Hepatic Lymphoma: an Imaging Approach with Emphasis on Image-Guided Needle Biopsy

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Abstract

Background: Involvement of the liver by lymphoma is almost always secondary. A definite diagnosis can be made only after histologic examination. Recently there has been a trend to replace surgical biopsies with percutaneous core-needle biopsies for the diagnosis of lymphoproliferative disorders.

Objectives: To describe our experience with percutaneous image-guided needle biopsies of the liver in 15 cases of primary and secondary hepatic lymphoma.

Methods: Between 1997 and 2002, 15 of all the percutaneous computerized tomography-guided core-needle liver biopsies performed at our institution yielded the diagnosis of lymphoma. We retrospectively reviewed the medical records of these patients.

Results: Seven patients had primary hepatic lymphoma (all non-Hodgkin's lymphoma) and eight had secondary (three Hodgkin's disease and five non-Hodgkin's lymphoma). No major complications were caused by the percutaneous biopsies, and all biopsies were diagnostic. The imaging findings were non-specific but were characteristic and similar to previously described series. Imaging demonstrated hypodense lesions by CT, or hypoechoic or anechoic lesions by ultrasound in all but two cases in which hilar lesions resulted in biliary dilatation, both demonstrated by ultrasound

Conclusions: Review of our primary cases indicated no association with cirrhosis or AIDS in contradistinction to the worldwide experience. There were no significant complications in the 15 patients in the study, and a definite diagnosis of lymphoma was made in all the cases with no need to proceed to surgical biopsy. We highly recommend image-guided core-needle biopsy of the liver as a reliable and useful tool for the diagnosis of hepatic lymphoma.

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Involvement of the liver in lymphoma usually occurs as a secondary process in the advanced stages of a widespread non-Hodgkin's lymphoma, and less commonly in Hodgkin's disease. Liver involvement is found in 25% of NHL and in 8% of HD patients at laparoscopy or laparotomy [1,2]. Nevertheless, it is not a common finding in cross-sectional studies of lymphoma patients, and some of these cases are not even detected by computed tomography [3,4]. Primary hepatic lymphoma, on the other hand, is an exceptionally rare disease, representing 0.4% of extranodal NHL and 0.016% of all NHL [5]. Lymphoma of the liver is considered primary in the absence of extra-hepatic involvement or in cases in which the predominant presentation is hepatic [6]. It usually belongs to the B cell lineage and shows diffuse large cell histology [7]. Hepatic lymphoma is more commonly encountered in patients with cirrhosis, mostly secondary to hepatitis C [8], AIDS [8–10], systemic lupus erythematosus [11], and in transplant recipients being treated with immunosuppressive drugs [5,12]. The prognosis appears to be favorable in patients diagnosed and treated early, unless there is an underlying disease [8].

The clinical presentation of lymphoma of the liver is generally non-specific, and so are the imaging findings, although certain characteristic features on CT, ultrasound and magnetic resonance imaging have been described in the literature [4–6,13,14]. The non-specific symptoms and laboratory findings make the diagnosis of hepatic lymphoma very difficult. In most cases the imaging findings do not lead to an accurate diagnosis and often it is not even suggested prior to biopsy. A definite diagnosis of liver lymphoma can be reached only after histologic examination. For many years surgical biopsy by laparotomy or laparoscopy has been the only procedure available for assessing liver infiltration by lymphoma [15]. In recent years, with the development of image-guided biopsy and cytopathologic diagnostic techniques, the safety and accuracy of the procedure has greatly improved [16]. Currently, percutaneous core-needle biopsies in lymphoproliferative disorders can be used not only for the simple distinction between benign and malignant disease, but also for the definitive subtyping of HD and NHL. Thus, a relatively simple procedure may enable therapeutic decisions to be made without the need for surgery and its associated morbidity [16–21]. A few series assessing the reliability of percutaneous needle biopsies in lymphoma have been described, including biopsies from different parts of the body, but none has specifically addressed its efficacy in the liver. We describe our experience with percutaneous image-guided needle biopsies of the liver in 15 cases of primary and secondary hepatic lymphoma.

Patients and Methods

A retrospective review of all percutaneous CT-guided liver biopsies performed at our institution between January 1997 and December 2002 yielded 15 biopsies with the eventual diagnosis of lymphoma. These 15 patients constituted the study population. Pathologic findings were grouped as either HD or NHL. The patients, 11 males and 4 females, ranged in age from 18 to 90 (mean 48 years). No patient had evidence of any other primary or secondary hepatic neoplasm. Eight patients had a history of lymphoma before biopsy and a new mass appearing in the liver. The medical records and imaging findings were retrospectively reviewed.

Cross-sectional imaging studies included CT in all 15 patients and ultrasonography in 11. All studies were performed within 3 weeks of the biopsy. All biopsies except for one, which was

NHL = non-Hodgkin's lymphoma
HD = Hodgkin's disease

performed under ultrasound guidance, were performed by two experienced staff radiologists under CT guidance (MxDual, Philips). Informed consent was obtained, and limited scanning was performed to localize the lesion. The puncture was performed by using a 20 or 22-gauge cutting edge Turner biopsy needle (Cook Co, Bloomington. IN, USA) and scanning was performed to document needle progression to the depth of the target. One to four passes were made for each patient [Figure 1]. One biopsy was performed under ultrasound control with a 14-gauge Biopty-cut biopsy needle (Bard, CR Bard Inc, Covington, GA). A 2 cm core was usually a satisfactory specimen for pathology. The specimen had a different color to that of normal liver tissue – white to gray as compared to the normal red to brown. Biopsies were fixed in 10% buffered formalin. Histologic results were based on the interpretation of biopsy material prepared by the standard techniques used in the pathology department of our hospital. In biopsies diagnosed as malignant lymphoma, a panel of antibodies was used to determine cell lineage and histologic subtype.

Results

Of the 15 biopsies 7 demonstrated primary liver lymphoma. The age of these patients was 23–59 years; six were male. The males did not have any underlying disease, while the one female patient had systemic lupus erythematosus. Histology in these seven cases demonstrated NHL, aggressive diffuse large B cell type. Imaging demonstrated a single lesion, hypodense and homogeneous by CT. There was no or minimal enhancement with iodinated contrast material. The rest of the liver was moderately enlarged but otherwise normal in five cases, and in the other two cases the lesion was located in the hilar region, causing biliary obstruction and intrahepatic billiary dilatation. Sonography showed the lesions to be hypoechoic in five patients and anechoic in the other two. They all demonstrated posterior enhancement. Intrahepatic biliary dilatation was demonstrated in the same two patients.

Eight patients, five males and three females, had secondary hepatic lymphoma. Histologically, three of them had HD and five had NHL, diffuse large B cell type. All eight had a known and biopsy-proven history of lymphoma. They were all in a late stage with disseminated overwhelming disease. Five of them died, three within a short time after the biopsy, during the same hospitalization. Two of them were immunosuppressed at the time of diagnosis of the hepatic lymphoma.

Imaging revealed multiple lesions in five patients and a single lesion in three. The characteristics of the lesions on CT were very similar to those of the primary hepatic lymphoma, except for the number of lesions [Figure 2]. The liver was enlarged in all of the patients. Ultrasonography demonstrated hypoechoic or anechoic lesions in five patients as seen in the primary cases, while the other three demonstrated some hyperechoic lesions [Figure 3]. None of our cases demonstrated a diffusely infiltrating pattern of the disease.

No major immediate or late complications were caused by the percutaneous biopsies. All biopsies were diagnostic and the patients received therapy on the basis of the core-needle biopsy results alone without the need for subsequent open biopsy.

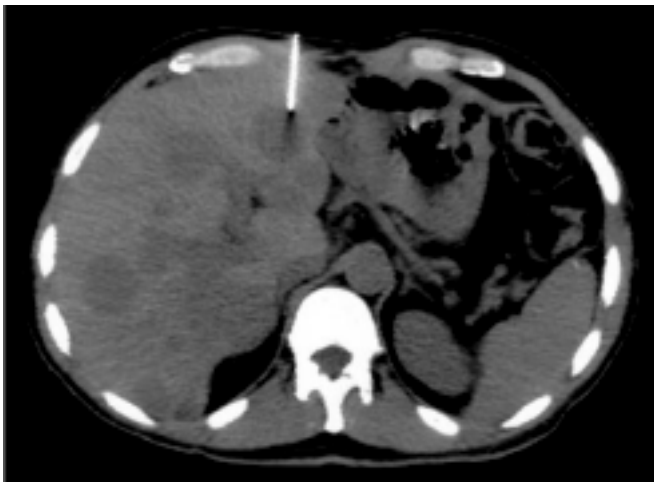

Figure 1. CT-guided liver biopsy from one of multiple hypodense lesions of secondary lymphoma.

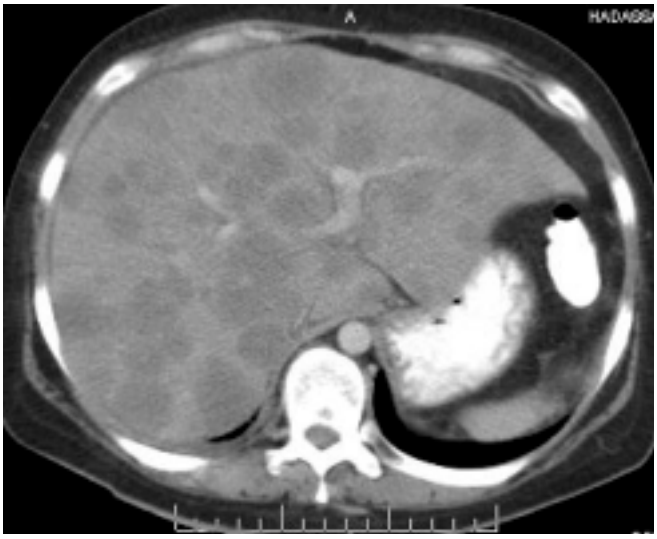

Figure 2. Enlarged liver with multiple hypodense masses.

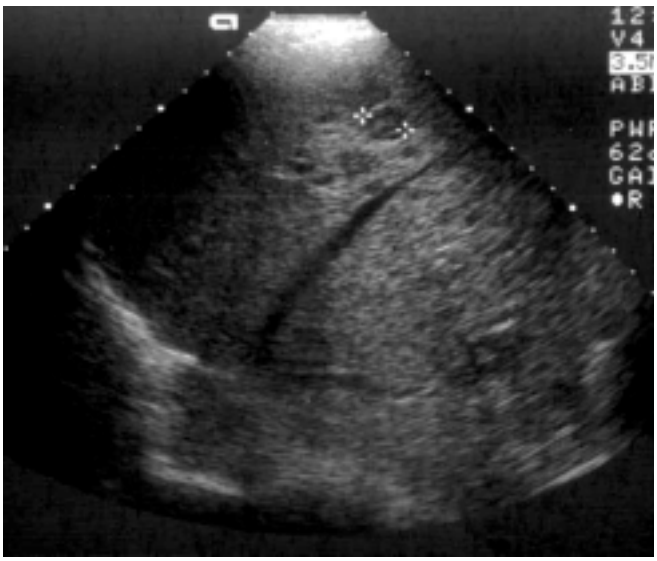

Figure 3. Liver ultrasound showing multiple small lesions of mixed echogenicity: secondary lymphoma.

Discussion

Liver involvement in lymphoma is not a common finding as a secondary process, and is a rare entity as a primary process. Of all the liver biopsies performed in our institution between 1997 and 2002, 15 demonstrated lymphoma at histology. Seven of them were primary and eight secondary. The relatively high percentage of the primary lymphoma in our results can be attributed to the fact that a reasonable number of the secondary hepatic lymphomas are diagnosed presumptively without histologic proof, with the support of the clinical history and other findings related to lymphoma, especially in advanced disease where involvement of the liver does not change the staging and where therapy for advanced disease would be administered anyway [22].

In our institution, core-needle biopsy rather than fine-needle aspiration is performed to obtain specimens for histologic examination. While cytology may suffice for the diagnosis of carcinoma, histology is required for the diagnosis of lymphoma.

Most of the patients with primary lymphoma in our series were middle-aged men. Despite the known association, none of them had cirrhosis or AIDS. In all the patients with secondary hepatic lymphoma, liver involvement occurred in a late stage with widespread disease. In five of them it occurred during regression of the disease after bone marrow transplantation and remission. The patients with the secondary disease had a very poor prognosis.

On imaging, the characteristics were quite similar to the descriptions in the literature. By CT scan it presented as hypodense homogenous lesions of variable size, with minimal or no enhancement [5,13,14]. On sonography, the lesions were hypoechoic or anechoic with posterior enhancement [4,6,13] in most of the patients, except for the three with secondary disease who exhibited hyperechoic lesions. In over half of the cases described in the literature primary hepatic lymphoma presented as a single lesion – 57% in the reviews of Gazelle et al. [4] and Maher et al. [13] – while the remainder presented as multiple lesions. Secondary lymphoma tends to present as multiple lesions in most cases, but can also show a single lesion or diffusely infiltrate the liver. In our series, primary hepatic lymphoma presented as a single lesion in all the cases, whereas secondary hepatic lymphoma demonstrated either single or multiple lesions, with a predilection for the latter. Hepatomegaly was almost invariably present.

Although the secondary lymphoma has a much more variable presentation in imaging, and the picture is not pathognomonic, recognizing the typical expected picture – with the combination of the clinical history, liver findings, and the presence of other supportive findings such as retroperitoneal lymphadenopathy – can lead to the correct diagnosis and spare invasive procedures in some cases.

The clinical diagnosis of primary lymphoma of the liver is difficult. In our series, as in others, the findings on imaging studies did not lead to suggestion of the correct diagnosis prior to biopsy in most of the cases. Primary lymphoma of liver in patients without underlying diseases is considered a potentially curable disease, especially when early diagnosis and aggressive treatment are available [8,13]. Although a rare diagnosis, primary hepatic lymphoma should be considered when solitary or multiple liver lesions with the characteristics described above are identified, especially in a middle-aged male patient without known malignancy, and particularly if there is a history of immunosuppression. Nevertheless, suggesting the correct diagnosis by imaging is not enough, and a definite histologic diagnosis has to be made. In recent years, image-guided core-needle biopsy has been more widely used, becoming a well-accepted alternative to the traditional open biopsy in laparotomy or laparoscopy. Previous studies [18–21] have shown a diagnostic accuracy of 68–94%. A study by Ben-Yehuda et al. [16] of 100 core-needle biopsies diagnosed as lymphoma showed that 86% of the patients were treated on the basis of core-needle biopsy results alone, and in 78% the needle biopsy was sufficient to save the patient from a more extensive surgical procedure. However, the biopsies in all these studies were taken from different sites, including mediastinum, retroperitoneum and abdominal masses, and only a minority was taken from the liver. Of 100 biopsies in the last study mentioned [16] for example, only one was a liver biopsy. In the present study, we exclusively used core-needle biopsies of the liver, with very good results, no significant complications, and definite diagnosis of lymphoma in all the cases with no need to proceed to surgical biopsy. We highly recommend this elegant and safe method of image-guided core-needle biopsy of the liver as a reliable and useful tool for the diagnosis of hepatic lymphoma

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A bank is a place where they lend you an umbrella in fair weather and ask for it back when it begins to rain

Robert Frost (1874-1963), American poet

Iron rusts from disuse, stagnant water loses its purity, and in cold weather becomes frozen, even so does inaction sap the vigors of the mind

Leonardo Da Vinci

Capsule

Mitochondria – culprits in metabolic disease

Hypertension and high levels of cholesterol are often associated with one another in the general population, notably in individuals who have "metabolic syndrome," a constellation of disorders that also includes insulin resistance and diabetes. Studying a large family with a high prevalence of hypertension, elevated cholesterol, and low serum levels of magnesium, Wilson et al. found that the causative mutation lies in an isoleucine transfer RNA gene encoded by the mitochondrial genome. Thus, the clustering of these three metabolic traits may arise from a single underlying factor – mitochondrial dysfunction. Coupled with previous evidence implicating mitochondrial dysfunction in insulin resistance and type 2 diabetes, this discovery raises the intriguing possibility that mitochondria play a key role in most components of metabolic syndrome, a disorder that may affect up to 25% of adults in the United States.

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E. Israeli

Capsule

Down syndrome critical region?

Down syndrome (DS) is thought to result from the expression of an additional copy of a gene, or set of genes, present within a critical region (CR) of chromosome 21, the chromosome present in triplicate in this condition (trisomy 21). Olson and team used a genetically manipulated mouse model for DS, in which the orthologs of the small number of human genes within the *DSCR* could be duplicated or deleted. Offspring generated by crossing these animals possessed one, two, or three copies of the *DSCR* and were compared with an established mouse model for DS with trisomy for a substantially larger region of the chromosome. Using primarily craniofacial and growth parameters, the mice with trisomy for *DSCR* genes did not possess DS-like features. Thus, DS may not result from simple overexpression of a small handful of genes, but involves instead a complex genetic and developmental interplay.

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