

## PERCUTANEOUS HISTOPATHOLOGIC EVALUATION OF LIVER IN TREATMENT OF NON-HODGKIN'S LYMPHOMA

BY

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### ABSTRACT

The results of 25 percutaneous biopsies of the liver from 24 patients with non-Hodgkin's lymphoma are reported. In all cases, the value of their serum biochemistry (LDH, GOT, GPT and/or alkaline phosphatase) was abnormal and sufficient tissue material was biopsied to obtain a histopathological evaluation.

Specimens from five ultrasonically suspected lymphoma of the liver showed tumor involvement histopathologically. Diffuse tumor involvement was also histologically found in three ultrasonically unsuspected livers. Six liver specimens showed degenerative and/or fibrotic change in the new and previously treated patients.

Key words: Malignant lymphoma, Biopsy, Ultrasound, Liver.

### INTRODUCTION

In patients with non-Hodgkin's lymphoma, hepatic tumor involvement is often found at the initiation and during the course of treatment. In addition, liver dysfunction is often also encountered in association with or without diffuse tumor involvement in the liver. Laparotomy has been proposed as a useful method for the diagnosis of hepatosplenic disease, though, it is an invasive procedure and can take much time at the expense of earlier initiation of treatment (Goffinet *et al.*[1]; Veronesi *et al.*[2]; Rosenberg *et al.*[3]; Moran *et al.*[4]; Heifetz *et al.*[5]; Chabner *et al.*[6]).

Focal lesions in the liver can usually be detected by imaging methods, such as computed tomography, isotope scans or sonography (Carrol *et al.*[7]; King *et al.*[8]).

Ultrasonically or CT-guided fine needle aspiration and percutaneous blind needle biopsy have become well-established techniques in the diagnosis of malignant neoplasms (Zornoza *et al.*[9]; Jansson *et al.*[10]; Solbiati *et al.*[11]; Pontifex *et al.*[12]; Erwin *et al.*[13]; Isler *et al.*[14]). Clinical validity and accuracy of these modalities in the diagnosis of non-Hodgkin's lymphoma is, however, still controversial (Maharaj *et al.*[15]).

The ultrasonically guided tissue biopsy technique has been used successfully for evaluating the kidney, liver and spleen and is now accepted (Lindgren *et al.*[16]; Torpederson *et al.*[17]; Yoshimatsu *et al.*[18]; Suzuki *et al.*[19]). The aim of this report was to know the usefulness of ultrasonically guided hepatic biopsy in the treatment of non-Hodgkin's lymphoma which shows liver dysfunction in the blood chemistry.

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### MATERIALS AND METHODS

Twenty-five liver biopsies on 24 patients were done at the Department of Radiology of the Tokyo Medical and Dental University. They were performed on patients admitted for the treatment of non-Hodgkin's lymphoma. The subjects ranged in age from 26 to 83 years and were previously diagnosed by their surgical specimens as having non-Hodgkin's lymphoma. Among these 25 specimens, 16 were biopsied as a part of an initial staging workup of non-Hodgkin's lymphoma. The clinical stages of these 16 patients were: 2 for stage-I, 2 for stage-II, 6 for stage-III and 6 for stage-IV. All 24 patients showed abnormal blood chemistry data. Seventeen patients had elevated serum values of LDH, GOT and GPT and a high alkaline phosphatase level. Eight patients showed an abnormality in one or two items of four enzymes. Pre-examination ultrasonography revealed three with hepatomegaly, seven with splenomegaly, five with intrahepatic mass and one with intrapancreatic mass. The liver in the 17 patients showed no abnormal findings ultrasonically. Other examination procedures included bipedal lymphography, bone marrow biopsy, barium enema, computed tomography, bone scintigraphy, blood sedimentation rate and other such diagnostic tests.

On laboratory examination, all had a platelet count greater than  $10 \times 10^4/\text{mm}^3$ , a prothrombin time within 12 seconds, an activated partial thromboplastin time within 40 seconds and a bleeding time within 5 minutes. The tissue core was obtained by a 21 gauge modified Menghini needle (Surecut) under sonographic control (Torp-Ederson *et al.*[17]; Yoshimatsu *et al.*[18]; Suzuki *et al.*[19]). This tissue core taken was then expelled into 10% formalin and was histologically examined. In the ultra-

sonically focally involved patient, at least two tissue cores were biopsied to gauge the nature of involvement in the several sites of the organ. In patients without a focal disease, two or three specimens from the different sites of the liver were also taken. The size of the biopsied specimens ranged from 1 cm to 5 cm in length. Cytological examination of these specimens was also conducted.

The specimens were sectioned for the whole length and stained by hematoxylin-eosin staining. Post-examination ultrasonography and a complete blood count were undertaken 24 hours after hepatic tissue biopsy.

### RESULTS

The results of clinical examination and hepatic histopathological findings are shown in Table 1. The histopathology of five ultrasonically suspected lymphomas of the livers showed the involvement of lymphoma cells and the clinical staging was confirmed histopathologically. Among the five livers which showed ultrasonically focal lesions, four showed only focal tumor involvements without further diffuse involvements (Fig. 1). The remaining one showed mixed focal and diffuse involvements histopathologically. Diffuse tumor cell involvement in the Glisson capsule and the sinusoid was detected in three ultrasonically and computed tomographically normal livers (Fig. 2). Among these three cases, one was an initial case and placed into stage-IV from the previous stage-II determinations. Six among the 25 liver specimens showed, histopathologically, a degenerative and/or fibrotic change without tumor cells. Two out of these 6 were diagnosed as having chronic liver disease at the initiation of treatment for malignant lymphoma and the other four were diagnosed as having degenerative changes that were suspected to be caused by the

Table 1. Clinical Evaluation and Histopathological Findings of Liver in 24 Patients (25 Biopsies) With non-Hodgkin's Lymphoma

No. of patient (age, sex)	Bio- Chemistry	Ultra- sonography	Histopathology of liver
Initial patients			
1. 58M	+	—	(-)
2. 72M	±	—	-
3. 70F	+	Intrahepatic mass	+
4. 68M	+	—	(-)
5. 55M	±	—	-
6. 26M	+	Hepatospleno- megaly	-
7. 83M	+	—	+
8. 54M	+	—	-
9. 41F	+	Intrahepatic mass	+
10. 47F	±	—	-
11. 69M	+	Intrahepatic mass	+
12. 74M	±	—	-
13. 48F	+	Splenomegaly	-
14. 52M	+	Hepatospleno- megaly	-
15. 61M	+	Splenomegaly	-
16. 65F	+	Intrahepatic mass	+
Follow up patients			
17. 58M	±	Pancreatic mass	-
59M	+	—	(-)
18. 69M	±	—	-
19. 51M	±	—	+
20. 75M	+	Intrahepatic mass	+
21. 53M	+	—	(-)
22. 52F	±	Hepatospleno- megaly	(-)
23. 56M	+	—	+
24. 57F	+	Splenomegaly	(-)

drugs taken during the course of chemotherapy for non-Hodgkin's lymphoma. The patient with intrapancreatic mass was diagnosed as having no tumor elsewhere and the treatment by radiation was undertaken.

Negative intraabdominal lymphadenopathy was found in six among 8 patients with liver involvement of the tumor on lymphography, CT and ultrasonography. One among 8 patients with liver involve-

ment had a positive bone marrow involvement of lymphoma. Histopathological diagnosis of the biopsied specimens was made within a few days after examination and the involved patients immediately underwent chemotherapy instead of other treatment. On the other hand, six patients showing histopathological degenerative changes in their livers were put on treatments taking their liver cell damage into consideration.

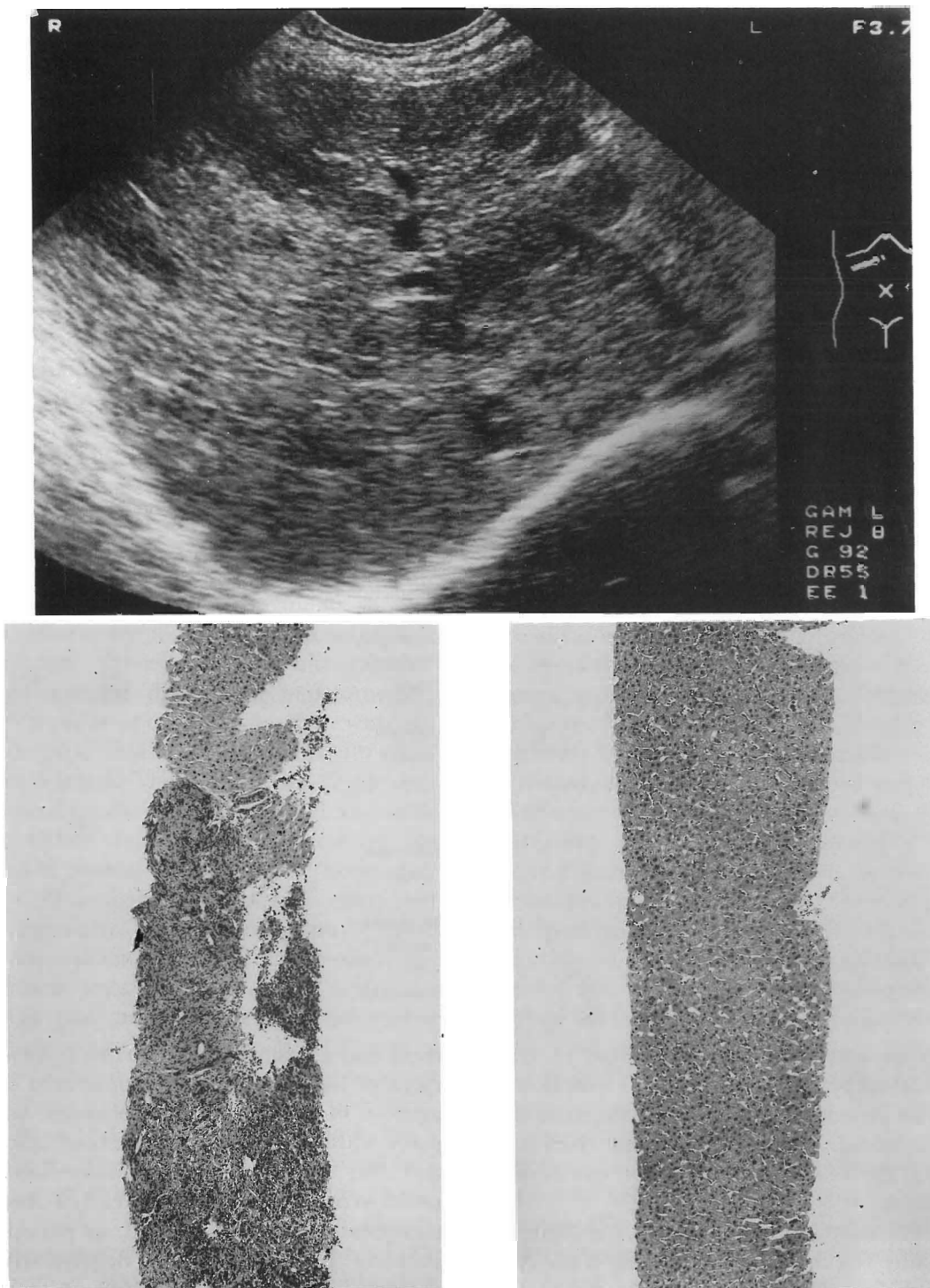


Fig. 1. Ultrasonography of the liver reveals multiple focal lesions (A). Histological liver specimen biopsied from focal lesion shows involvement of non-Hodgkin's lymphoma (B) ( $\times 67$ ). Another specimen biopsied from ultrasonically normal liver shows no involvement of lymphoma (C) ( $\times 67$ ).

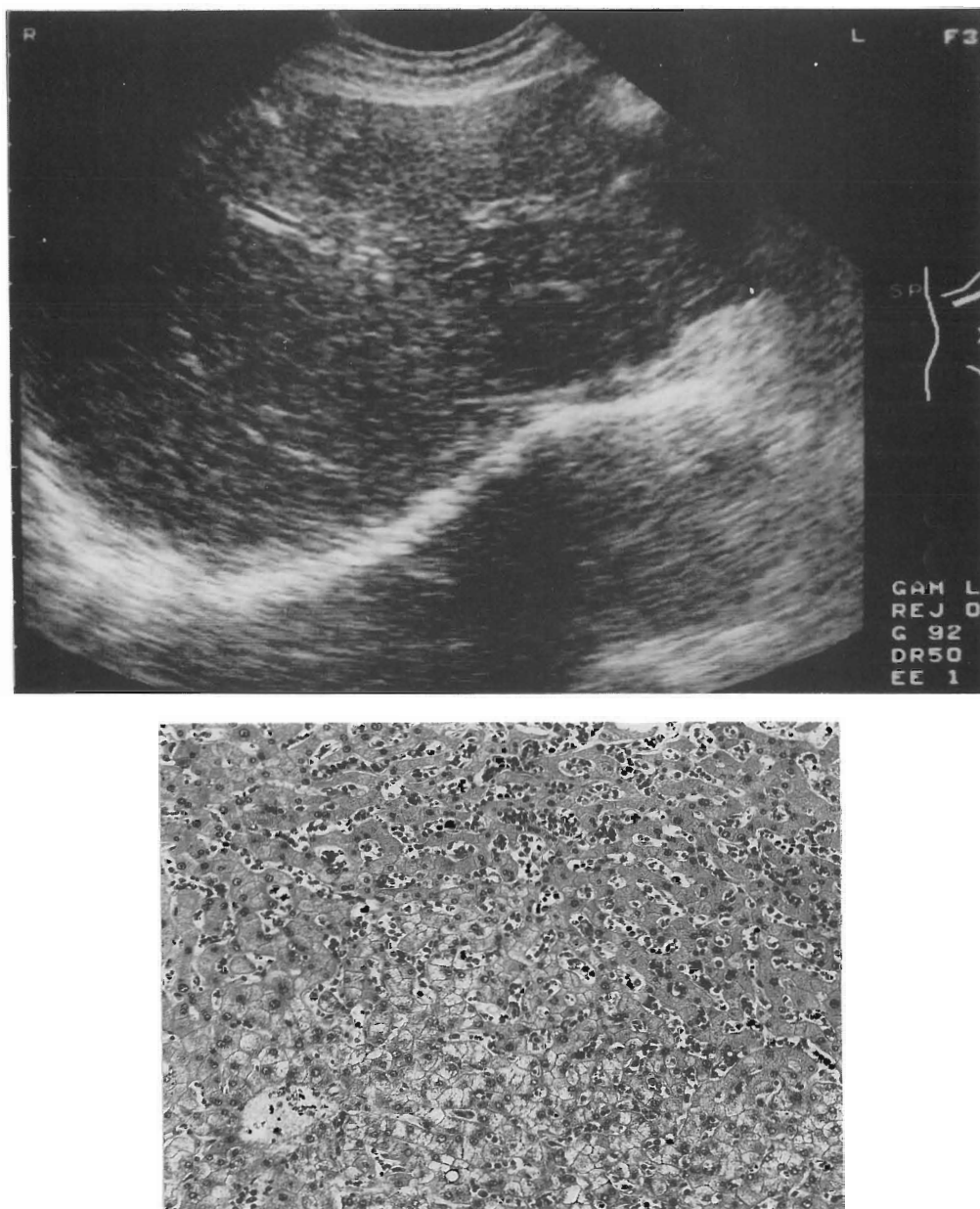


Fig. 2. Ultrasonography of the liver reveals no pathological finding (A). Histological liver specimen shows diffuse infiltration of lymphoma cells in the sinusoid (B) ( $\times 130$ ).

No complications such as bleeding has been found in the laboratory data as a result of these ultrasonic examinations up to 24 hours following the examinations.

#### DISCUSSION

To improve the treatment result for non-Hodgkin's lymphoma, the confirma-

tion of a hepatic condition has become important for the rapid initiation of therapy. Quite a number of patients with non-Hodgkin's lymphoma have abnormal liver dysfunction without tumor involvement. Among the 25 patients showing abnormal pre-examination data on blood chemistry, only 8 had tumor involvement histopathologically. It should also be noted that chemotherapeutic drugs can often induce damage to the liver cells and cause liver dysfunction. Hepatic tumor involvement without negative lymphography is also not a rare condition in non-Hodgkin's lymphoma (Veronesi *et al.*[2]; Chabner *et al.*[6]) and six such cases were found among the 22 patients examined. Patients with non-Hodgkin's lymphoma have been said to be older than those with Hodgkin's disease and older patients have been shown to experience more difficulty with laparotomy (Rosenberg *et al.*[3]). The usefulness of a percutaneous tissue core biopsy is characterized by the lack of any complications and is time-saving (Lindgren *et al.*[16]; Torp-pederson *et al.*[17]; Yoshimatsu *et al.*[18]; Suzuki *et al.*[19]).

There have been many studies on hepatic diseases conducted through imaging methods and aspiration biopsy, but none of these examinations has been fully satisfactory for the diagnosis of the hepatic tumor involvement of non-Hodgkin's lymphoma (King *et al.*[8]; Zornoza *et al.*[9]; Pontifex *et al.*[12]; Erwin *et al.*[13]). Histopathological examination, therefore, is indispensable to fully diagnose the condition of the liver and/or other organs (Chabner *et al.*[6]; Jansson *et al.*[10]; Lindgren *et al.*[16]). Through our procedure, a percutaneous hepatic tissue core sampling was accomplished with a minimum invasion at the bedside under local anesthesia and sufficient material for histological diagnosis was obtained.

In the examination of percutaneous

hepatic biopsy, it should be noted that negative results for tumor involvement do not always represent true negative depending on the localization of the tumor. The possibility of false negative biopsy from an involved organ would be minimized by the accurate estimation of the target in the organ and the long tissue cores. In the cases with no focal disease, more than one biopsy should be recommended to avoid the false negative result. Also in cases with focal hepatic lymphoma, biopsies from ultrasonically normal liver would give the information on the diffuse lymphomatous involvement and other liver parenchymatous diseases. The presence of abnormal liver parenchymatous disease would give a chance in the selection of drugs for chemotherapy.

This ability to obtain a quick, accurate diagnosis of a hepatic disease at the outset and during the early course of treatment has made a significant change in the treatment and follow-up care of patients with non-Hodgkin's lymphoma.

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