European Review for Medical and Pharmacological Sciences 2016; 20: 1691-1698

# Image-guided percutaneous liver biopsy in hepatosplenic gamma-delta T-cell lymphoma: a single centre experience

C.-C. WANG, L.-Y. CHEN, K. LIU, X.-Q. LIU, D.-J. LI

Center of Infectious Diseases, West China Hospital of Sichuan University, Chengdu, Sichuan Province, China

**Abstract. – OBJECTIVE: This study was to determine whether Image-Guided Percutaneous Liver Biopsy (IGPLB) is a safe and accurate procedure in patients with Hepatosplenic Gamma-Delta T-Cell Lymphoma (HSTCL) characterized by hepatosplenomegaly, and provide a rapid and safe diagnostic approach in this rare group of patients with a generally poor outcome.**

**PATIENTS AND METHODS: We report five patients who underwent IGPLB for an initial diagnosis of HSTCL, in whom diagnosis by bone marrow biopsy and blood smear had failed. The patients presented with fever of undetermined origin, fatigue, night sweats and abdominal pain. Percutaneous liver biopsies were performed following location of the puncture point under the guidance of computed tomography (CT) or ultrasonography (US).**

**RESULTS: CT and US can detect prominent hepatosplenomegaly without significant lymphadenopathy. IGPLB, assessed by immunohistochemical and molecular pathological analyses, was then performed without complications, which resulted in the diagnosis of HSTCL and facilitated treatment in a timely manner.**

**CONCLUSIONS: IGPLB is a safe and accurate procedure in patients with suspected underlying malignant lymphoma characterized by hepatosplenomegaly, especially in those without readily accessible tissue amenable to biopsy.**

*Key Words:*
Image-Guided Percutaneous Liver Biopsy (IGPLB), Diagnosis, Hepatosplenic Gamma-Delta T-Cell Lymphoma (HSTCL).

## Introduction

Hepatosplenic Gamma-Delta T-cell Lymphoma (HSTCL) is a rare hematological neoplasm and accounts for approximately 3% of all T-cell lymphoma subtypes in the United States, 2.3% in Europe, and 0.2% in Asia[1-4]. HSTCL is a diagnostic challenge and a treatment-resistant lymphoid neoplasm characterized by primary extranodal proliferation of neoplastic cells with typical intrasinusoidal infiltration of the bone marrow, liver and spleen, resulting in marked hepatosplenomegaly and peripheral blood cytopenia. In non-Hodgkin lymphomas (NHLs), the liver is less involved than the lymph nodes, bone marrow and spleen, with the majority of secondary dissemination in advanced disease rather than primary hepatic involvement[5,6]. However, in HSTCL there is a high frequency (80-88.2%) of liver involvement[2,7].

As pathological examination is thought to be the standard diagnostic strategy in the clinical setting, obtaining timely and sufficient materials from accessible tissues by bone marrow, liver, spleen or lymph node biopsy is extremely significant as prompt diagnosis can improve the clinical outcome of malignancies[2,5]. Traditionally, bone marrow biopsy is regarded as the gold standard in the diagnosis of HSTCL, as bone marrow involvement is seen in 72% of patients at diagnosis[5]. However, the accurate diagnosis of malignant lymphoma in those without identifiable indications using bone marrow biopsy or blood smear is difficult, which prompted us to try other accessible methods for the diagnosis of this disease. HSTCL is characteristically associated with sinusoidal or sinusal infiltration of the liver and the spleen by malignant cells. The utility of liver biopsy as a diagnostic method has been shown to be safe and accurate with a high diagnostic yield if no alternative tissue is amenable to biopsy[2,3,7,8].

Based on the above findings and the presence of prominent hepatosplenomegaly, we performed IGPLB in our patients suspected of having malignant lymphoma who had negative bone marrow biopsy or blood smear results. The diagnosis of HSTCL was established in all patients. There-

*Corresponding Author:* Dajiang Li, MD; e-mail: Dajiang1012@aliyun.com

fore, an early awareness that IGPLB is a safe and accurate procedure in patients suspected of having malignant lymphoma is necessary for correct diagnosis.

Overall, this work demonstrated that IGPLB is a safe and accurate procedure in patients with suspected underlying malignant lymphoma characterized by hepatosplenomegaly, and provides a rapid and safe diagnostic approach in this rare group of patients with a generally poor outcome.

## Patients and Methods

Based on the Hospital Information System (HIS), we retrospectively searched for patients with a definite diagnosis of lymphoma by liver biopsy at a single center between January 2005 and June 2014. Following careful screening, the following patients were excluded: those with previously confirmed HSTCL on initial bone marrow biopsy or other biopsies and patients with sophisticated malignant systema sanguineum diseases or other undistinguishable lymphatic disorders diagnosed by liver biopsy. Liver biopsy specimens were reviewed (A.R.) and patients without a diagnosis of lymphoma were excluded. Thus, five cases of HSTCL following liver biopsy were identified and analyzed. According to the World Health Organization classification of tumors in hematopoietic and lymphoid tissues, the diagnosis of lymphoma was confirmed based on its characteristic clinical, histologic, and immunophenotypic features. Staging of HSTCL was carried out according to the Ann Arbor system (1971).

All patients underwent a comprehensive examination and obtained a specific diagnosis. First, history taking and physical examination were performed followed by hematologic and biochemical evaluations, computed tomography (CT) or ultrasonography (US) examinations of the chest and abdomen, bone marrow aspiration, liver biopsy and then precise techniques for diagnosis.

Percutaneous liver biopsies were performed following location of the puncture point under the guidance of computed tomography (CT) or ultrasonography (US). The patients' vital signs were closely monitored, both before and after liver biopsy, to exclude the possible related complications of arterial embolization or hematoma due to hemorrhage.

## Results

### Clinical Manifestations

The clinical and peripheral laboratory characteristics are shown in Table I. The patients were admitted or transferred to the hematology department in our hospital, initially due to various clinical presentations, particularly fever of undetermined origin, fatigue, night sweats and abdomi-

**Table I.** The clinical and peripheral laboratory characters.

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Age/gender | 21/male | 22/male | 28/male | 21/female | 15/female |
| Diagnosis | HSTCL | HSTCL | HSTCL | HSTCL | HSTCL |
| Clinical features | | | | | |
| Fever | + | + | + | + | + |
| Fatigue | + | – | – | – | – |
| Abdominal pain | – | + | – | – | – |
| Night sweat | + | + | – | – | – |
| Weight loss | – | – | – | – | – |
| Loss of appetite and nausea. | – | – | – | – | – |
| B-symptoms | + | + | + | + | + |
| Hepatic insufficiency | | | | | |
| CT imaging | | | | | |
| Hepatomegaly | + | + | + | + | + |
| Splenomegaly | + | + | + | + | + |
| HIV/HBV/HCV/EBV infection | – | – | – | – | – |
| Blood pancytopenia | + | + | + | + | + |
| Bone marrow First/second | –/– | –/– | –/+ | –/– | –/+ |
| Liver biopsy | + | + | + | + | + |
| Hepatic sinusoidal infiltration | + | + | + | + | + |

nal pain. Our patients seldom exhibited weight loss. All five patients had persistent fever, accompanied by fatigue in two cases, night sweats in two and abdominal pain in one patient. Fever in two cases was alleviated in the short-term by anti-inflammatory treatment; however, fever recurred repeatedly. The clinical presentations were similar to those previously described for lymphoma. The patients were young, with a median age of 22 years (15-28 years) at presentation, and included three males and two females.

During the initial physical examinations, hepatomegaly and splenomegaly were common, and superficial lymph node enlargement was absent. Peripheral laboratory test results included hematologic and biochemical parameters such as blood count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, and lactate dehydrogenase (LDH) levels, and enzymes related to blood coagulation or inflammation. On blood examination, immune-related pancytopenia was observed in almost all cases, as shown in Table I. Suppressed hematopoiesis manifesting as cytopenia may have been due to hypersplenism, bone marrow infiltration, or cytokines such as interferon-γ released by neoplastic γδ T cells. There were no specific findings of lymphocytosis in peripheral blood, as this is presumed to occur in the terminal stage of the disease accompanied by lymphocytic and blastic evolution[9]. The biochemical results included an elevated LDH level and a range of increases in ALT and AST due to hepatic dysfunction. Improvements in total bilirubin, direct bilirubin and gamma-glutamyl transpeptidase (GGT) were found in one patient, which were suspicious for co-existing biliary disease.

CT or abdominal US findings were available for all patients with hepatosplenomegaly. CT demonstrated multiple, space-occupying lesions in the liver in four patients, while hepatomegaly without obvious lesions on CT scanning was detected in one patient. In one case, chest CT identified inflammation in the right lung, suggesting respiratory tract infection. We suspected possible pulmonary tuberculosis prior to accurate diagnosis. Considering the subsequent accurate diagnosis of HSTL, tuberculosis was excluded.

During the initial diagnosis of patients with systemic B symptoms (fever of undetermined origin, fatigue, night sweats and abdominal pain) and characteristic hepatosplenomegaly at our hospital, we initially performed bone marrow biopsy, but with unsatisfactory results. Following bone marrow biopsy, liver biopsy was performed in all patients after location of the puncture point, due to the presence of marked hepatosplenomegaly, during which tumor cells were found to have predominantly invaded the hepatic sinusoids or portal tracts. We performed a second bone marrow biopsy in these patients during the later disease course, and two cases with positive lymphocyte proliferation were identified.

Bone marrow biopsy was performed two or three times in all cases. However, no typical malignant cells were discovered in the first bone marrow aspirates. Three cases had active bone marrow hyperplasia. One had a major proliferation of neutrophils and lymphocytes accounting for 26% of all mature lymphocytes. One patient had active hyperplasia, in which malignant lymphoma was suspected due to a large number of primitive cells in bone marrow aspirates, but no further abnormal cells were identified. The remaining patient had hyperplasia on bone marrow biopsy, in which granulocytes accounted for 52% and primitive cells accounted for 70%, with difficulties in separation. The other 2 cases were characterized by low bone marrow hyperplasia, in which three series decreased and three cell morphologies did not show abnormalities.

### Liver Biopsy Results

Following bone marrow biopsy, IGPLB was performed in all patients after location of the puncture point, due to the presence of marked hepatosplenomegaly, which resulted in the prompt and accurate diagnosis of HSTCL due to irregular sinusoidal infiltration by medium-sized lymphocytes.

The liver was an accessible site for biopsy, with or without the identification of space-occupying lesions in the liver. Major complications were not observed in any of the patients after this procedure. Combining subsequent Flow Cytometry Method (FCM) and immunohistochemistry technology, the diagnosis of HSTCL was further defined. In all five patients, we observed the predominant infiltration of recognizable small- to medium-size neoplastic cells in the hepatic sinusoids. The neoplastic lymphocytes were homogeneously and predominantly distributed in the hepatic sinusoids referred to as a dense infiltrate[10] with visible and basophilic nuclei, and mildly dispersed chromatin. The nucleus was round or oval, and the cytoplasm showed moderately pale-

staining with obscure cellular borders in patients with HSTCL. Subsequent TCRγ gene cloning rearrangement was performed to support the diagnosis in 4/5 patients with HSTCL.

IGPLB was found to be a safe and accurate procedure in patients with suspected underlying malignant lymphoma characterized by hepatosplenomegaly, and none of the patients developed bleeding complications. All patients experienced temporary manageable pain treated with local anesthesia.

### Immunophenotype

The immunophenotype results are shown in Table II. In all patients diagnosed with HSTCL, the lymphoid cells presented CD3, CD3p and TIA-1 antigen expression, but lacked CD20 and granzyme B. A negative reaction for TCRβF1 (the marker of αβ T-cells) was detected in all 5 patients, coinciding with the diagnosis of γδ T-cell lymphoma. The CD56 antigen was frequently expressed in four cases, and three cases were positive for CD45, CD16 as well as CD7 antigen.

## Discussion

HSTCL was initially reported by Farcet et al[11] in 1990 and first incorporated into the Revised European American Lymphoma (REAL) classification system in 1994. HSTCL is regarded as a distinct rare lymphoma entity of peripheral T-cell lymphoma (PTCL) derived from a small subgroup of γδ T-cell receptor-expressing lymphocytes. It may be associated with genetic abnormalities such as isochromosome 7q (i7q), trisomy 8 and loss of the Y chromosome in genetic analysis and cytogenetic studies[12]. HSTCL has an aggressive clinical course, a poor outcome and poor prognosis. Susceptibility to PTCL, particularly HSTCL, is observed in patients with immunosuppression, especially in those who have undergone solid organ transplantation and those with autoimmune disorders, such as inflammatory bowel diseases and rheumatoid arthritis, leading to a poor prognosis[12-14]. HSTCL represents a diagnostic challenge and is a treatment-resistant lymphoid neoplasm characterized by primary extranodal proliferation of neoplastic cells with typical intrasinusoidal infiltration in the bone marrow, liver and spleen, as well as the skin, oral mucosa, and kidney during progression[13], resulting in marked hepatosplenomegaly and peripheral blood cytopenia. The diagnostic approach in this disorder is challenging, due to its extremely rare occurrence or prevalence, in conjunction with its propensity to mimic other specific pathological entities, owing to its easily confused clinical presentation, including fever and hepatosplenomegaly in the absence of overt lymphadenopathy and cytopenia. Based on the above, awareness of HSTCL is of paramount importance and HSTCL must be distinguished from other entities. Indeed, within the HSTCL hypothesis, a straightforward diagnostic algorithm that may include the analysis of bone marrow, peripheral blood, liver and spleen would help achieve an accurate diagnosis. In the past, splenectomy was frequently performed for diagnostic and therapeutic purposes. However, bone marrow biopsy, peripheral blood smear and image–guided biopsy of the liver are now performed for diagnostic evaluation.

In previous studies[2,3,13], splenectomy was performed for approximately half of diagnostic or therapeutic purposes in HSTCL, which was like-

**Table II.** Immunophenotype in this study.

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Diagnosis | HSTCL | HSTCL | HSTCL | HSTCL | HSTCL |
| CD3 | + | + | + | + | + |
| CD56 | + | + | + | + | – |
| TIA–1 | + | + | + | + | + |
| CD20 | – | – | – | – | – |
| CD3p | + | + | + | + | + |
| CD45 | + | / | + | + | / |
| CD16 | + | – | + | + | / |
| CD7 | + | – | + | + | / |
| CD5 | – | – | + | – | – |

ly due to the underestimation of bone marrow and liver examinations. It appears that infiltration into bone marrow was initially overlooked in some cases in the present series, but was easily documented by histological review associated with appropriate immunostaining[13]. Although a few case reports have suggested that splenectomy could be important in selected patients, either in those with extreme forms of splenomegaly-associated cytopenia, including splenic rupture[15], or in those whose platelet counts increased after the procedure, making them suitable for further chemotherapy treatment[16], splenectomy has not been routinely undertaken in patients with HSTCL since 1995. It is not only a very invasive procedure, but is also not particularly helpful in the long-term treatment, as splenomegaly and thrombocytopenia can develop due to the involvement of malignant lymphocytes in the spleen. Thrombocytopenia is recognized to result partly from hypersplenism; however, some reports have demonstrated that cytokine secretion by neoplastic γδ T cells, such as interferon-γ, may contribute to the suppression of hematopoiesis and an autoimmune mechanism of γδ T cells could also explain thrombocytopenia[13,17-19]. Even in patients who underwent splenectomy, recurrent thrombocytopenia paralleled disease progression, and favors the second explanation[13,20]. In addition, the occurrence of consequent thrombocythemia may lead to the misdiagnosis of idiopathic thrombocytopenia or other hematological disorders, along with an increased risk of potentially fatal clot formation[3]. The post-splenectomy state is associated with an increased risk of sepsis due to encapsulated organisms (such as *Haemophilus influenzae* and *Streptococcus pneumoniae*)[17]. Therefore, splenectomy may not be suitable and could be phased out in patients with malignant lymphoma.

The high occurrence or prevalence of bone marrow involvement in HSTCL is well known. According to the literature, bone marrow involvement in HSTCL is found in 72% of patients at diagnosis and in 50% of peripheral blood samples[2]. Bone marrow biopsy assessed by morphological and molecular investigations together with appropriate immunophenotypic analysis, including TCRγ rearrangement and flow cytometry phenotype, is an important part of the initial evaluation of patients with malignant lymphoma[13]. It typically shows a neoplastic intrasinusoidal infiltration of homogeneous medium-sized neoplastic lymphoid cells. However, as bone marrow involvement is usually subtle, it is difficult to recognize without immunohistochemistry, making the accurate diagnosis of HSTCL from an initial bone marrow biopsy or aspirate unsatisfactory and sometimes misleading. Studies have demonstrated that 6/19 (31.5%) positive bone marrow biopsies have been missed, leading to misdiagnoses including reactive hypercellular marrow and chronic myelomonocytic leukemia at initial examination[13]. The recognition of lymphoma infiltration would be enabled by appropriate solutions that may allow careful histologic and immunohistologic evaluation of bone marrow biopsy specimens, and alternative tissues amenable to biopsy, such as the liver.

Traditionally, bone marrow biopsy is regarded as the gold standard in the diagnosis of HSTCL due to the high occurrence or prevalence of bone marrow involvement. However, the accurate diagnosis of malignant lymphoma in patients with a negative bone marrow biopsy or peripheral blood smear, prompted us to identify other accessible methods for the diagnosis of this lymphoma. HSTCL is characteristically associated with sinusoidal or sinusal infiltration of the liver and spleen by malignant cells. The utility of liver biopsy as a diagnostic method has been shown to be safe and accurate with a high diagnostic accuracy if no alternative tissue is amenable to biopsy[2,3,7,8]. Based on the above, and prompted by prominent hepatosplenomegaly, we performed IGPLB in our patients with suspected malignant lymphoma who had negative bone marrow biopsy or blood smear results, and the diagnosis of HSTCL was made in all patients. Thus, an early awareness that IGPLB is a safe and accurate procedure in most patients with hepatosplenomegaly and suspected underlying malignant lymphoma is necessary for correct diagnosis.

Although primary hepatic lymphoma is rare[21], the liver is involved in HSTCL in 88% of patients; thus, core needle biopsy of the liver can be used for the diagnosis of lymphoma secondary to bone marrow biopsy[1,5,22,23].

In patients with suspected lymphoma, but without identifiable indications (negative bone marrow biopsy or blood smear), liver biopsy can yield crucial primary diagnostic information[14,24]. Successful liver biopsy and the importance of a positive biopsy increase the outcome of a positive HSTCL diagnosis and prove that liver biopsy is an adequate and feasible procedure for identifying liver involvement in lymphoma. It can reveal a previously unknown lymphoma with the

aid of immunohistochemistry or TCR rearrangement analysis during the evaluation of a solid hepatic mass[25]. In previous studies[2,3,5,7,13], liver biopsy was performed less frequently than splenectomy and bone marrow biopsy for the diagnosis of HSTCL, mainly due to the risks of hemorrhage, which can easily occur during a blind biopsy in the absence of imaging guidance. In most patients who have successfully undergone liver biopsy, a hepatic involvement of malignant lymphocytes has been detected, illustrating the high diagnostic yield of liver biopsy. Liver biopsy also has a high diagnostic rate (41.2%) in China[7]. In addition, liver biopsy has significant diagnostic value in other lymphoma entities besides HSTCL. In 64% of cases[5], liver biopsy identified the primary diagnosis of lymphoma in patients with no positive results following extrahepatic biopsy or peripheral blood analysis. We found that a second bone marrow biopsy detected characteristic lymphocytes in several cases (13%), in which the first bone marrow evaluation failed due to identify mild infiltration[5].

However, HSTCL is frequently associated with thrombocytopenia either due to hypersplenism, bone marrow infiltration, the release of cytokines from neoplastic T-cells or to an autoimmune mechanism of CD T cells[19]. The risk of related post-procedural complications, especially major hemorrhage and even death, are still of great importance, making clinicians and pathologists reluctant to perform a liver biopsy. The proportion of hemorrhage-related deaths after liver biopsy was reported to be 0.11%[26,27]. Major risks during this procedure could be avoided with inchoate platelet elevation[19]. With the use of functional imaging, including CT, ultrasound and 18 F-FDG-PET, and with the technical improvements by biopsy specialists, the risk of hemorrhage is reduced, and percutaneous liver biopsy can be performed preferentially with expected complications and high diagnostic value.

In the present study, no major complications after percutaneous liver biopsy were observed, however, several patients complained of slight abdominal pain for 1 day after the procedure.

Factors statistically associated with bleeding include baseline platelet counts of less than 60 * 10 9/L and baseline INRs of more than 1.5. Clinically, a biopsy directed at a focal lesion has been suggested to increase the risk of hemorrhage[26]. The contraindications of liver biopsy along with the patient's clinical condition should be considered to avoid major complications. Clinicians and pathologists should strictly obey the guidelines for biopsy practice and highlight bleeding risk assessment, hemostasis and pre-biopsy assessment of coagulation parameters due to the high frequency and potential severity of major hemorrhage. Special consideration should be paid to patients with thrombocytopenia or dysfunctional platelets with regard to INR levels and platelet levels before the procedure[26,28,29].

We must point out that this study has imperfection of selection bias and the number of cases is small. Moreover, due to the misleading clinical picture at presentation, an accurate diagnosis is generally made in an advanced disease stage in the vast majority of cases. Thus, the development of rapid and safe diagnostic methods to facilitate therapy for this deadly disease is essential.

## Conclusions

We consider that the liver is an accessible tissue for biopsy puncture, and IGPLB is a safe and accurate procedure in patients with suspected underlying malignant lymphoma characterized by hepatosplenomegaly, especially in those without readily accessible tissue amenable to biopsy.

### Acknowledgements

This study was funded in full by "Science and Technology Support Plan, Department of Technology, Sichuan Province", grant number is 2012SZ0020.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

## References

1) Salmon JS, Thompson MA, Arildsen RC, Greer JP. Non-Hodgkin's lymphoma involving the liver: clinical and therapeutic consideration. Clin Lymphoma Myeloma 2006; 6: 273-280.
2) Weidmann E. Hepatosplenic T cell lymphoma. A review on 45 cases since the first report describing the disease as a distinct lymphoma entity in 1990. Leukemia 2000; 14: 991-997.
3) El-Sharkawi D, Ramsay A, Cwynarski K, Hughes D, Prentice A, Davies N, Goode A, Wylie P, Malhotra A, Warbey V, Dooley J, McNamara C. Clinicopathologic characteristics of patients with hepatic lymphoma diagnosed using image-guided liver biopsy techniques. Leuk Lymphoma 2011; 52: 2130-2134.

4) Stancu M, Jones D, Vega F, Medeiros LJ. Peripheral T-cell lymphoma arising in the liver. Am J Clin Pathol 2002; 118: 574-581.

5) Loddenkemper C, Longerich T, Hummel M, Ernestus K, Anagnostopoulos I, Dienes HP, Schirmacher P, Stein H. Frequency and diagnostic patterns of lymphomas in liver biopsies with respect to the WHO classification. Virchows Archiv 2007; 450: 493-502.

6) Raja P, Jackel JN, Li S, Heard IM, Bisaro DM. Arabidopsis double-stranded RNA binding protein DRB3 participates in methylation-mediated defense against geminiviruses. J Virol 2013; 88: 2611-2622.

7) Lu CL, Tang Y, Yang QP, Wang M, Zhao S, Bi CF, Jiang NG, Zhang WY, Liu JP, Xu X, Liu WP. Hepatosplenic T-cell lymphoma: clinicopathologic, immunophenotypic, and molecular characterization of 17 Chinese cases. Hum Pathol 2011; 42: 1965-1978.

8) Falchook GS, Vega F, Dang NH, Samaniego F, Rodriguez MA, Champlin RE, Hosing C, Verstovsek S, Pro B. Hepatosplenic gamma-delta T-cell lymphoma: clinicopathological features and treatment. Ann Oncol 2009; 20: 1080-1085.

9) Visnyei K, Grossbard ML, Shapira I. Hepatosplenic γδ T-cell lymphoma: an overview. Clin Lymphoma Myeloma Leuk 2013; 13: 360-369.

10) Wilson AL, Swerdlow SH, Przybylski GK, Surti U, Choi JK, Campo E, Trucco MM, Van Oss SB, Felgar RE. Intestinal gammadelta T-cell lymphomas are most frequently of type II enteropathy-associated T-cell type. Human Pathol 2013; 44: 1131-1145.

11) Farcet JP, Gaulard P, Marolleau JP, Le Couedic JP, Henni T, Gourdin MF, Divine M, Haioun C, Zafrani S, Goossens M, et al. Hepatosplenic T-cell lymphoma: sinusal/sinusoidal localization of malignant cells expressing the T-cell receptor gamma delta. Blood 1990; 75: 2213-2219.

12) Tamaska J, Adam E, Kozma A, Gopcsa L, Andrikovics H, Tordai A, Halm G, Bereczki L, Bagdi E, Krenacs L. Hepatosplenic gammadelta T-cell lymphoma with ring chromosome 7, an isochromosome 7q equivalent clonal chromosomal aberration. Virchows Archiv 2006; 449: 479-483.

13) Belhadj K, Reyes F, Farcet JP, Tilly H, Bastard C, Angonin R, Deconinck E, Charlotte F, Leblond V, Labouyrie E, Lederlin P, Emile JF, Delmas-Marsalet B, Arnulf B, Zafrani ES, Gaulard P. Hepatosplenic gammadelta T-cell lymphoma is a rare clinicopathologic entity with poor outcome: report on a series of 21 patients. Blood 2003; 102: 4261-4269.

14) Ashmore P, Patel M, Vaughan J, Wiggill T, Willem P, van den Berg E, Philip V, Lakha A. Hepatosplenic T-cell lymphoma: a case series. Hematol Oncol Stem Cell Ther 2015; 8: 78-84.

15) Nguyen BM, Halprin C, Olimpiadi Y, Traum P, Yeh JJ, Dauphine C. Core needle biopsy is a safe and accurate initial diagnostic procedure for suspected lymphoma. Am J Surg 2014; 208: 1003-1008.

16) Gumbs AA, Zain J, Neylon E, MacGregor-Cortelli B, Patterson M, O'Connor OA. Importance of early splenectomy in patients with hepatosplenic T-cell lymphoma and severe thrombocytopenia. Ann Surg Oncol 2009; 16: 2014-2017.

17) Working Party of the British Committee for Standards in Haematology Clinical Haematology Task Force. Guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen. Br Med J 1996; 312: 430-434.

18) Vandervelde C, Kamani T, Varghese A, Ramesar K, Grace R, Howlett DC. A study to evaluate the efficacy of image-guided core biopsy in the diagnosis and management of lymphoma--results in 103 biopsies. Eur J Radiol 2008; 66: 107-111.

19) Motta G, Vianello F, Menin C, De Nicolo A, Agata S, Altavilla G, Pietrogrande F, Girolami A. Hepatosplenic gammadelta T-cell lymphoma presenting with immune-mediated thrombocytopenia and hemolytic anemia (Evans' syndrome). Am J Hematol 2002; 69: 164-170.

20) Shimizu I, Okazaki Y, Takeda W, Kirihara T, Sato K, Fujikawa Y, Ueki T, Hiroshima Y, Sumi M, Ueno M, Ichikawa N, Kobayashi H. Use of percutaneous image-guided coaxial core-needle biopsy for diagnosis of intraabdominal lymphoma. Cancer Med 2014; 3: 1336-1341.

21) Mastoraki A, Stefanou MI, Chatzoglou E, Danias N, Kyriazi M, Arkadopoulos N, Smyrniotis V. Primary hepatic lymphoma: dilemmas in diagnostic approach and therapeutic management. Indian J Hematol Blood Transfus 2014; 30: 150-154.

22) Bagley CM Jr, Thomas LB, Johnson RE, Chretien PB, DeVita VT Jr. Diagnosis of liver involvement by lymphoma: results in 96 consecutive peritoneoscopies. Cancer 1973; 4: 840-847.

23) Murase T, Yamaguchi M, Suzuki R, Okamoto M, Sato Y, Tamaru J, Kojima M, Miura I, Mori N, Yoshino T, Nakamura S. Intravascular large B-cell lymphoma (IVLBCL): a clinicopathologic study of 96 cases with special reference to the immunophenotypic heterogeneity of CD5. Blood 2007; 109: 478-485.

24) Vose J, Armitage J, Weisenburger D; International T-Cell Lymphoma Project. International peripheral T-cell and natural killer/T-cell lymphoma study: pathology findings and clinical outcomes. J Clin Oncol 2008; 26: 4124-4130.

25) Khan NN, Jijina FF, Joshi AS, Gupte PA, Chaturvedi RA. Hepatosplenic T cell lymphoma. Indian J Hematol Blood Transfus 2014; 30: 21-23.

26) Howlett DC, Drinkwater KJ, Lawrence D, Barter S, Nicholson T. Findings of the UK national audit evaluating image-guided or image-assisted liver biopsy. Part II. Minor and major complications and procedure-related mortality. Radiology 2013; 266: 226-235.

27) Aoki Y, Takamiya M, Satoh T, Fujita S, Kato H, Maeno Y. A fatal case of hemoperitoneum after ultrasound-guided liver biopsy in a patient with intravascular large B-cell lymphoma. Leg Med 2011; 13: 191-195.

28) Seeff LB, Everson GT, Morgan TR, Curto TM, Lee WM, Ghany MG, Shiffman ML, Fontana RJ, Di Bisceglie AM, Bonkovsky HL, Dienstag JL; HALT–C Trial Group. Complication rate of percutaneous liver biopsies among persons with advanced chronic liver disease in the HALT-C trial. Clin Gastroenterol Hepatol 2010; 8: 877-883.

29) Sekiguchi N, Joshita S, Yoshida T, Kurozumi M, Sano K, Nakagawa M, Ito T, Matsushita T, Komatsu D, Komatsu M, Ito T, Umemura T, Ikeda S, Kadoya M, Ishida F, Tanaka E. Liver dysfunction and thrombocytopenia diagnosed as intravascular large B-cell lymphoma using a timely and accurate transjugular liver biopsy. Intern Med 2013; 52: 1903-1908.