Peripheral T-Cell Lymphoma Arising in the Liver

Mirela Stancu, MD, Dan Jones, MD, PhD, Francisco Vega, MD, PhD, and L. Jeffrey Medeiros, MD

Key Words: Peripheral T-cell lymphoma; Primary; Liver; Immunohistochemistry

Abstract

We report 3 cases of primary hepatic peripheral T-cell lymphoma (PTCL). All patients were men, 50 to 57 years of age, who sought care because of systemic symptoms including fever, fatigue, and weight loss. Physical examination revealed hepatomegaly in 2 patients, associated with jaundice in 1. Two patients had abnormal serum liver enzyme levels and coagulation profiles. Imaging studies demonstrated marked hepatomegaly without focal lesions in 1 patient and multiple discrete tumor masses in 2 patients. Tumor infiltrates in biopsy specimens were heterogeneous with a large cell component in 2 cases. An inflammatory background was present in all cases, complicating the histologic recognition of PTCL. Immunohistochemical studies showed that all tumors were of T-cell lineage, and 2 cases had monoclonal T-cell receptor gamma chain gene rearrangements. One patient died of disease shortly after diagnosis, and 2 patients treated with multiagent chemotherapy are in clinical remission with 12 and 84 months of clinical follow-up, respectively. PTCL may rarely arise in the liver. These neoplasms respond to chemotherapy, suggesting that this disease is curable if diagnosed at an early stage.

Secondary liver involvement is common in patients with non-Hodgkin lymphoma (NHL), detected in up to 50% of patients who undergo pathologic staging. In contrast, NHL arising in the liver is uncommon, and most cases are diffuse large B-cell lymphomas that manifest as space-occupying lesions. Low-grade B-cell lymphomas of mucosa-associated lymphoid tissue arising in the liver also have been reported and may transform to diffuse large B-cell lymphoma in some cases. Approximately 50 cases of primary hepatic B-cell lymphoma have been reported in the literature.

By contrast, peripheral T-cell lymphoma (PTCL) arising in the liver is rare. Although patients with PTCL who sought care because of hepatic symptoms are described, many of these patients had systemic disease at the time of diagnosis, shown by tissue biopsy, bone marrow aspiration and biopsy, or radiologic studies. Although some of these NHLs may have arisen in the liver and subsequently disseminated, it is likely that most of these tumors were systemic and secondarily involved the liver.

In our review of the literature, we identified only 11 well-documented, localized (Ann Arbor stage IE or IIE) primary hepatic PTCLs. In this article, we report 3 additional cases of localized hepatic PTCL and discuss some of the reactive histologic findings that occur at this site and make recognition of PTCL difficult.

Case Reports

Case 1

A 57-year old man, with a history of chronic alcoholism and a 2-month history of fever up to 40.6°C, rigors, and night sweats, was admitted to the hospital. His relevant medical
history included idiopathic thrombocytopenic purpura for which he had undergone splenectomy. The physical examination revealed no palpable hepatomegaly or lymphadenopathy. A CBC count was normal. Liver function tests showed an aspartate aminotransferase level of 113 U/L (reference range, 15-46 U/L), an alkaline phosphatase level of 372 U/L (reference range, 38-126 U/L), and a lactate dehydrogenase level of 1,360 U/L (reference range, 87-202 U/L). Coagulation studies showed a partial thromboplastin time of 39 seconds (reference range, 25-37.1 seconds) and a normal prothrombin time. Viral serologic testing results for hepatitis B and C were negative, as was an infectious disease workup. A computed tomography (CT) scan of the abdomen showed 2 hypodense liver nodules and regional lymphadenopathy; no distant lymphadenopathy was identified. A CT scan–guided needle biopsy of the liver initially was interpreted as nonspecific granulomatous hepatitis. The patient did not respond to empiric antibiotic therapy or to a 2-week course of corticosteroids. An open wedge biopsy of the liver and excision of a regional lymph node was performed, and the diagnosis of PTCL was established. A staging bone marrow biopsy was negative for lymphoma. The patient was treated with 6 cycles of chemotherapy using the CHOP regimen (cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisone), and he was in clinical remission 12 months after diagnosis.

Case 2

A 54-year-old man, with a remote history of hepatitis A virus infection and intravenous drug abuse, had a 4-month history of fatigue, weight loss, and right upper quadrant pain for which he was admitted to the hospital. The physical examination revealed hepatomegaly palpable 8 cm inferior to the right costal margin. No lymphadenopathy or splenomegaly was identified. Results of a CBC count and liver function tests were normal. The serum calcium level was 13.8 mg/dL (3.45 mmol/L; reference range, 8.4-10.2 mg/dL [2.10-2.55 mmol/L]). Serologic test results for HIV, hepatitis B virus, hepatitis C virus, and human T-lymphotropic virus 1 were negative. A CT scan of the abdomen showed multiple liver nodules and regional lymphadenopathy. No distant lymphadenopathy was identified. A CT scan of chest was negative. An open wedge biopsy of liver revealed PTCL. A staging bone marrow biopsy was negative. The patient received 4 cycles of chemotherapy using the CHOP and DHAP (dexamethasone, cytarabine, and cisplatin) regimens, but he could not tolerate additional courses of chemotherapy. The patient was in clinical remission 84 months after diagnosis.

Case 3

A 50-year-old man, with a 6-month history of pancytopenia and the presumptive diagnosis of myelodysplastic syndrome, developed a fever (temperature, 39.5°C) and cough, prompting hospitalization. The physical examination showed jaundice and hepatomegaly palpable 6 cm inferior to the right costal margin. There was no evidence of lymphadenopathy. A CBC count revealed the following: WBC count, 2,400/µL (2.4 × 10⁹/L; reference range, 4,000-11,000/µL [4.0-11.0 × 10⁹/L]); hemoglobin, 10.0 g/dL (100 g/L; reference range, 14.0-18.0 g/dL [140-180 g/L]); and platelet count, 27 × 10⁹/µL (27 × 10⁹/L; reference range, 140-440 × 10⁹/µL [140-440 × 10⁹/L]). Liver function tests showed an alanine aminotransferase level of 146 U/L (reference range, 7-56 U/L) and a lactate dehydrogenase level of 1,396 U/L. The total bilirubin level was elevated to 10.0 mg/dL (171 µmol/L; reference range, 0.0-1.0 mg/dL [0.0-17.1 µmol/L]). Coagulation studies showed a prothrombin time of 15 seconds (reference range, 10.8-13.9 seconds), a partial thromboplastin time of 50 seconds, and a decreased fibrinogen level of 0.06 g/dL (1.8 µmol/L) (reference range, 0.20-0.40 g/dL [5.9-11.8 µmol/L]). These findings indicated disseminated intravascular coagulation. A CT scan of the abdomen showed hepatomegaly without discrete masses or regional lymphadenopathy. Bilateral pleural effusions and multiple lung densities clinically considered most likely to have an infectious cause were demonstrated by a CT scan of the chest. No mediastinal or hilar lymphadenopathy was identified. A CT-guided needle biopsy of the liver revealed PTCL. A staging bone marrow biopsy was negative for lymphoma or myelodysplastic syndrome. Despite aggressive supportive and antibiotic therapy, the patient died of acute liver failure 4 days after diagnosis. A postmortem examination was not performed.

Materials and Methods

Three cases of PTCL arising in the liver were identified in the T-cell lymphoma database of the Department of Hematopathology, M.D. Anderson Cancer Center, Houston, TX. This database includes data for 1,100 patients with T-cell lymphomas accessioned at this institute between 1985 and 2001. Five criteria were used to define primary PTCL of the liver for the present study: (1) tumor of T-cell lineage; (2) symptoms, signs, or laboratory findings attributable to liver involvement; (3) no evidence of distant or systemic lymphadenopathy; regional lymphadenopathy was accepted; (4) no history of PTCL; and (5) no evidence of peripheral blood or bone marrow involvement at the time of diagnosis. These criteria excluded types of PTCL known to commonly involve the liver as part of systemic disease, such as hepatosplenic T-cell lymphoma. These criteria also excluded recurrence of PTCL in the liver, as the liver commonly is involved at time of relapse.

Clinical data and pathologic specimens were reviewed. Material available for histologic review included 1 needle (case 3) and 2 wedge (cases 1 and 2) biopsy specimens of 575
the liver and 1 lymph node biopsy specimen. The initial needle biopsy specimen of case 1 was not available for review. All biopsy specimens were processed routinely and embedded in paraffin. The lesions were classified according to the criteria for PTCL, unspecified, as stated in the World Health Organization classification.18

Lineage was determined by immunohistochemical methods. In 3 cases, these studies were performed using fixed, paraffin-embedded tissue sections and included various combinations of monoclonal antibodies specific for CD3, CD8, CD20, CD43, and CD45RO (DAKO, Carpinteria, CA); CD4 (Novoceastra, Newcastle upon Tyne, England); and TIA-1 (Immunotech, Westbrook, ME), as described previously.19 In 1 case, immunohistochemical studies also were performed using frozen tissue and monoclonal antibodies specific for CD3, CD5, CD20, and TIA-1.

Molecular studies to assess for immunoglobulin heavy chain (IgH) and T-cell receptor gamma chain gene rearrangements were performed successfully using polymerase chain reaction–based assays in 2 cases, as described previously.19,20 For these assays, the DNA was extracted from fixed, paraffin-embedded tissue using standard methods. In case 3, DNA extracted from fixed, paraffin-embedded tissue was of inadequate quality, precluding molecular studies, because the beta-globin control was not amplified.

Results

Clinical Findings

The clinical and laboratory findings are summarized in Table 1. The patients were 3 men, 50, 54, and 57 years old, who all sought care because of systemic (B) symptoms. The most common symptom was fever in 2 patients. Other symptoms included night sweats, right upper quadrant pain, and weight loss in 1 patient each. The physical examination revealed hepatomegaly in 2 patients, associated with jaundice in 1 patient. One patient had no physical findings. No patients had palpable lymphadenopathy. Two patients had abnormal liver function test results and coagulation profiles. One of these patients (case 3) also had pancytopenia and a markedly elevated total bilirubin level. Staging bone marrow biopsy specimens were negative for lymphoma in all cases. Computerized tomography scans demonstrated 2 or multiple liver masses without distant lymphadenopathy in 2 cases and diffuse hepatomegaly in 1 case.

The clinical course and follow-up information were available for all patients. One patient (case 3), who had an acute hepatobiliary disease-like picture, had rapidly progressive disease and died 4 days after diagnosis. Two patients (cases 1 and 2), treated with 6 and 4 cycles of multiagent chemotherapy, were alive with no evidence of disease at 12 and 84 months after diagnosis, respectively.

Pathologic Findings

All cases were classified as PTCL, unspecified, according to the World Health Organization classification,18 and the histologic findings are summarized in Table 2. The liver biopsy specimens were diffusely (2 cases) or focally (1 case) effaced by an infiltrate of predominantly small and intermediate-sized lymphoid cells (3 cases) with variably irregular nuclear contours, inconspicuous nucleoli, and clear cytoplasm Image 1 and Image 2. Scattered large cells were present in all cases and were relatively numerous in case 2. The large cells had vesicular nuclei with round to variably irregular nuclear contours and inconspicuous nucleoli. In case 3 with focal liver involvement, the infiltrate was located predominantly within portal tracts and periportal regions. Sinusoids were not involved in any cases. The mitotic rate ranged from 1 to 9 per 10 high-power (×400) microscopic fields. In case 1, a para-aortic lymph node adjacent to the liver also was biopsied and showed complete replacement by PTCL with cytologic features similar to those seen in the liver specimen.

Unusual histologic features that complicated diagnosis in the liver biopsy specimens included numerous histiocytes in all cases, associated with a prominent number of eosinophils in 2 cases Image 3. In case 1, numerous multinucleated giant cells

<table>
<thead>
<tr>
<th>Case No./ Sex/Age(y)</th>
<th>Initial Symptoms and Signs</th>
<th>Imaging Studies</th>
<th>Elevated LFT Results</th>
<th>Total Bilirubin Studies</th>
<th>Altered Coagulation Studies</th>
<th>Bone Marrow Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/57</td>
<td>Fever; night sweats</td>
<td>Two hypodense liver nodules; regional lymphadenopathy</td>
<td>Normal</td>
<td>Yes</td>
<td>Normal</td>
<td>Elevated PTT</td>
</tr>
<tr>
<td>2/M/54</td>
<td>Fatigue; weight loss; RUQ pain; hepatomegaly</td>
<td>Multiple liver masses; regional lymphadenopathy</td>
<td>Normal</td>
<td>No</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>3/M/50</td>
<td>Fever; jaundice; hepatomegaly</td>
<td>Hepatomegaly without focal lesions</td>
<td>Pancytopenia</td>
<td>Yes</td>
<td>Elevated</td>
<td>Elevated PT and PTT; decreased fibrinogen level</td>
</tr>
</tbody>
</table>

LFT, liver function tests; NA, not available; PT, prothrombin time; PTT, partial thromboplastin time; RUQ, right upper quadrant.
### Table 2
Histologic Features of Primary Hepatic Peripheral T-Cell Lymphoma

<table>
<thead>
<tr>
<th>Case No./Liver Sample Type</th>
<th>Histologic Pattern</th>
<th>Location of Infiltrate</th>
<th>Size</th>
<th>Nucleus</th>
<th>Cytoplasm</th>
<th>Mitotic Figures (10 HPF)</th>
<th>Secondary Features in Nonneoplastic Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/Wedge</td>
<td>Diffuse and focal</td>
<td>Portal and focal</td>
<td>Small, medium, and occasional large</td>
<td>Irregular with small nucleoli</td>
<td>Moderate, clear to amphophilic</td>
<td>1</td>
<td>Prominent inflammatory cells (histiocytes, eosinophils) and granulomas; minimal lymphocytic exocytosis in the biliary duct epithelium; parenchymal and bile duct necrosis and inflammatory changes</td>
</tr>
<tr>
<td>2/Wedge</td>
<td>Diffuse</td>
<td>Portal and lobular</td>
<td>Equal numbers of small, medium, and large cells</td>
<td>Irregular with small nucleoli</td>
<td>Moderate, clear</td>
<td>6</td>
<td>Prominent inflammatory background (histiocytes, eosinophils, neutrophils); reactive hepatocytes and cholangiocytes</td>
</tr>
<tr>
<td>3/Needle</td>
<td>Patchy</td>
<td>Portal and periportal</td>
<td>Small, medium, and occasional large cells</td>
<td>Irregular with occasional conspicuous chromocenters</td>
<td>Clear to amphophilic</td>
<td>9</td>
<td>Prominent histiocytes; minimal lymphocytic exocytosis in the biliary duct epithelium; periportal hepatocyte necrosis and inflammatory changes</td>
</tr>
</tbody>
</table>

HPF, high-power microscopic field (×400).

**Image 1** (Case 1) **A**, Peripheral T-cell lymphoma with sharp tumor-liver interface (H&E, ×40). **B**, The neoplasm is composed of a mixed population of small, intermediate, and occasional large lymphocytes with irregular nuclear contours and clear cytoplasm (H&E, ×400). **C**, CD3 is expressed by the neoplastic cells with a strong cytoplasmic and membranous pattern (immunoperoxidase with hematoxylin counterstain, ×400).
and poorly formed granulomas were present that partly obscured the neoplastic lymphoid infiltrate and prompted the initial diagnosis of granulomatous hepatitis. In case 2, the focal presence of spindle-shaped histiocytes forming vague fascicles imparted an inflammatory myofibroblastic tumor-like appearance. Adjacent uninvolved liver parenchyma in all cases showed reactive and degenerative changes including hepatocyte swelling or atrophy, nucleomegaly, nuclear hyperchromasia, binucleation, and prominent nucleoli. Focal clustering of hepatocytes in small nests was noted, imparting an alveolar appearance, reminiscent of acute viral hepatitis. Large areas of parenchymal collapse were present in case 1, and focal periportal necrotic hepatocytes were present in case 3. Minimal lymphocytic exocytosis into the portal biliary duct epithelium was present in cases 1 and 3. The extent of the intraepithelial lymphocytes varied in different microscopic fields and did not correlate with the severity of disease.

Immunohistochemical studies showed that all neoplasms were of T-cell lineage. Each neoplasm was positive for CD3 and negative for CD20. All neoplasms were positive for TIA-1. Other markers assessed included CD43 and CD45RO, each positive in 2 cases assessed; CD4 was positive in 1 of 2 cases studied; and CD8 was positive in 1 case. Frozen section immunohistochemical studies performed on the wedge biopsy specimen of case 2 demonstrated that the neoplasm was positive for CD3 and CD5 and negative for CD20.

Extracted DNA was of sufficient quality for polymerase chain reaction studies in cases 1 and 2. In case 1, a monoclonal T-cell receptor gamma chain gene rearrangement was identified. The IgH gene analysis revealed a faint smear consistent with polyclonal B cells. In case 2, monoclonal T-cell receptor gamma chain and IgH gene rearrangements were identified. This result is attributed to lineage infidelity, as IgH gene rearrangements can occur infrequently in mature T-cell lymphomas.

**Discussion**

Including the 3 patients described herein, 14 cases of primary hepatic PTCL have been reported in the literature.
Table 3. The median age of these patients is 51.5 years (mean, 52.4 years) with an age range from 22-82 years. Only 1 patient was younger than 40 years. Most patients sought care because of systemic symptoms, including fever in 8 patients, weight loss in 7 patients, and night sweats in 3 patients. Eight patients had abdominal, right upper quadrant, or epigastric pain. The most common physical finding was jaundice, noted in 7 patients. Ann Arbor stage, as determined by biopsy and radiologic studies, was IE in 12 patients and IIE in 2 patients. Liver function tests were abnormal in 11 of 12 patients for whom data were available. In most cases reported previously, the results of coagulation tests were not reported, but 2 of 3 patients in our study had coagulopathy. The treatments received by these patients were variable. Eight patients received some form of chemotherapy, 1 patient was treated by surgery alone, 4 patients received only supportive therapy, and no treatment information was available for 1 patient. Eight patients died, 7 of disease, within 27 months after diagnosis. Thus, patients with primary hepatic PTCL described in the literature, despite their low clinical stage, have had an aggressive disease course. Nevertheless, 2 patients in the present study completely responded to multiagent chemotherapy and were in clinical remission at last follow-up, suggesting that this disease is curable if diagnosed and treated while the neoplasm is localized.

In previous studies, 9 of 11 primary hepatic PTCLs were composed of a predominant population of small lymphoid cells with a portal and periportal distribution. Using the Kiel classification, 7 of these 9 tumors were classified as pleomorphic small cell (n = 4), T zone (n = 2), and centrocytic (n = 1). Two other cases were classified as small lymphocytic lymphoma and PTCL using the Working Formulation and revised European-American classification of lymphoid neoplasms, respectively. In 2 of 11 cases, a diffuse large cell lymphoid infiltrate completely obliterated the liver architecture. Both of these cases were classified as diffuse large noncleaved cell using the Working Formulation. The 3 cases in the present study differed somewhat...
from these descriptions in the literature. In all cases, the neoplasms were composed of a mixture of small and medium-sized cells, with occasional large cells. In the limited sampling of the third case, the neoplasm was relatively focal and limited to the portal and periportal regions.

Anthony and coworkers\textsuperscript{12} reported the presence of eosinophils among the neoplastic infiltrate in 2 of 7 cases, whereas a small number of epithelioid histiocytes were noted in the case reported by Kim and coworkers.\textsuperscript{14} In all 3 cases we report, an inflammatory background composed of histiocytes, eosinophils, neutrophils, and plasma cells was noted. Histiocytes were numerous in all cases, and eosinophils were prominent in cases 1 and 2. Poorly formed granulomas, multinucleated giant cells, focal streaming of spindle-shaped histiocytes, and patchy parenchymal collapse were additional features present in 1 or more cases. Marked reactive atypia of hepatocytes and cholangiocytes at the periphery of the neoplastic infiltrate was present in all cases in the present study, as has been described by others.\textsuperscript{12}

As has been emphasized previously, the histologic diagnosis of primary hepatic PTCL can be difficult. The most common erroneous diagnoses are idiopathic granulomatous hepatitis,\textsuperscript{14} chronic active hepatitis, granulomatous cholangitis, inflammatory myofibroblastic tumor,\textsuperscript{12} and hepatocellular carcinoma.\textsuperscript{11,12} As described in case 1 of the present study, numerous granulomas with or without multinucleated giant cells may mimic granulomatous inflammation. As occurred in case 2, spindle-shaped histiocytes admixed with lymphocytes and plasma cells can be prominent, mimicking an inflammatory myofibroblastic tumor. Case 3 had a focal neoplastic infiltrate composed predominantly of small cells in a portal and periportal distribution, suggesting the differential diagnosis with chronic hepatitis virus infection. Diagnostic errors may be avoided by recognizing the destructive growth pattern of

<table>
<thead>
<tr>
<th>Reference/Patient</th>
<th>Initial Symptoms and Signs</th>
<th>Stage</th>
<th>Altered LFT</th>
<th>Diagnosis</th>
<th>Therapy</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andreola et al\textsuperscript{11}</td>
<td>Fever; pruritus; jaundice; RUQ pain</td>
<td>IE</td>
<td>NA</td>
<td>Diffuse large noncleaved cell (WF)</td>
<td>Surgery</td>
<td>NED, 62 mo</td>
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<td>Anthony et al\textsuperscript{12}</td>
<td>Fever; weight loss; abdominal pain; hepatomegaly</td>
<td>IE</td>
<td>Yes</td>
<td>Centrocytic (Kiell)</td>
<td>Chemotherapy</td>
<td>DOD, 27 mo</td>
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<td></td>
<td>Night sweats; weight loss; jaundice; abdominal pain; hepatomegaly</td>
<td>IE</td>
<td>Yes</td>
<td>Pleomorphic small cell (Kiell)</td>
<td>Prednisone; chemotherapy</td>
<td>DOD, 15 mo</td>
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<td></td>
<td>Jaundice; abdominal pain; hepatomegaly</td>
<td>IE</td>
<td>Yes</td>
<td>T zone (Kiell)</td>
<td>Prednisone; antibiotics</td>
<td>NED, 36 mo</td>
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<td></td>
<td>Fever; weight loss; hepatomegaly; celiac disease for 4 y</td>
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<td>Pleomorphic small cell (Kiell)</td>
<td>Antibiotics</td>
<td>DOD, 18 mo</td>
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<td>CHF; weight loss; jaundice; hepatomegaly</td>
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<td>Yes</td>
<td>T zone (Kiell)</td>
<td>Prednisone</td>
<td>Died of unrelated cause, 1 wk</td>
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<td>Fever; weight loss; jaundice; abdominal pain; hepatomegaly; alcoholism</td>
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<td>Yes</td>
<td>Pleomorphic small cell (Kiell)</td>
<td>Chemotherapy</td>
<td>NED, 72 mo</td>
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<td>Intermittent fever and chills for 12 y</td>
<td>IE</td>
<td>NA</td>
<td>Peripheral T-cell lymphoma, unspecified (REAL)</td>
<td>Chlorambucil; prednisone</td>
<td>DOD, 2.4 mo</td>
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<td>Anorexia; fatigue; epigastric pain; weight loss</td>
<td>IE</td>
<td>No</td>
<td>Diffuse large noncleaved cell (WF)</td>
<td>Chemotherapy</td>
<td>NED, 15 mo</td>
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<tr>
<td></td>
<td>Fever; night sweats; hepatomegaly</td>
<td>IIE</td>
<td>Yes</td>
<td>Peripheral T-cell lymphoma, unspecified (WHO)</td>
<td>Chemotherapy</td>
<td>NED, 12 mo</td>
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<td>Fatigue; weight loss; RUQ pain; hepatomegaly</td>
<td>IIE</td>
<td>Yes</td>
<td>Peripheral T-cell lymphoma, unspecified (WHO)</td>
<td>Chemotherapy</td>
<td>NED, 84 mo</td>
</tr>
<tr>
<td></td>
<td>Fever; jaundice; hepatomegaly</td>
<td>IIE</td>
<td>Yes</td>
<td>Peripheral T-cell lymphoma, unspecified (WHO)</td>
<td>Antibiotics</td>
<td>DOD, 4 d</td>
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</table>

CHF, congestive heart failure; DOD, died of disease; LFT, liver function test; NA, not available; NED, alive, no evidence of disease; REAL, revised European-American classification of lymphoid neoplasms; RUQ, right upper quadrant; WF, Working Formulation; WHO, World Health Organization.

Table 3
Clinical Features of Primary Hepatic Peripheral T-Cell Lymphomas Reported in the Literature
PTCL, the mixed cellular composition, and the cytologic atypia of the lymphocytes. Immunostains can help distinguish primary PTCL from chronic active hepatitis C virus infection. In 60% of the latter cases, germinal centers or aggregates of B cells, surrounded by a zone of CD8+ T cells, are present in portal tracts.22,23 This type of zonation has not been reported in PTCLs, which usually are associated with few B cells. As shown in 2 cases in the present study, molecular studies to assess clonality of the T-cell receptor and immunoglobulin genes also can be helpful.

The neoplastic cells of PTCL also can be large and epithelioid, raising the possibility of a hepatocellular carcinoma. This diagnostic error may be avoided by searching for intracytoplasmic bile and/or bile canaliculi formation by the malignant cells, features that are present only in hepatocellular carcinoma. Immunohistochemical studies are very helpful to ascertain the epithelial or lymphoid origin of a poorly differentiated neoplasm and may be mandatory for small needle core biopsy specimens.

Primary hepatic PTCL may be detected at an early stage because these neoplasms impair hepatic function, resulting in elevated serum liver enzyme levels and coagulopathy. Although patients with these neoplasms are reported to have a poor prognosis in the literature, 2 of 3 patients in the present study treated with chemotherapy completely responded and were in clinical remission at last follow-up. Thus, correct diagnosis is essential. Knowledge that primary hepatic PTCL, particularly in small biopsy specimens, can be partly obscured by a necroinflammatory and granulomatous background that may mimic inflammatory processes will help to prevent misdiagnosis.

From the Division of Pathology and Laboratory Medicine, University of Texas M.D. Anderson Cancer Center, Houston.

Address reprint requests to Dr Medeiros: Division of Pathology and Laboratory Medicine, Box 72, M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030.

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