Case report

Successful diagnosis of primary splenic diffuse large B-cell lymphoma by percutaneous splenic biopsy using a core-needle in a patient with rapid progressive splenomegaly: a case report

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Abstract:

Background: *Primary splenic lymphoma has been reported as a rare subtype of non-Hodgkin lymphoma. The common presentations are splenomegaly and splenic mass and this malignancy is extremely rare to diagnose from splenic infarction.* ***Case presentation:*** *A 47-year-old Thai female presented acute abdominal pain for 1 week and fever with thrombocytopenia for 2 days. Her fever failed to respond to antibiotics, and she continued to experience constant high grade fever with abdominal pain. She was followed up by physical examination, and developed progressive splenomegaly 5 cm below the left costal margin. Her serological workups for endemic tropical infections and microbiological results were all negative. A bone marrow study did not reveal an aggregation of lymphoid cells. A contrast abdominal computed tomography was repeated; although it did not detect any lymphadenopathies or masses; it found progressive hepatosplenomegaly and splenic infarction. To make a differential diagnosis between splenic infarction and splenic collection, an ultrasound-guided percutaneous splenic biopsy was performed. Histological analysis of the splenic biopsy revealed few small aggregates and infiltration of large atypical lymphoid cells with mild degree of nuclear pleomorphism. The nuclei are hyperchromatic with scant cytoplasm and an irregular nuclear outline. Mitotic figures are frequently observed. The red pulps are congested with a focal infarct area. The focal aggregates of atypical lymphoid cells-CD20(+), CD3(-), cyclin D1(-), CD10(-), BCL6(-), and MUM1(+)-with Ki-67 show high activity in more than 80% of tumor cells. This finding was consistent with diffuse large B-cell lymphoma, nongerminal center subtype.* ***Conclusion:*** *In patients with progressive splenomegaly and splenic infarction, Carrying out a differential diagnosis of aggressive lymphomas would be important. In addition to splenectomy, a percutaneous fine needle biopsy of the spleen can help make a definite diagnosis of primary splenic lymphoma.*

Keywords : ● *DLBCL* ● *Primary splenic lymphoma* ● *Splenic infarction*

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รายงานผู้ป่วย

การให้การวินิจฉัย primary splenic diffuse large B-cell lymphoma โดยการทำ percutaneous splenic biopsy using a core-needle ในผู้ป่วยที่มีม้ามโตอย่างรวดเร็ว

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บทคัดย่อ

Primary splenic lymphoma เป็น subtype ของ non-Hodgkin lymphomas ที่พบได้น้อย อาการแสดงที่พบได้บ่อยของมะเร็งต่อมน้ำเหลืองชนิดนี้คือมีม้ามโตหรือมีก้อนที่ม้าม การวินิจฉัยมะเร็งชนิดนี้จาก splenic infarction พบได้น้อยมาก ในรายงานผู้ป่วยฉบับนี้กล่าวถึง ผู้ป่วยหญิง 47 ปี มีอาการปวดท้อง 1 สัปดาห์ และมีเกล็ดเลือดต่ำ 2 วัน โดยไม่ตอบสนองต่อยาปฏิชีวนะ ผู้ป่วยได้รับการตรวจร่างกายติดตามพบว่ามีม้ามโตขึ้น สามารถคลำได้ขนาด 5 เซนติเมตรจากชายโครงซ้าย ผลการตรวจเลือดไม่พบการติดเชื้อที่เป็นสาเหตุ การตรวจไขกระดูกไม่พบว่ามีความผิดปกติของเม็ดเลือดขาวชนิด lymphoid ผู้ป่วยได้เข้ารับการทำเอกซเรย์คอมพิวเตอร์ช่องท้องซ้ำ ไม่พบต่อมน้ำเหลืองโต ไม่พบก้อนในช่องท้อง แต่มีตับม้ามโตขึ้นและมี splenic infarction ผู้ป่วยได้รับการทำ ultrasound-guided percutaneous splenic biopsy เพื่อแยกภาวะ splenic infarction และ splenic collection ผล Histological analysis เข้าได้กับ Diffuse large B-cell lymphoma, non-germinal center subtype ดังนั้นจึงมีความสำคัญที่จะคิดถึง aggressive lymphoma ในผู้ป่วยที่มี progressive splenomegaly and splenic infarction และนอกเหนือไปจากการตัดม้าม การทำ fine needle biopsy ที่ม้าม มีประโยชน์ในการได้ histopathological analysis เพื่อการวินิจฉัยและรักษาต่อไป

คำสำคัญ : ● *มะเร็งต่อมน้ำเหลืองชนิด* ● *DLBCL* ● *มะเร็งที่ม้าม* ● *ภาวะม้ามขาดเลือด*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2565;32:157-63.

Introduction

Primary splenic lymphomas (PSLs) are defined as lymphomas involving the spleen without any other sites of lymphadenopathy, with the possible exception of splenic hilar lymphadenopathy[1]. This rare subtype, involving 2% of non-Hodgkin's lymphomas [NHLs], is exclusively B cell in origin, and comprises low, intermediate and high grade histologic subtypes[2]. PSLs are usually curable after splenectomy and chemotherapy[3]. Splenectomy is the only procedure for pathologic diagnosis when a PSL is suspected. Recently, an ultrasound-guided percutaneous splenic biopsy using a core-needle has been employed as a less invasive alternative procedure. Here, we report a case initially suspected with infectious disorders with progressive splenomegaly and splenic infarction. In this setting, an ultrasound-guided, percutaneous, splenic biopsy using a core-needle yielded the definite diagnosis after four weeks of comprehensive investigations, during which all other diagnostic options were excluded.

Case presentation

A previously healthy 47-year-old Thai female presented to the emergency room with abdominal pain for one week and fever without night sweat or weight loss for two days. The initial physical examination revealed a low grade fever (38.0°C), generalized abdominal tenderness without guarding or rigidity, an inability to palpate the liver and spleen, an absence of splenic dullness, and no sign of superficial lymphadenopathy. Active pulmonary disease was undetected by chest radiography, and free intraperitoneal air was not visible in abdominal radiography. A computerized tomography (CT) scanning was performed and the only abnormality finding was an ovarian cyst (2.6 x 1.3 cm) in the left adnexa. According to the CT result, she was discharged and given oral medications for supportive and symptomatic treatment.

Ten days later, she revisited the emergency room because of her persistent fever and abdominal pain. At this time, she was readmitted to determine the etiology of her fever and abdominal pain. A physical examination revealed no superficial lymphadenopathy, an enlarged liver, 2 cm below the right costal margin, with a liver span of 16 cm, and enlarged section, 5 cm below the left costal margin. Her complete blood count showed hemoglobin of 13 g/dL, a white blood cell count of 11,400 cells/mm^3 (neutrophils 53%, lymphocytes 26%, reactive lymphocytes 8%, monocytes 9%), and a platelet count of 102,000 cells/mm^3. Her blood chemistry was also worked up. The results were BUN 8 mg/dL, creatinine 0.80 mg/dL, albumin 3.1 mg/dL, globulin 3.5 mg/dL, total bilirubin 0.5 mg/dL, direct bilirubin 0.1 mg/dL, aspartate aminotransferase 149 U/L, alanine aminotransferase 18 U/L, alkaline phosphatase 121 U/L, and lactic acid 1.41 mmol/L. Her bacterial cultures, anti-HIV, scrub typhus titer, Dengue IgM, IgG, Dengue NS1 and melioid titer were all negative. In addition, an echocardiogram performed could exclude infectious endocarditis.

The second abdominal CT scan performed on the second day of admission revealed splenomegaly with multifocal splenic infarction, patent splenic vein, no significant mediastinal and abdominal lymphadenopathy. The two abdominal CT scans performed at the initial visit and at this admission, demonstrated that her splenic volume increased from 317.89 mL to 821.49 ml (Figure 1).

In the second week of this admission, the patient developed a persistent high grade fever of 39°C and progressive left upper quadrant abdominal pain. As an empirical therapy for meliodosis, the patient initially received ceftriaxone intravenously for 5 days and was subsequently given ceftazidime intravenously for 14 days. Because the patient had a fever of unknown origin and thrombocytopenia, a bone marrow study was performed revealing normal myelopoiesis without any abnormal lymphoid cell aggregates.

Due to the worsening clinical course of the patient, an ultrasound-guided, percutaneous splenic biopsy using a core-needle was performed. The histologic finding of the splenic tissue showed focal aggregates of atypical

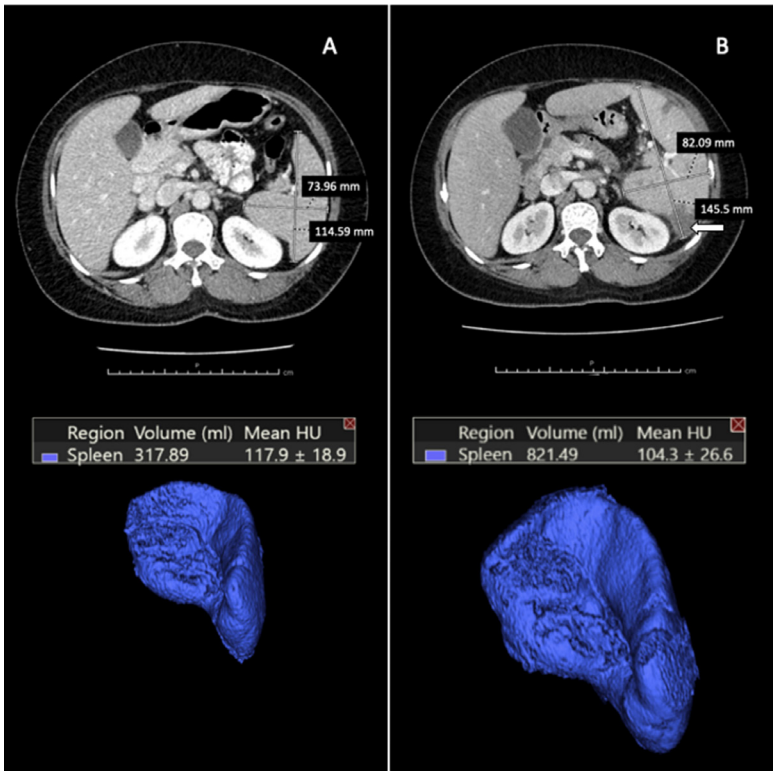

Figure 1 A) Contrast computed tomography scan performed at the first admission. **B**) Second contrast computed tomography scan, taken at the second week, showing progressive hepatosplenomegaly with multifocal splenic infarction without splenic vein thrombosis. An ultrasound-guided, percutaneous splenic biopsy was performed at the posterior aspect of the spleen (arrow).

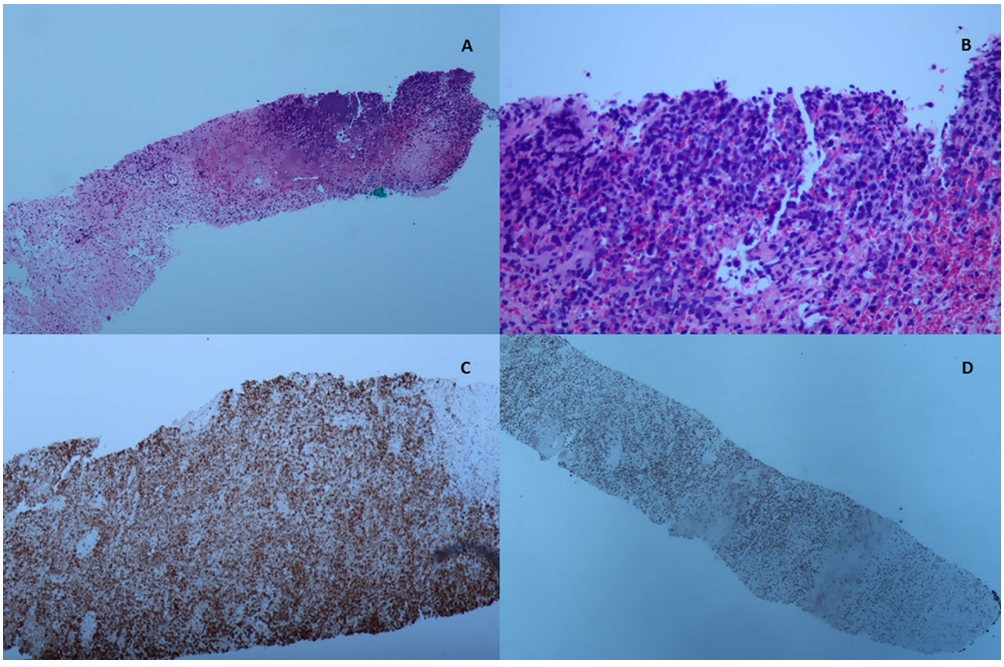

Figure 2 This hematoxylin and eosin-stained splenic section shows a few small aggregates and some infiltration of atypical large lymphoid cells with mild degree nuclear polymorphism. The nuclei are hyperchromatic with scant cytoplasm and exhibit an irregular nuclear outline. Mitotic figures are frequently observed. **A, B)** Red pulp is congested with focal infarction areas. **C)** Immunohistochemistry features of the spleen signify that these atypical large lymphoid cells are CD20 positive. **D)** Ki-67 staining shows a high activity in more than 80% of the tumor cells.

large lymphoid cells - CD20(+), CD3(-), Cyclin D1(-), CD10(-), BCL6(-), and MUM1(+) - with high (> 80%) Ki-67 positivity. The finding was consistent with diffuse large B-cell lymphoma (DLBCL), nongerminal center subtype (Figure 2).

The patient received standard R-CHOP chemotherapy. After the first cycle of R-CHOP, her fever and constitutional symptoms disappeared and her abdominal pain improved. After the third R-CHOP, the third abdominal CT scan demonstrated a dramatic decrease in the spleen size and regression of the multifocal splenic infarcts. A timeline of a long term treatment of the patient is provided in Supplementary Data 1.

Discussion

DLBCL is the most common lymphoma subtype, accounting for 40% of all lymphoma cases. This lymphoma subtype usually presents with lymphadenopathy but can frequently involve extranodal sites, for example, the brain, bones, kidneys, adrenal glands and soft tissues[4]. Immunohistochemistry is the gold-standard diagnostic tool for subtyping diagnoses, even in countries with limited resources. Additionally, gene expressing profiling and next-generation sequencing, increasingly have been used in Western countries to facilitate further stratifying of patients and personalizing of therapy[5]. Using standard frontline therapy among young patients, the current 6-year event-free survival rate of DLBCL is approximately 70%[6].

DLBCL diagnosis is challenging among patients without peripheral lymphadenopathy and deep organ involvement, inaccessible to fine-needle biopsy. At presentation, 30% to 40% of patients with NHLs have splenic involvement[7]; however, in the vast majority of cases, the NHLs are disseminated rather than being confined to the spleen. Splenic involvement of lymphomas can be classified in primary and secondary types. While primary solitary splenic lymphoma is very rare, accounting for only 2% of all NHLs, secondary splenic involvement of NHL is common[2]. Primary splenic lymphoma is classified in three disease stages: stage 1 refers to a disease that is present only in the spleen; stage 2 involves spleen and hilar lymph node involvement and stage 3 signifies extra-splenic nodal or hepatic involvement[8]. Imaging studies of splenic lymphomas usually show a single splenic mass and multiple focal splenic masses[7] but splenic infarction is extremely rare. The reported patient had a quickly deteriorating condition with rapid progression of splenomegaly, which is why we did not opt for a spleen biopsy due to its high risk of bleeding complications. Therefore, before committing to the procedure, we reviewed the safety reports of ultrasound-guided percutaneous splenic biopsies[9]. Therefore, the splenic biopsy was undertaken, during the fourth week from clinical onset and without bleeding sequelae.

This case constituted an unusual presentation of DLBCL with splenic infarction without splenic masses or lymphadenopathy. The clinical course of the patient mimicked infectious causes that are far more common in Thailand. The need existed to make a differential diagnosis between splenic infarction and splenic collection among our patients. Because the patient was unwilling to undergo any major operation, a splenectomy was not performed. Instead, a splenic biopsy was deemed a safe procedure by our surgeon. Because the spleen is a hypervascular organ, ultrasound-guided, percutaneous splenic biopsy using a core-needle was decided to be carried out because the benefits outweighed the risk of major bleeding sequelae. The main limitation of this case report is that a completed cytogenetic workup and immunostaining of tissue biopsy could not be performed due to the limited resources in our institute.

Conclusion

This report showed the benefit of the ultrasound-guided, percutaneous splenic biopsy for obtaining adequate splenic tissue to diagnose primary splenic lymphoma.

Supplementary Data 1

Dates	**Relevant Past Medical History and Interventions**		
	She did not have any history of previous medical illness and underlying diseases.		
Dates (Place)	Summaries from Initial and Follow-up Visits	Diagnostic Testings	Interventions
5 Oct 2020 (Emergency room)	She presented to the emergency room with clinical abdominal pain for a week and acute fever for 2 days without night sweats or weight loss.	The investigations for diagnosis acute abdominal pain consisted of: CBC: Hb 15 g/dL, WBC 17.4 $x10^9$/L, Platelet 115 $x10^9$/L Chest radiography: no active pulmonary disease Abdominal radiography: no free intraperitoneal air Computerized tomography (CT) scanning: an ovarian cyst (2.6 x 1.3 cm) in the left adnexa, otherwise unremarkable.	According to the CT result, she was discharged and given oral medications for supportive and symptomatic treatment.
15 Oct 2020 (IPD)	she still had a fever and abdominal pain, she revisited the emergency room. This time, she was admitted for a work-up etiology of her fever and abdominal pain.	The investigations for a work-up etiology of her fever and abdominal pain consisted of: CBC: Hb 13 g/dL, WBC 11.4 $x10^9$/L, Platelet 102 $x10^9$/L BUN 8 mg/dl, Cr 0.80 mg/dL Albumin 3.1 mg/dL, globulin 3.5 mg/dL, TB 0.5 mg/dL, DB 0.1 mg/dL, AST 149 U/L, ALT 18 U/L, ALP 121 U/L Lactic acid 1.41 mmol/L anti-HIV, scrub typhus titer, Dengue IgM, IgG, Dengue NS1, and melioid titer: all negative Hemoculture: NG Echocardiogram: no infectious endocarditis	Ceftriaxone iv for 5 days
16 Oct 2020 (IPD)	A physical examination revealed an enlarged liver (2 cm below the right costal margin, with a liver span of 16 cm), and her spleen could be palpated 5 cm below the left costal margin.	The investigations for diagnosis of progressive hepatosplenomegaly: The second abdominal CT scan: splenomegaly with multifocal splenic infarction, patent splenic vein, no significant mediastinal, and abdominal lymphadenopathy, splenic volume had increased from 317.89 mL to 821.49 mL within 11 days	Ceftazidime iv for 14 days
21 Oct 2020 (IPD)	Her fever did not respond to empirical antibiotic and therapy for melioidosis. Given that the patient had a fever of unknown origin as well as thrombocytopenia.	A bone marrow study was conducted; it revealed normal myelopoiesis and no lymphoid cell aggregates	none
10 Nov 2020 (IPD)	She still had fever, abdominal pain, progressive splenomegaly with splenic infarction.	A splenic core-needle biopsy: focal aggregates of atypical lymphoid cells; CD20(+), CD3(-), Cyclin D1(-) and CD10(-) with high (> 80%) Ki-67 positivity. The finding was consistent with diffuse large B-cell lymphoma	1st R-CHOP D1= 11 Nov 2020

Supplementary Data 1 (continue)

8 Dec 2020 (OPD hemato)	After the first cycle, her clinical status was dramatically improved, the fever had disappeared, and there was an improvement in her abdominal pain and constitutional symptoms	CBC: Hb 11.3 g/dL, WBC 6.2 x 10^9/L, Platelet 292 x 10^9/L	2nd R-CHOP D1= 9 Dec 2020 3rd R-CHOP D1= 6 Jan 2021
30 Jan 2021 (OPD hemato)	After the third cycle of R-CHOP, there was an improvement in her abdominal pain	The third abdominal CT scan: a dramatic decrease in the size of the spleen and regression of the multifocal splenic infarcts.	Continue R-CHOP every 4 weeks and plan follow up the abdominal CT scan after 6th R-CHOP

Declarations

Ethics approval and consent

This case report was approved by the Chiang Rai Hospital Ethics Committee.

Consent for publication

Written informed consent was obtained from patients to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

Availability of data and materials is not applicable

Competing interests

The authors declared that they have no competing interests.

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Authors' contributions

WP contributed manuscript writing, ethics approval and patient consent form, CC provided CT abdomen reconstruction for splenic volume. NK provided the spleen and bone marrow pathologic report and morphology. AL performed a percutaneous biopsy of the spleen. WO and PH wrote, reviewed and approved the manuscript. All authors read and approved the final manuscript.

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