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Tumor Discovery

CASE REPORT

Diffuse large B-cell lymphoma in the splenic hilar lymph node mimicking an intrasplenic lesion

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Abstract

Diffuse large B-cell lymphoma (DLBCL) in the splenic hilar lymph node mimicking an intrasplenic lesion is considered rare in the literature. This case is discussed as a form of a primary splenic DLBCL and as a stage I/II abdominal DLBCL. Primary splenic DLBCL was previously defined as a lymphoma confined to the spleen, with or without involvement of the hilar lymph node or distant lesions. However, the condition is not included in the 5th edition of the World Health Organization classification. In this report, we describe the case of a 63-year-old Japanese male who presented with a 5 cm ^{18}F-fluorodeoxyglucose-avid mass identified on imaging, presumed to be an intrasplenic mass. Subsequent splenectomy confirmed that the mass was DLBCL originating from the splenic hilar lymph node, distinctly separated from the spleen and the tail of the pancreas. Postoperatively, the patient responded well to treatment comprising three courses of a combined regimen of polatuzumab vedotin, rituximab, cyclophosphamide, daunorubicin, and prednisolone. This case underscores the importance of caution when diagnosing intrasplenic lesions based on imaging, as the lesions may be located outside the spleen.

Keywords: Diffuse large B-cell lymphoma; Splenic hilar lymph node; Non-intrasplenic lymphoma; Positron emission tomography-computed tomography

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1. Introduction

Splenic neoplasms encompass various tumors, such as splenic hemangioma, lymphangioma, various subtypes of lymphomas, and angiosarcoma, which must be differentiated for accurate diagnosis and management. In the 5th edition of the World Health Organization classification of splenic B-cell lymphomas and leukemias, diffuse large B-cell lymphoma (DLBCL) is not listed as a specific subtype.[1] However, although rare, primary splenic DLBCL has been documented in several case reports and case series[2-13] (Table 1). According to Shimizu-Kohno *et al*.,[2] an analysis of 115 specimens of splenic lymphoid neoplasms in Japan revealed that DLBCL was the most common

Table 1. Subtypes of non-Hodgkin lymphomas in the spleen

Subtypes	References
B-cell type	
[a]Splenic diffuse red pulp small B-cell lymphoma	1
[a]Splenic marginal zone lymphoma	1
[a]Splenic B-cell lymphoma/leukemia with prominent nucleoli	1
[a]Hairy cell leukemia	1
Primary splenic diffuse large B-cell lymphoma	2-10
Fibrin-associated large B-cell lymphomas in splenic cysts	11
Primary splenic CD10-positive small B-cell lymphoma/ follicular lymphoma.	12
T-cell and other cell type	
[a]Hepatosplenic T-cell lymphoma	1
Splenic T/NK cell lymphoma	2
Splenic micronodular T-cell/histiocyte-rich large B-cell lymphoma	13

Note: [a]Refers to the World Health Organization Classification of Tumors, 5th edition (Hematolymphoid tumors-Part B).[1] Other splenic lymphomas are based on literature surveys.
Abbreviation: NK: Natural killer.

type (46 cases), followed by splenic marginal zone lymphoma (28 cases), and follicular lymphoma (11 cases).[2] Shimono *et al.*[3] classified primary splenic DLBCL into two categories: (i) type A, which includes cases with or without lymphadenopathy of splenic hilum, and (ii) type B, characterized by cases with involvement of the bone marrow, liver, or peripheral blood, in addition to the splenic lesions.[3] Here, we report a rare case in which an intrasplenic mass was initially suspected based on imaging studies but was later identified as DLBCL in the splenic hilar lymph node without intrasplenic lesions after splenectomy examination.

2. Case presentation

A 63-year-old Japanese man (174 cm, 64 kg), a hepatitis B virus carrier, presented with a hypoechoic spleen mass discovered during a routine annual abdominal ultrasound. Notably, he reported no symptoms of left upper abdominal pain or splenomegaly. His laboratory findings included a white blood cell count of 5,100 cells/μL, hemoglobin at 14.5 g/dL, platelet count of 250,000 platelets/μL, alanine aminotransferase at 14 U/L, lactate dehydrogenase at 209 U/L (reference range: 124 – 222), total bilirubin of 0.58 mg/dL, total protein of 7.3 g/dL, and albumin at 4.5 g/dL. Serological markers indicated active hepatitis B infection (HBsAg positive, HBsAb negative, HBcAb positive, HBeAb positive, and HCVAb negative). In addition, serum C-reactive protein was 0.1 mg/dL, with immunoglobulin G and immunoglobulin M levels recorded at 1,140 mg/dL and 47 mg/dL, respectively. Tumor marker studies showed a slightly high soluble interleukin-2 receptor (666 U/mL, reference range: 122 – 496), whereas other tumor markers (CA19-9 and CEA, determined by chemiluminescent enzyme immunoassay, DUPAN-2, determined by enzyme immunoassay, and SPAN-1, determined by radioimmunoassay) were within normal limits.

Contrast-enhanced computed tomography (CT) revealed a mass measuring 5 cm × 4 cm with indistinct margins in the middle of the spleen (Figure 1A). ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-CT confirmed the presence of an FDG-positive mass measuring 5 cm with a maximum standardized uptake value of 28.3 (Figure 1B). These imaging studies suggested an intrasplenic lymphoma.

The spleen (where the mass was initially thought to be located) and the tail of the pancreas were resected *en bloc* through robot-assisted laparoscopic surgery, along with dissection of regional small lymph nodes. Gross examination revealed a white, well-defined 5 cm soft mass between the spleen and pancreas (Figure 1C).

Formalin-fixed paraffin-embedded tissue specimens were stained with hematoxylin-eosin and specific antibodies, including CD3 (Roche Diagnostics, United States), CD5 (Roche Diagnostics, United States), CD10 (Nichirei Biosciences, Japan), CD20 (Roche Diagnostics, United States), CD23 (Nichirei Biosciences, Japan), BCL-2 (Roche Diagnostics, United States), BCL-6 (Roche Diagnostics, United States), Ki-67 (Roche Diagnostics, United States), and MUM-1 (Roche Diagnostics, United States), for immunohistochemistry (IHC). IHC was considered positive if more than 30% of tumor cells were positively stained. Ki-67 labeling index was estimated on the "hot spot" by simple visual inspection ("eyeballing").

Microscopic examination of the resected mass revealed that it did not invade the splenic parenchyma or pancreatic tissue, and no lymphoma cells were found in the regional lymph nodes. Histopathological analysis confirmed the diagnosis of DLBCL, specifically of the germinal center B-cell type (Figure 1D-F). The bone marrow was free from lymphoma cell involvement, leading to a diagnosis of stage I DLBCL originating from the splenic hilar lymph node. The karyotype was not assessed in this case. Fluorescence *in situ* hybridization (Vysis™ LSI® IGH/MYC, CEP 8 Tri-color, Dual Fusion Translocation Probe, Abbott Molecular Inc., United States) analysis was performed on the lymphoma cells from the DLBCL tissue. Results indicated negative for the *IGH-MYC* translocation, t(8;14)(q24;q32).

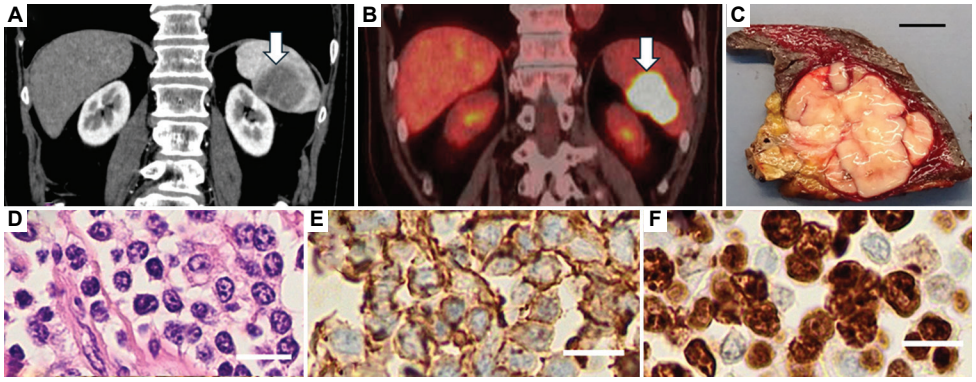


Figure 1. Enhanced computed tomography shows a 4 cm × 3 cm mass (white arrow) in the middle of the spleen. (A) The margin of the mass was indistinct. (B) Positron emission tomography-computed tomography demonstrates an ^{18}F-fluorodeoxyglucose-avid mass in the same area (arrow). (C) A white, well-defined 5 cm soft mass (shown as a dissected surface) is located outside the spleen, magnification: ×4, scale bar: 1 cm. Histology of the mass derived from the splenic hilar lymph node revealed diffuse large B-cell lymphoma as described in the text: (D) Hematoxylin & Eosin stain, (E) CD20 stain, and (F) Ki-67, magnification: 400×, scale bar: 50 μm. Positive stains for CD10, BCL-2, and BCL-6 are not shown.

Postoperatively, the patient experienced minor complications related to pancreatic leakage during the first 2 months but did not encounter any serious side effects, except for grade 1/2 cytopenia following three cycles of polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, and prednisolone combination therapy (PvRCHP regimen).[14] As of 5 months post-diagnosis, the patient has been doing well without any recurrence of lymphoma.

3. Discussion

This case was initially suspected to involve a primary splenic mass based on imaging studies that mimicked an intrasplenic lesion (Figure 1A and B). As listed in Table 1, several B-cell and other lineage lymphomas must be differentiated if an intrasplenic lymphoma is considered. However, in this case, gross and microscopic examinations of the formalin-fixed specimen revealed that the lymphoma originated from the splenic hilar lymph node rather than from within the spleen. The enhanced CT showed a mass with an indistinct margin (Figure 1A), which did not resemble typical imaging of a splenic cyst found in the fibrin-associated large B-cell lymphoma, a rare subtype of Epstein-Barr virus-associated lymphoma and distinct from typical DLBCL.[11,15] In retrospect, it was hypothesized that the CT appearance was due to external compression of the spleen by the mass.

In our search for literature on DLBCL localized to the splenic hilar lymph node, similar to our case, we found no relevant reports in PubMed or Google Scholar. This absence raises a critical question regarding the classification of our DLBCL: Is it classifiable as a primary splenic DLBCL-related lymphoma or as one of the abdominal nodular DLBCLs? Shimono *et al.*[3] conducted a comparative study of primary splenic DLBCL (66 cases) and control DLBCL (309 cases). They noted that patients with primary splenic DLBCL exhibited specific clinical characteristics, including a higher hepatitis C virus antibody prevalence, the presence of B symptoms, poor performance status, and CD5 positivity. Notably, the response to initial treatment was better in the primary splenic DLBCL group ($P < 0.05$), whereas the control group required radiation therapy.[3] However, our case did not exhibit these characteristics associated with primary splenic DLBCL.

The outcomes of primary splenic DLBCL demonstrate varying treatment responses and survival rates across different populations. In Japan, a study reported that among 66 patients, 40 patients received R-CHOP therapy, with 39 achieving complete remission.[3] Conversely, in Israel, among 87 patients, splenectomy was carried out in 39 patients, with the majority receiving chemotherapy. At a 5-year follow-up, the overall survival rate was observed to be 77%, whereas the disease-free survival rate was 67%.[16] In addition, Yonghao *et al.*[7] conducted an analysis involving 347 patients with primary splenic DLBCL. They found that combined treatment with splenectomy and chemotherapy demonstrated better outcomes compared to other treatment modalities, such as no treatment, splenectomy alone, or chemotherapy alone.

In contrast, regarding stage I/II DLBCL treatment outcomes, Persky *et al.*[17] reported on 132 patients with non-bulky (<10 cm) stage I/II DLBCL, who received three cycles of R-CHOP (with an additional cycle for cases showing negative PET/CT). In this cohort, only six patients experienced disease progression, and three succumbed to lymphoma, with a median follow-up of 4.92 years (range: 1.1 – 7.7 years).[17] Although previous chemotherapy utilized four cycles of R-CHOP on primary splenic DLBCL

and stage I/II DLCBL,[3,4,6,8,10,17] our case was managed postoperatively with three courses of the PvRCHP regimen due to concerns regarding potential poor prognosis.

4. Conclusion

In this case, after surgical resection and subsequent gross and microscopic examinations, it was determined that the mass originated from the splenic hilar lymph node, despite pre-operative imaging studies (CT, PET/CT) suggesting an intrasplenic tumor. Thus, even when imaging studies indicate an intrasplenic mass, caution must be exercised regarding the possibility of lymphoma located outside the spleen, potentially within the splenic hilar lymph node.

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Conflict of interest

The authors declare no conflicts of interest.

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Ethics approval and consent to participate

The work was carried out following the Declaration of Helsinki as revised in 2013. This case report was approved by the institutional review board (Uji-Tokushukai Medical Center Ethics Committee; IRB approval No. 2024-45). The patient provided written consent to participate in this study.

Consent for publication

Written informed consent was obtained from the patient.

Availability of data

Data are available upon request from the authors.

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