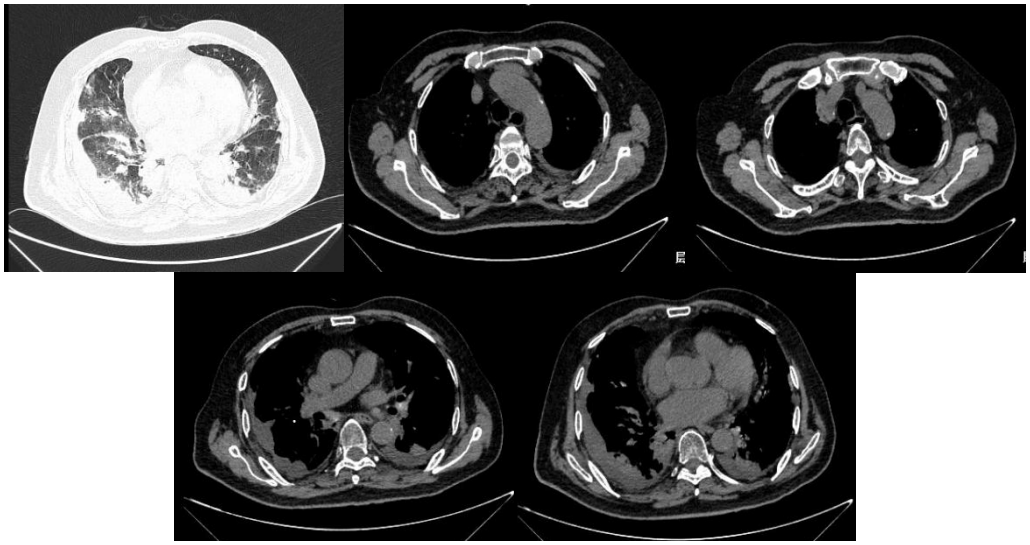

Figure 3 Patient 2023.11.24 Chest CT

Figure 3 Patient 2023.11.24 Chest CT suggested scattered multiple patchy ground glass shadows in both lungs, and multiple enlarged lymph nodes in mediastinum with calcifications. There was a slightly reduced absorption in some patchy foci in both lungs compared with the anterior comparison

3. Discussion

Diffuse large B-cell lymphoma (DLBCL) is a group of malignant tumors with great heterogeneity in clinical manifestations and prognosis, mainly showing rapid growth in lymph node areas or extranodal tissues and organs. The primary sites of DLBCL are mostly located in the lymph nodes, and the most common primary site of extranodal disease is the gastrointestinal tract, which also increases the complexity of the disease and the difficulty of diagnosis[8,9].Tuberculosis and primary pulmonary diffuse large B-cell lymphoma (PPL-DL BCL) showed some similar imaging features on CT scans, such as patchy or irregular consolidation, with or without ground glass shadows, and single or multiple nodules or large masses. The CT imaging characteristics of pulmonary tuberculosis mainly include uneven density, focal nodules, calcification, morphological changes and possible mass. A PET / CT examination of the primary lung with diffuse large B-cell lymphoma (PPL-DLBCL) shows a significant increase in glucose metabolism in the lung lesions. On CT scan, PPL-DLBCL may present as a more dense mass in the right upper lobe, indistinct margins, uneven density, with air bronchial signs, and mild to moderate enhancement. Although these two diseases may show some similar imaging features in CT scan, there are significant differences in their pathogenesis, clinical manifestations, and treatment options[10], In addition to imaging reports, lymphoma should also be diagnosed according to clear pathological histology. Clinical symptoms of lymphoma and tuberculosis are atypical, and chest images lack specificity, making them more prone to misdiagnosis and miss diagnosis[11].

In Chinese areas with high prevalence of TB, approximately 10% – 20% of lymphoma patients have a history of TB infection[12].The relationship between lymphoma and TB exists in three ways: ① patients have a history of TB or are experiencing TB before being diagnosed with lymphoma. The occurrence of lymphoma may be affected by tuberculosis, but the link between the two needs further research.② After the diagnosis of lymphoma, the patient was found to have tuberculosis. This may be due to the treatment of lymphoma or the development of the disease, increasing the risk of infection with tuberculosis bacilli.③ Tuberculosis and lymphoma occur almost simultaneously, which may be due to the existence of some common etiology or trigger between them. Doctors need to consider the characteristics of the two diseases and develop appropriate treatment plans[13].This case is in the second scenario, where the patient has severely impaired cellular immunity due to immunosuppressive therapy after chemotherapy and an increased risk of latent TB reactivation[8].The typical symptoms of lymphoma are painless enlargement of lymph nodes, local mass, fever, night sweats, weight loss and so on[14].The clinical manifestations of pulmonary tuberculosis may also have similar respiratory symptoms. The clinical manifestations of tuberculosis and lymphoma alone (e. g., fever, night sweats, fatigue, weight loss) may lead to misdiagnosis. The patient had recurrent clinical symptoms of fever during the treatment period. Secondly, the clinical manifestations of lymphoma with tuberculosis are

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not typical, and fever is a common clinical manifestation. However, it is difficult to distinguish whether the cause of fever is caused by lymphoma or infection. In addition to evaluating the activity of lymphoma, it is necessary to look for evidence of tuberculosis infection[15].The risk of TB in patients with malignancy is due to immunosuppression due to the tumor itself or chemotherapy, and local structural changes in the lung due to a primary lung cancer or metastasis[16].LTBI screening and treatment should be performed at cancer diagnosis to prevent opportunistic infections[17].After the fifth chemotherapy treatment, the PET / CT suggested new onset and multiple hypermetabolic ground glass shadows in both lungs, and the presence of lymphoma metastasis should be considered. According to the pathogenic detection of acid-fast bacilli in the other hospital, the sputum culture results in this hospital did not detect the detection of Mycobacterium tuberculosis. In addition, after a period of anti-tuberculosis treatment, the absorption of the lesions was improved, which can be confirmed that this case is the change of lung ground glass shadow caused by tuberculosis. In this case, the patient had respiratory failure due to the infection of tuberculosis. The reason for this serious consequence may be that the medical staff did not know enough about tuberculosis. When the patient had symptoms, the medical staff did not test the patient for acid-fast bacteria, and the delay of the condition led to serious consequences.

Latent tuberculosis infection (LTBI) is caused by the infection of mycobacterium tuber-culosis (MTB), which increases significantly when the body resistance decreases. The vast majority of infected people are in the state of Mycobacterium tuberculosis latent infection (LTBI), but no clinical symptoms appear. The final outcome of the infection depends mainly on the interaction between the host immune system and the pathogen[2], Latent TB may develop active TB when the bodys immunity decreases. Patients with leukemia, lymphoma, or silicosis may activate Mycobacterium tuberculosis, and people with latent TB infection should decide on receiving treatment based on the risks and benefits of developing active TB[18].For the cases of pulmonary tuberculosis with intervariable diffuse large B cell lymphoma, the principle of comprehensive treatment should be adopted. Anti-tumor therapy should be used both for lymphoma and anti-tuberculosis therapy for tuberculosis. Due to anti-TB drug treatment, active TB can affect the chemotherapy effects in cancer patients[19].Some studies have shown that anticancer drugs do not reduce the efficacy of anti-TB drugs against TB[20], but the simultaneous administration of anti-tumor and anti-tuberculosis drugs still needs to consider drug interactions and the side effects of multiple drug use[18].

In conclusion, lymphoma has similar clinical manifestations and imaging characteristics, no specificity and easy to misdiagnosis with each other. Lymphoma patients are at high risk for TB due to immunosuppression caused by the tumor itself or chemotherapy. After the diagnosis of TB in lymphoma patients, anti-tumor and anti-tuberculosis drugs can be treated simultaneously, but the side effects of drug interactions and multiple drug use still need to be considered.

4. Conclusion

This case highlights the clinical complexity and challenges of managing diffuse large B-cell lymphoma (DLBCL) complicated by pulmonary tuberculosis (TB), particularly in regions with a high prevalence of latent TB infection (LTBI). The co-occurrence of these two conditions poses significant diagnostic, therapeutic, and prognostic challenges due to overlapping clinical presentations, imaging findings, and the immunosuppressive effects of lymphoma and its treatment. Based on the insights from this case, several key conclusions and implications for clinical practice can be drawn.

First, the immunosuppressive environment induced by both the malignancy itself and the administration of chemotherapy significantly increases the risk of reactivating latent TB. In DLBCL patients undergoing R-CHOP chemotherapy, as observed in this case, impaired cellular immunity creates a favorable condition for Mycobacterium tuberculosis (MTB) reactivation. Early and systematic screening for LTBI in lymphoma patients should be a standard practice, particularly in endemic regions. Diagnostic tools such as interferon-gamma release assays (IGRAs) and T-SPOT.TB should be considered as part of the pre-treatment workup to detect latent TB. Prophylactic anti-TB therapy for LTBI-positive patients can be a critical intervention to reduce the risk of TB activation during immunosuppressive treatments.

Second, the diagnostic challenges of differentiating TB from lymphoma-related pulmonary lesions emphasize the need for a multimodal approach. In this case, overlapping symptoms such as fever, night sweats, and weight loss, combined with radiological findings like ground-glass opacities and nodular lesions, initially complicated the differentiation. PET/CT scans, while useful for lymphoma staging,

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lack specificity in distinguishing between infectious and malignant causes of lung lesions. Histopathological confirmation through biopsy and microbiological testing for MTB, including acid-fast bacillus (AFB) smear, GeneXpert, and culture, remain essential in confirming TB diagnosis. Early integration of TB-specific diagnostic protocols into oncology settings is vital to avoid delays in initiating appropriate therapy.

Third, the co-administration of anti-TB and anti-tumor therapies requires careful management due to potential drug-drug interactions and overlapping toxicities. For instance, rifampin, a cornerstone anti-TB drug, is a potent inducer of cytochrome P450 enzymes, potentially reducing the efficacy of chemotherapeutic agents. Conversely, chemotherapy-related myelosuppression and hepatotoxicity may exacerbate the adverse effects of anti-TB drugs. In this case, a tailored treatment approach balancing both anti-tumor efficacy and TB control was implemented, involving the selection of anti-TB regimens with minimal interactions and supportive therapies such as nutritional supplementation and hepatic protection. Such strategies are critical in managing patients with dual diagnoses.

Fourth, this case underscores the importance of multidisciplinary collaboration in managing complex conditions like lymphoma with concomitant TB. Effective communication and coordination among oncologists, infectious disease specialists, pulmonologists, and radiologists are essential to develop comprehensive treatment plans. Multidisciplinary teams can ensure timely diagnosis, optimize therapeutic strategies, and monitor for complications, ultimately improving patient outcomes.

Finally, public health implications cannot be overlooked. The increasing burden of TB in cancer patients necessitates enhanced awareness and education for healthcare providers, particularly in TB-endemic regions. Establishing institutional protocols for TB screening, monitoring, and management in oncology settings can mitigate the risks of delayed diagnosis and treatment failure.

In conclusion, the co-occurrence of DLBCL and pulmonary TB presents a challenging clinical scenario that requires early detection, tailored therapy, and coordinated care. This case serves as a reminder of the intricate interplay between malignancy and infection, reinforcing the importance of integrating TB control strategies into cancer management. Future research should focus on optimizing diagnostic tools, exploring safer therapeutic combinations, and developing evidence-based guidelines to address the unique challenges posed by this dual pathology.

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