



## Diffuse Large B cell Lymphoma with Primary Spleen Involvement: Report of Three Cases

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### Abstract

*The spleen is the primary organ of lymphoma in only 1–2 % of all lymphoma patients. We presented three cases of primary splenic involvement of lymphoma that were treated. Presentation of cases: In the first case, four solid lesions were detected, and in the second case, a hypodense lesion of 3 cm was detected in the spleen. Two cases underwent splenectomy. No complication and recurrence were observed during 22 - 21 months follow-up, respectively. In the third case, a splenic mass invading pancreas was detected. Splenectomy and distal pancreatectomy were performed. No recurrence was observed during 8-year follow-up. In postoperative period, all cases were treated with cyclophosphamide, vincristine, doxorubicin, prednisone plus rituximab for 6 cycles. Primary splenic lymphoma refers to the involvement of the spleen only or with splenic hilar lymph node or local invasion without liver involvement. The pathologic diagnosis was diffuse large B-cell non-Hodgkin's lymphoma in the all cases. Splenic mass biopsy has some complication risks. Aspiration biopsy of splenic mass was performed in one of the three cases. Invasions should be evaluated in terms of malignancy during splenectomy, and liver biopsy and biopsies of lymph nodes can be performed in case of lymphoma. Additionally diagnosis should be confirmed via post-operative bone marrow biopsy and positron emission tomography screening. Primary splenic involved lymphoma must be kept in mind for differential diagnosis in cases with splenic mass. Splenectomy is one of the most common modality for primary splenic lymphomas in terms of both diagnostic and curative treatment.*

**Key words:** Non-hodgkin lymphoma, splenic involvement, splenectomy

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## Introduction

More than half of patients affected by Hodgkin's disease, and about a third of those with non-Hodgkin lymphoma have splenic involvement [1]. Splenic lymphomas (SL) are composed of a wide and heterogeneous array of diseases whose clinical behavior spans from indolent to highly aggressive [2] (Table 1). Primary and metastatic tumors of spleen are quite rare. The spleen is the primary organ of lymphoma in only 1–2% of all lymphoma patients [3,4]. Primary splenic lymphoma (PSL) is the involvement of the spleen or splenic hilar lymph node, not of any other organ. Before confirming the diagnosis of PSL, the authors recommend that the 6-month relapse-free period should exist after removal of the spleen [5]. On the other hand, some authors suggested that the diagnosis of PSL can be made if splenomegaly is a predominant feature in any lymphoma involving the spleen [6-8].

Merely radiologic methods are still insufficient for the diagnosis of masses. If the imaging studies strongly suggest the presence of PSL, fine needle aspiration biopsy (FNAB) or core biopsy of the spleen may be substituted for splenectomy as a diagnostic tool [5]. Splenectomy and pathologic examination are generally necessary for the final diagnosis of PSL.

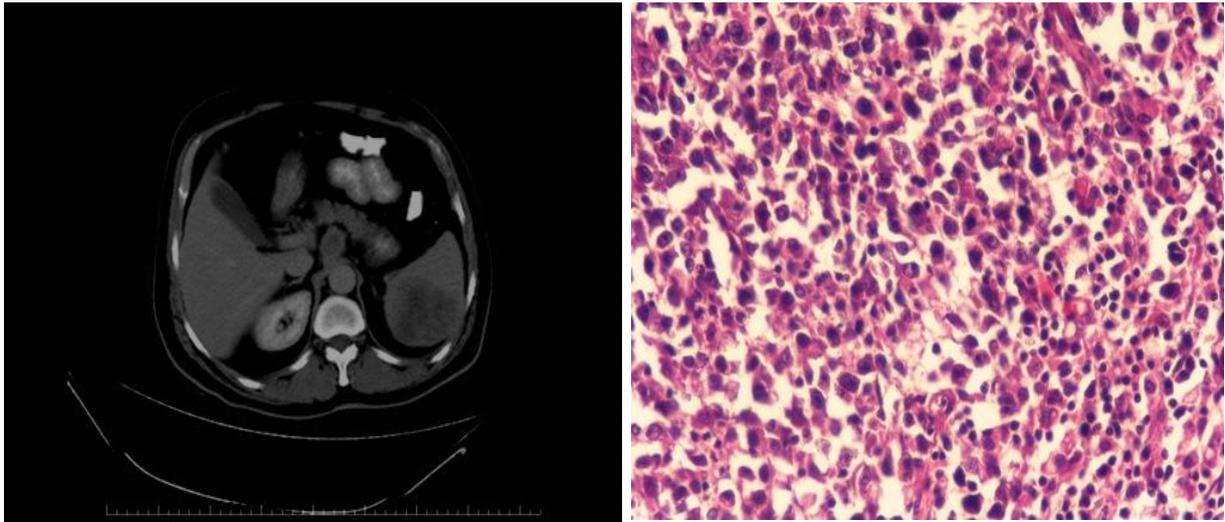
As PSL is a rare disease, the present study reports on three cases, considering the findings in the literature.

## Presentation of Cases

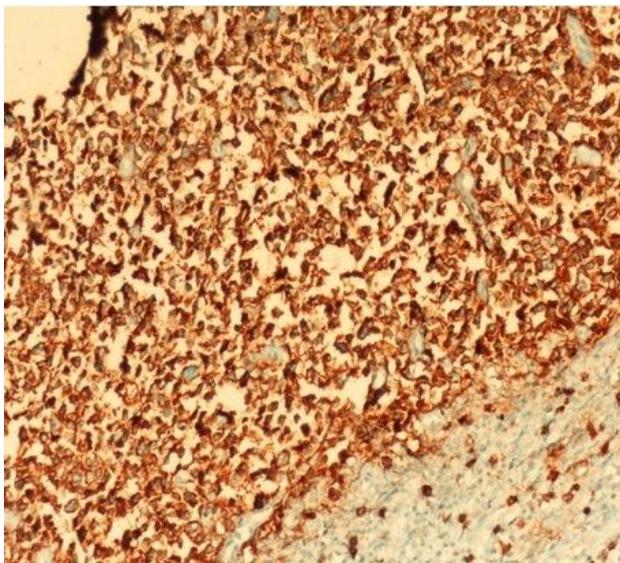
**Case 1:** A 61-year-old man presented with left upper quadrant (LUQ) abdominal pain that began one month ago, and continued to the back. Splenomegaly was found during physical examination. Hemoglobin 127 g/L, leukocyte count  $10.9 \times 10^9/L$  (NE-50.2%, LY-29.7%, MO-19%, EO-0.8%), thrombocyte count  $285 \times 10^9/L$ . Abdomen CT revealed splenomegaly, irregularly-contoured, heterogeneous, hypodense, solid lesions (Figure 1-A). Exploratory laparotomy was done because of the splenomegaly, and symptomatic tumor in the spleen. The spleen was found to be enlarged, and involved in three semi-solid, irregularly-contoured masses the largest of which was 8 cm. No abdominal lymphadenomegaly or liver involvement were observed. Total splenectomy was performed. The spleen's weight was 535 gr., and was including four partly necrotic lesions. The largest of which was  $8 \times 6.5 \times 6$  cm.

**Table 1.** Lymphoid malignancies that may present as SLs

<b>Lymphomas commonly/typically presenting as SLs</b>
Splenic marginal zone lymphoma
Splenic lymphoma/leukemia unclassifiable
Splenic diffuse red pulp B-cell lymphoma
Hairy cell leukemia variant
Hairy cell leukemia
LL
B-PLL
T-cell large granular lymphocytic leukemia
Hepatosplenic T-cell lymphoma
<b>Primary splenic presentations of nodal lymphomas</b>
Mantle cell lymphoma
Follicular lymphoma
Diffuse large B-cell lymphoma - not otherwise specified
Micronodular T-cell/histiocyte-rich large B-cell lymphoma



**Figure 1.** Abdominal CT image for case 1(A), atypical large diffuse lymphocytic infiltration is seen (x400, H.E ) (B), CD20 positivity is seen on the large cell lymphocytes (x400, Immunohistochemical Stain) (C).



Microscopically atypical large diffuse lymphocytic infiltration and sparse atypical large cell lymphocytes were observed (Figure 1-B).

Immunohistochemical staining revealed CD20 (+) (Figure 1-C), CD79a (+), Cyclin D1 (-), CD3 (-), CD5 (-) CD10 (-), BCL6 (-), MUM1 (-).

Pathology confirmed diffuse large B-cell lymphoma(DLBCL).

**Case 2:** A 68-year-old woman presented with LUQ pain and fatigue. Physical examination was normal. Abdominal US revealed a hypoechoic area of 34×24 cm in the spleen.

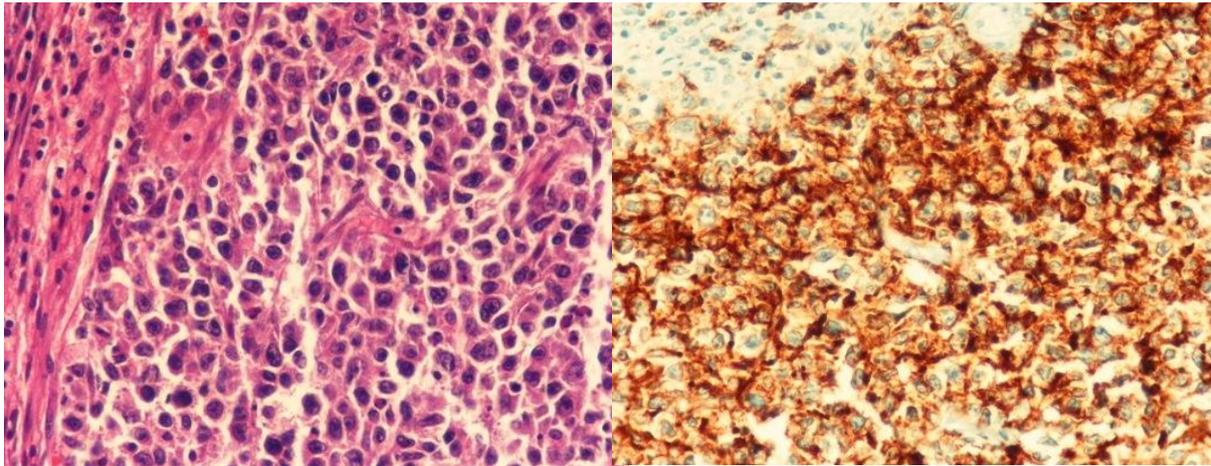
Abdominal CT revealed a regularly-contoured hypodense lesion of 3 cm in the spleen. Hemoglobin 122 g/L, leukocyte count  $10.9 \times 10^9/L$  (NE-69.5%, LY-20.5%, MO-6.7%, EO-3%, BA-0.3%), thrombocyte count  $300 \times 10^9/L$ . Total splenectomy were performed. The spleen's weight was 200gr, and was including a subcapsular lesion of 3x2x2 cm in diameter (Figure 2-A).

Microscopically was revealed atypical large diffuse lymphocytic infiltration (Figure 2-B). Immunohistochemical staining revealed CD20 (+) (Figure 1-C), CD79a (+), Cyclin D1 (-), CD3 (-), CD5 (-) CD10 (-), BCL6 (-), MUM1 (-).

Pathology confirmed DLBCL.



**Figure 2.** It is included a 3x2x2 cm in diameter subcapsular mass lesion in splenectomy specimen for case 2(A), atypical large diffuse lymphocytic infiltration is seen (x400, H.E )(B), CD20 positivity is seen on the large cell lymphocytes (x400, Immunohistochemical Stain)(C).

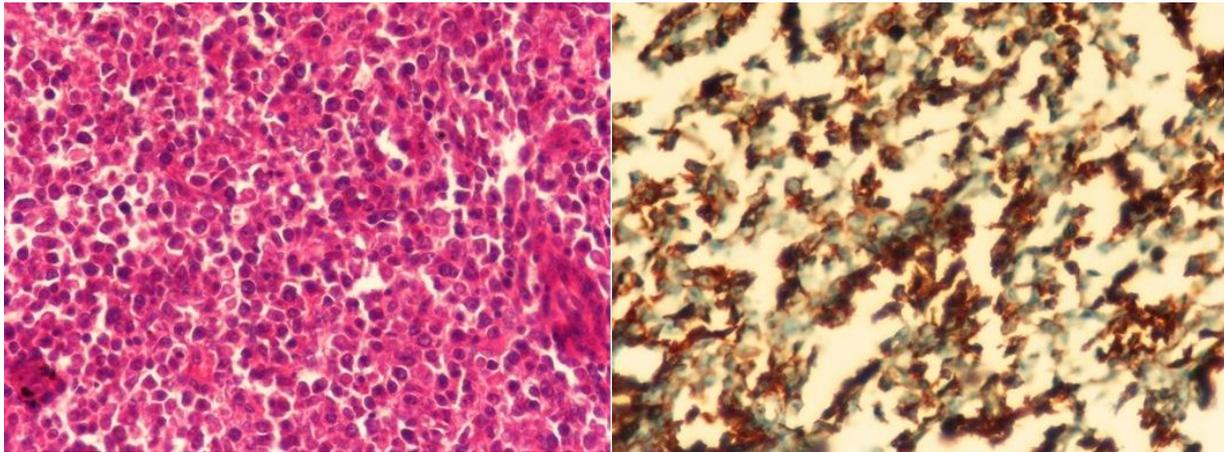


**Figure 2.** It is included a 3x2x2 cm in diameter subcapsular mass lesion in splenectomy specimen for case 2(A), atypical large diffuse lymphocytic infiltration is seen (x400, H.E )(B), CD20 positivity is seen on the large cell lymphocytes (x400, Immunohistochemical Stain)(C).

**Case 3:** A 50-year-old woman presented with a diagnosis of tumoral mass in the spleen. Physical examination revealed a mass in the LUQ, and no peripheral lymphadenomegaly was observed. Abdominal CT revealed an invasive pancreatic and splenic mass of 10×8 cm. Hemogram was normal. Fine-needle aspiration biopsy (FNAB) was tried but technically wasn't successful. Abdominal exploration was decided because of the symptomatic large mass in the spleen and the pancreas. An invasive pancreatic mass of 12 cm, which included the splenic hilum was detected during the procedure. Total splenectomy, distal pancreatectomy, and liver tissue biopsy were performed. Spleen and distal pancreas pathology's examinations were revealed atypical large diffuse lymphocytic infiltration (Figure 3-A).

Immunohistochemical staining revealed CD20 (+) (Figure 3-B), CD79a (+), Cyclin D1 (-), CD3 (-), CD5 (-) CD10 (-), BCL6 (-), MUM1 (-).

Pathology confirmed DLBCL.



**Figure 3.** Atypical large diffuse lymphocytic infiltration is seen in Case 3 (x400, H.E )(A), CD20 positivity is seen on the large cell lymphocytes (x400, Immunohistochemical Stain)(B).

In the three cases, the fever, the night sweats, and the weight loss weren't observed. Hemograms and peripheral blood smears were normal. No abdominal lymphadenomegaly and liver involvement were observed. Postoperatively the patients were managed by the department of medical hematology - oncology, and no involvement was observed in whole body in postoperative positron emission tomography (PET) imaging and bone marrow biopsy. The all cases received cyclophosphamide, vincristine, doxorubicin, prednisone plus rituximab (R-CHOP) for 6 cycles, after only rituximab for 2 cycles. Three cases are in complete remission respectively, for 22,21 month, and 8 years.

### Discussion

Primary splenic lymphoma refers to the involvement of the spleen only, or with splenic hilar lymph node and local invasion without liver involvement. Ahmann and Kiely [9] classified PSL and patient survival times were reported to decrease with disease progression. Two of the cases in the present study were stage II, while the third was stage III. A direct pancreatic invasion was observed in the stage-III patient, and splenectomy along with distal pancreatectomy was performed. That patient has surviving for eight years without recurrence. Because of considering the lymphoma pre-diagnosis, a liver biopsy was performed during the operations of all three patients, and no liver involvement was observed. This finding is considered to contribute to the prognosis of the patients.

The three cases presented have the same pathology. DLBCLs with strong CD 20 staining were detected in all three cases. According to the literature, the incidence rate of B-cell lymphomas is immunophenotypically higher than T-cell lymphomas [10]. The incidence of DLBCL in PSL varies between 22% and 77% [11]. Grosskreutz [11] determined DLBCL in 8 of 10 patients according to the Revised European–American Lymphoma Classification (REAL). Three patients with DLBCL in the present study support reports that it is the most common pathologic subtype in PSL.

PSL can be observed as homogeneous, miliary, multiple masses, or solitary masses according to various microscopic types [12]. One of the three cases had multiple masses, while the other two had solitary masses.

Splenic biopsy is not widely practiced in the United States because of the risk of bleeding. Lindgren [13] reported 13 % major complication rates for percutaneous biopsy of the spleen performed with a 14 gauge needle. However, subsequent reports of FNAB of the spleen under radiologic or ultrasound guidance have indicated much lower complication rates using smaller diameter needles (18 gauge or smaller), allowing for a safer procedure along with avoidance of the need for major surgical intervention [14-18]. In this study, FNAB was tried in one of the three cases (Case 3). No trial was performed in the other two cases because of their symptomatic course and mass localizations. However FNAB could be performed the other two cases, it changed treatments, was it? This circumstance can be considered a shortcoming.

Exploratory laparotomy, laparoscopy, and splenectomy are generally used for diagnosis and treatment in the patients that detected masses in their spleen that couldn't be defined from the patient's medical history, physical examination, or laboratory tests. Additionally, during the operation, invasions are evaluated in terms of malignity, and liver biopsy - biopsies of lymph nodes can be performed in case of lymphoma.

Total splenectomy was performed in the three cases after a multidisciplinary approach. It may be appropriate to adopt a multidisciplinary approach when deciding on the options of total splenectomy and/or chemotherapy in the treatment of PSL cases. DLBCLs of the spleen behave as aggressive neoplasm as those arising in lymph nodes and other extranodal sites do. Hence, treatment of these SLs should be guided by the same general recommendations proposed for DLBCLs [19].

Postoperatively, patients with SL were confirmed as not involving other distal organs through a combination of CT, PET scan and bone marrow biopsy in the pathologic diagnosis and post-operative staging. However, to date there is no indication for routine PET scan in the diagnostic approach and staging of SLs, but it can be performed pretreatment staging procedures in high grade SLs [2].

### Conclusion

Three cases have been complete remission respectively for 22, 21 month, and 8 years. In the light of the findings in the literature, early splenectomy and chemotherapy are the most important processes for primary splenic lymphomas and lymphomas with limited splenic hilum in terms of both diagnostic and curative treatment [1,20-22].

### Conflict of Interest Statement

No authors of this paper have a conflict of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included in this manuscript.

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### References

1. Gobbi PG, Grignani GE, Pozzetti U, Bertoloni D, Pieresca C, Montagna G, Ascari E. Primary splenic lymphoma; does it exist? *Haematologica*. 1994;79(3):286-93.
2. Lannitto E, Tripodo C. How I diagnose and treat splenic lymphomas. *Blood*. 2011;117(9):2585-95
3. Healy NA, Conneely JB, Mahon S, O'Riardon C, McAnena OJ. Primary splenic lymphoma presenting with ascites. *Rare Tumors*. 2011;3(2):e25.
4. Shao-Min H, Chieh-Lin T, Guang-Yuh H, Guan C, Che-An T. Primary splenic lymphoma which was associated with haemophagocytic lymphohistiocytosis which was complicated with splenic rupture. *J Chin Med Assoc*. 2008;7:210-3.
5. Kim JK, Hahn JS, Kim GE, Yang WI. Three cases of diffuse large B cell lymphoma presenting as primary splenic lymphoma. *Yonsei Med J*. 2005;46(5):703-9.
6. Kehoe J, Straus D. Primary lymphoma of the spleen. Clinical Features and Outcome after splenectomy. *Cancer*. 1988;62(7):1433-8.

7. Skarin AT, Davey FR, Moloney WC. Lymphosarcoma of the spleen. *Arch Intern Med.* 1971;127(2):259-65.
8. Dachman AH, Buck JL, Krishnan J, Aguilera NS, Buetow PC. Primary non-Hodgkin's splenic lymphoma. *Clin Radiol.* 1998;53(2):137-42.
9. Ahmann DL, Kiely JM, Harison EG, Paine WS. Malignant lymphoma of the spleen. *Cancer.* 1966;19(4):461-9.
10. Burke JS. The spleen In: Sternberg SS, ed. *Diagnostic Surgical Pathology*, Chapter 18. Lippincott Williams and Wilkins, 1999;779-802.
11. Grosskreutz C, Troy K, Cuttner J. Primary splenic lymphoma: report of 10 cases using the REAL classification. *Cancer Invest.* 2002;20(5-6):749-53.
12. Rosai J. Spleen. In: Rosai J, ed, *Ackerman's Surgical Pathology*. 8th edition. Mosby Year Book Ins, St.Louis, 1996;1775-96.
13. Lindgren PG, Hagberg H, Eriksson B, Glimelius B, Magnusson A, Sundström C. Excision biopsy of the spleen by ultrasonic guidance. *Br J Radiol.* 1985;58(693):853-7.
14. Silverman JF, Geisinger KR, Raab SS, Stanley MW. Fine needle aspiration biopsy of the spleen in the evaluation of neoplastic disorders. *Acta Cytol.* 1993;37(2):158-62.
15. Moriarty AT, Schwenk GR Jr, Chua G. Splenic fine needle aspiration biopsy in the diagnosis of lymphoreticular diseases. A report of four cases. *Acta Cytol.* 1993;37(2):191-6.
16. Civardi G1, Vallisa D, Bertè R, Giorgio A, Filice C, Caremani M, Caturelli E, Pompili M, De Sio I, Buscarini E, Cavanna L. Ultrasound-guided fine needle biopsy of the spleen: high clinical efficacy and low risk in a multicenter Italian study. *Am J Hematol.* 2001;67(2):93-9.
17. Lieberman S1, Libson E, Maly B, Lebensart P, Ben-Yehuda D, Bloom AI. Imaging-guided percutaneous splenic biopsy using a 20- or 22-gauge cutting-edge core biopsy needle for the diagnosis of malignant lymphoma. *AJR Am J Roentgenol.* 2003;181(4):1025-7.
18. Gómez-Rubio M1, López-Cano A, Rendón P, Muñoz-Benvenuty A, Macías M, Garre C, Segura-Cabral JM. Safety and diagnostic accuracy of percutaneous ultrasound-guided biopsy of the spleen: a multicenter study. *J Clin Ultrasound.* 2009;37(8):445-50.
19. Armitage JO. How I treat patients with diffuse large B-cell lymphoma. *Blood.* 2007;110(1):29-36.
20. Abraksia S, Dileep KP, Kasal J. Two unusual lymphomas. *J Clin Oncol.* 2000;18(21):3731-3.
21. Cavanna L1, Artioli F, Vallisa D, Di Donato C, Bertè R, Carapezzi C, Feroni R, Del Vecchio C, Lo Monaco B, Prati R. Primary lymphoma of the spleen. report of a case with diagnosis by fine needle guided biopsy. *Haematologica.* 1995;80(3):241-3.
22. Makni A, Magherbi H, Ksantini R, Azzouz H, Ayadi O, Jouini M, Kacem M, Ben Safta Z. Primary splenic lymphoma. *Tunis Med.* 2011;89(10):800-2.