

The Treatment of Diffuse Large B-Cell Lymphoma (Triple Expression) Involving the Breast, Spleen, and Bone in a Male Patient with Viral Hepatitis B: A Rare Case Report

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Background: Diffuse large B-cell lymphoma (DLBCL) involving the breast, spleen, and bone in a male patient with hepatitis B virus (HBV) infection is extremely rare in clinical practice.

Case Presentation: We report a case of DLBCL involving the breast, spleen, and bone (triple expression of Bcl-2⁺, Bcl-6⁺, and 70% positive C-myc) in a male patient with HBV admitted to our hospital. The patient was treated with EPOCH×4, lenalidomide +EPOCH×2 chemotherapy, intermittent methotrexate intrathecal injections to prevent central invasion, and autologous stem cell transplantation (ASCT). The patient is currently in complete remission, and the follow-up time was 43 months.

Conclusion: A patient with DLBCL involving the breast, spleen, and bone can be treated with a combination of multiple regimens. If the patient's economic conditions permit it, ASCT can be considered.

Keywords: breast, viral hepatitis B, diffuse large B-cell lymphoma, triple expression, autologous stem cell transplantation

Introduction

The prevalence of any breast malignancy is very low in the male population, and male breast diffuse large B-cell lymphoma (DLBCL) is even rarer. Male breast cancer accounts for about 1% of all breast malignancies.¹ Moreover, primary DLBCL of the breast accounts for only about 0.5% of breast tumors;^{2–4} this may be attributed to the fact that breast tissue contains fewer lymph nodes. Correspondingly, there is no effective unified treatment program.

As far as we know, there have been no large-scale reports and few reports about male breast DLBCL, which have mostly been reported as individual cases. Only a few male breast DLBCL cases can be found worldwide. We report the case of a male patient with chronic hepatitis B virus (HBV) infection complicated with DLBCL (triple expression: Bcl-2⁺, Bcl-6⁺, and 70% positive C-myc, involving the breast, spleen, and bone).

Case Presentation

In June 2019, a 45-year-old man found a mass about the size of an egg in the left breast without obvious pain. He had been diagnosed with HBV 20 years previously. The patient's disease course and treatment history is summarized in Figure 1. Ultrasonography indicated the following: an extremely hypoechoic nodule with a size of 3.3×2.9×1.2cm was observed in the subcutaneous fat layer in the outer upper quadrant of the left breast, showing a large lobulated regular shape with a clear boundary,

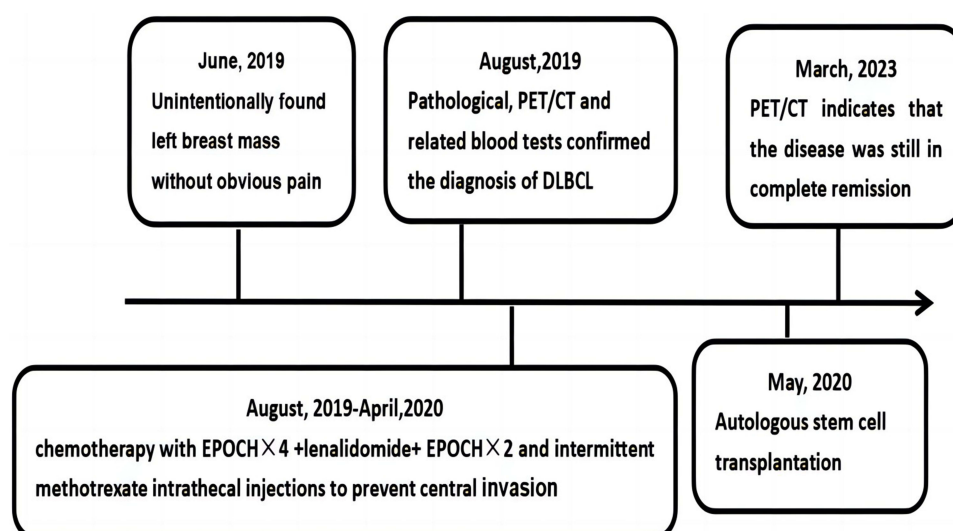


Figure 1 Summary of disease course and treatment situation.

an uneven internal echo, an enhanced peripheral soft tissue echo, and no abnormal axillary lymph nodes (Figure 2). In accordance with the examination results, a breast biopsy was performed. The pathology indicated a malignant tumor, and immunohistochemistry was recommended to exclude lymphoma (Figure 3). The immunohistochemistry results indicated the following: CD20⁺, Ki-67 (80% positive cells), Bcl-2⁺, Bcl-6⁺, C-myc (70% positive), CD3⁻, AE1/AE3⁻, CD2⁻, CD30⁻, CD1⁻, CD5⁻, and MUM1⁻. The in situ hybridization results were EBER⁻, and the puncture tissue was considered to be non-Hodgkin's lymphoma, which is consistent with DLBCL. Further gene fluorescence in situ hybridization (FISH) detection showed no recombination of Bcl-2, Bcl-6, and C-myc. During the first admission, there were no obvious abnormalities in the blood routine, coagulation function, β 2 microglobulin, sedimentation rate, liver and kidney function and bone marrow aspiration. Lactate dehydrogenase (LDH) was 400 U/L \uparrow and hepatitis B DNA quantitative was 5.27×10^5 IU/mL \uparrow . PET/CT (Figure 4) showed soft tissue nodules in the upper quadrant of the left breast, abnormal high glucose metabolism in the corresponding parts on PET (SUV_{max} 9.9), multiple circular low density in the spleen (SUV_{max} 15.8), mass soft tissue density in the right posterior chest wall, and the cortex of the adjacent posterior ribs of the right 10th was blurred, seemingly discontinuous. Uneven density in the medullary cavity (SUV_{max} 15.1) with the possibility of multiple site invasion of lymphoma, was considered high. The patient had a history of chronic viral hepatitis B and no history of other chronic diseases or malignant tumors. Due to active virus replication, the patient was treated with EPOCH (vindesine 1 mg + pirarubicin hydrochloride 19.4 mg + etoposide 0.097 g \times 4d + cyclophosphamide 1.45 g \times 1d) chemotherapy based on liver protection and antiviral replication. He was admitted to hospital for the second time in



Figure 2 In the left breast, there was an extremely low echo nodule about 3.3*2.9*1.2cm in size, which was large lobulated, regular in shape, clear in boundary, and uneven in internal echo before therapy.

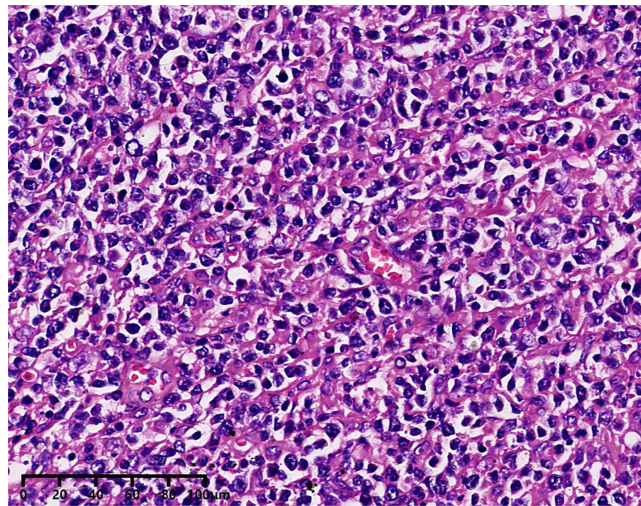


Figure 3 HE staining showed diffuse, relatively uniform, medium sized cells with obvious atypia, considering to be diffuse large B-cell lymphoma. The ruler in indicates 20 μ m.

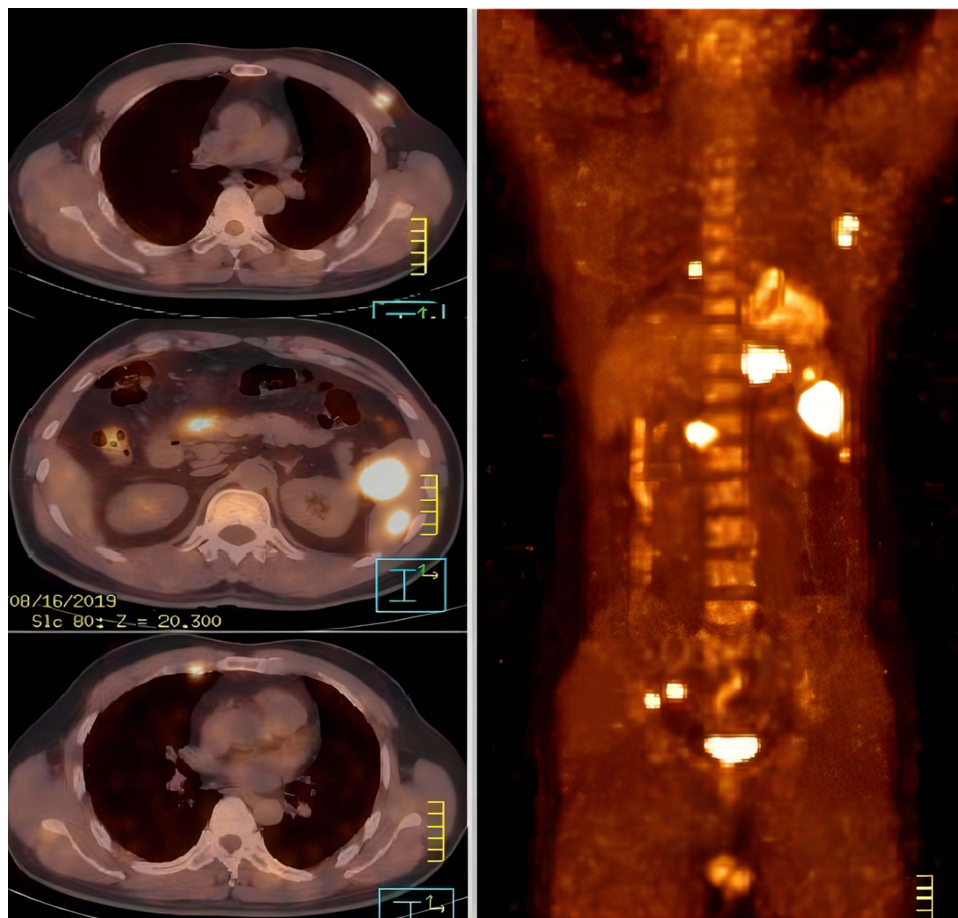


Figure 4 PET/CT showed diffuse large B-cell lymphoma involving breast, spleen, and bone.

September 2019, when a gene mutation test showed CD70 mutation, indicating a poor prognosis, indicating first-line auto-transplantation; lenalidomide + EPOCH chemotherapy was given to the patient. Considering the high risk of central invasion of the patient's primary disease, a large methotrexate dose was given to prevent central invasion after chemotherapy. Fully explain



Figure 5 The ultrasound and PET/CT indicated complete remission of the DLBCL.

Autologous stem cell transplantation (ASCT) related side effects to patients and their families, including high-dose chemotherapy may cause damage to important organs, gastrointestinal reactions, bone marrow suppression, bleeding, infection, hemolytic reaction, etc., and do a good job in psychological counseling and emotional stability of patients. ASCT carried out successful under full assessment and preparation. Although various complications such as bone marrow suppression and infection occurred in this patient, he was obviously alleviated after symptomatic treatment. After chemotherapy with EPOCH \times 4, lenalidomide + EPOCH \times 2, intermittent methotrexate intrathecal injections to prevent central invasion and the ASCT, the patient was in complete remission. The latest review was in March 2023 (Figure 5), when the breast ultrasound showed no obvious space occupation, PET/CT showed small flakes with slightly low density in the splenic parenchyma, the margin was not clear, and no obvious abnormal glucose hypermetabolism was observed on PET, which was considered to be the change after the lymphoma treatment, the disappearance of the breast and bone tumors. The patient and their families were satisfied with our overall treatment.

DLBCL of the breast is relatively rare, and DLBCL of the male breast is even rarer. Only one case was found in lymphoma patients in our hospital over the past 15 years.

Discussion

DLBCL is made up of mature B-cells and is one of the most common types of non-Hodgkin's lymphoma (NHL). DLBCL is a potentially curable disease that usually responds to systemic chemotherapy and synchronous or adjuvant radiotherapy.⁵ Many patients are misdiagnosed with breast cancer and receive surgical treatment. However, one study showed that surgical treatment did not improve patient survival.² Our rare case was a male patient with hepatitis B involving breast, spleen, and bone DLBCL. We treated the patient with EPOCH \times 4, lenalidomide +EPOCH \times 2 chemotherapy and ASCT. The patient is in complete remission and has been followed up for 43 months.

ASCT refers to the harvesting of autologous stem cells into foreign blood and the transplantation of the purified stem cells back into the body. ASCT has shown strong advantages in the treatment of recurrent lymphoma or refractory lymphoma and could improve the survival time of patients.^{6–8} Due to the small number of cases, there is no exact and effective treatment plan for breast DLBCL at present. This case achieved an ideal therapeutic effect through chemotherapy and ASCT, which could provide a reference for the formulation of future treatment plans.

HBV, tuberculosis, and acquired immune deficiency syndrome are the three most common infectious diseases in the world. In 2015, there were 257 million chronic HBV carriers worldwide, of whom 887,000 died from HBV-related complications, mainly cirrhosis and hepatocellular carcinoma.⁹ A large Italian study showed an increased risk of DLBCL in HBsAg-positive patients (hazard ratio 1.74; 95% CI 1.45–2.09).¹⁰ However, the mechanism by which HBV may induce NHL is not clear and may be related to chronic B-cell activation that promotes DNA damage and transformation into NHL,¹¹ explaining the clinical existence of many hepatitis patients with lymphoma. In addition, the presence of immune and inflammatory cells helps regulate tumor growth and invasion in hematologic malignancies and DLBCL.

DLBCL cells interact with mature stromal cells and blood vessels to confer tumor protection and suppress the immune response while providing nutrients and oxygen supply.¹² Therefore, tumor microenvironment analysis is an important aspect of assessing DLBCL progression.

Limitations

This is a single case report, and further studies are needed to determine the generalizability of the treatment approach used in this case.

Conclusion

In this case, a male patient with DLBCL involving the breast, spleen, and bone, who was treated with a combination of multiple regimens, showed a good response without signs of recurrence after 43 months of follow-up. Therefore, if the patient's economic conditions are relatively good, this treatment plan combined with ASCT can be considered. As this is only an individual case, more cases are needed to verify this result.

Ethics Statement

The study was reviewed and approved by the Ethic Committee of the The Fourth Hospital of Hebei Medical University (approval number, 2022KY384).

Informed Consent Statement

Informed consent was obtained from the patient involved in this study.

Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors disclose no conflicts of interest related to this work.

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