

## CASE REPORT

### PRIMARY LIVER AIDS-RELATED LYMPHOMA

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#### SUMMARY

Non-Hodgkin's lymphomas (NHL) are the second most frequent malignancies in AIDS patients. The majority of NHL associated with AIDS involves extranodal sites, especially the digestive tract and the central nervous system. Primary liver lymphoma (PLL) is an uncommon neoplasm among these patients. Ultrasonography and computed tomography scans may be helpful in the diagnosis of focal hepatic lymphoma. Image-guided fine-needle biopsy with histopathology of the liver lesions is the gold standard for the diagnosis of hepatic lymphoma. We report a case of PLL as the initial manifestation of AIDS in a patient without any previous infection by hepatitis C or B virus, presented as multiple and large hepatic masses.

**KEYWORDS:** AIDS; non-Hodgkin lymphoma; Primary liver lymphoma.

#### INTRODUCTION

Liver involvement is common in disseminated non-Hodgkin's lymphoma (NHL), however only less than 1% of extranodal lymphomas appears in the liver<sup>4</sup>.

The hepatic involvement of NHL, either primary or secondary, includes a diffuse parenchymal infiltration or it presents as single or multiple liver masses<sup>5</sup>.

We report a case of primary liver lymphoma (PLL) in a patient infected with the human immunodeficiency virus (HIV) presenting as multiple occupying hepatic masses.

#### CASE REPORT

A 27-year-old male infected by HIV was admitted with a 1-month history of mild fever, abdominal pain, weight loss and night sweats. He did not have previous diagnosis of AIDS and he had never received highly active antiretroviral therapy. He had no past history of blood transfusions, heavy alcohol use or injection drug use. Physical examination revealed abdominal distension, tender hepatomegaly of 7-cm below the right costal margin and a small left supraclavicular adenopathy. Significant laboratory findings showed hemoglobin 9.2 g/dL, hematocrit 31%, platelets 212,000/mm<sup>3</sup>, alkaline phosphatase 7,787 U/L (normal 90-240 U/L), lactate dehydrogenase 1,239 U/L (normal 230-460 U/L). Transaminase and alpha-fetoprotein levels were normal. Hepatitis B surface antigen and anti-hepatitis C antibodies were also

negative. The CD4 T-lymphocytes count was 266 cells/ $\mu$ L and the plasma viral load was over 500 000 copies/mL.

Abdominal ultrasound showed a large mass of 7.3 x 5.9 cm in the right hepatic lobe (Fig. 1) and another two large hypoechoic solid lesions of 11.0 x 8.0 cm and 8.3 x 6.1 cm, respectively, occupying the left lobe of the liver (Fig. 2) with regional hilar hepatic adenopathies. Scan computed tomography (CT) confirmed hepatomegaly and low attenuation lesions in both lobes of the liver, without contrast-enhancement. CT scan of the thorax and pelvis were normal. Bone marrow biopsy and histopathological examination of supraclavicular lymph node did not show atypical cells.



Fig. 1 - Abdominal sonogram showing another large hypoechoic mass in the left lobe.

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Fig. 2 - Abdominal sonography showing a large lesion occupying the right liver lobe.

CT percutaneous-guided fine needle liver biopsies were performed; histopathological examination of biopsy smears showed an aggressive infiltration with replacement of the normal liver histoarchitecture by large cells with hyperchromatic central nuclei, various nucleoli near the basal membrane and abundant eosinophilic cytoplasm (Fig. 3). The histologic findings were consistent with the diagnosis of high-grade non-Hodgkin's lymphoma. Immunostaining with monoclonal antibodies demonstrated that the atypical cells showed reactivity for anti-CD20 (B-cell phenotype) (Fig. 4). Epstein-Barr virus (EBV)-

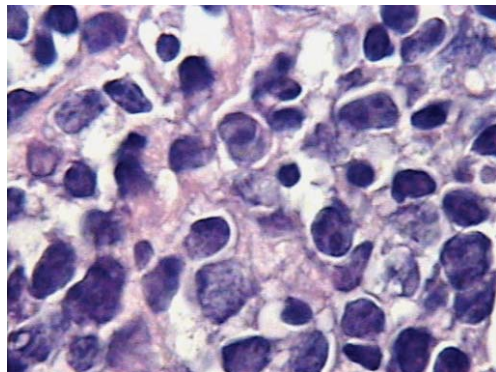


Fig. 3 - Liver biopsy revealed the existence of an atypical infiltrate consistent with the diagnosis of high-grade non-Hodgkin lymphoma.

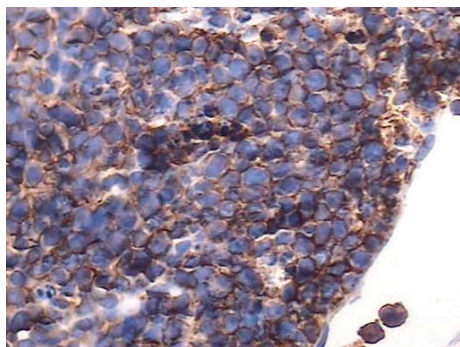


Fig. 4 - Immunostaining with monoclonal antibodies demonstrating the reactivity for anti-CD20 (B-cell phenotype).

encoded mRNAs were detected by *in situ* hybridization (ISH) in tumour cells.

The patient died one month after the diagnosis; his physical condition did not allow him to receive any specific chemotherapy.

## DISCUSSION

In an effort to standardize the nomenclature, improve diagnostic accuracy, and promote international consensus, the World Health Organization (WHO) has developed a different classification of lymphomas. In particular, the more commonly observed HIV-associated large-cell lymphomas are now classified as either diffuse large B-cell lymphoma/centroblastic or diffuse large B-cell lymphoma/immunoblastic<sup>5</sup>.

PLL is a very rare condition while the secondary involvement of the liver is relatively common including 50% to 80% of Hodgkin's or non-Hodgkin's lymphomas at autopsies<sup>7,9</sup>. The first case of PLL associated with AIDS was reported by REICHERT *et al.*<sup>10</sup> in 1983 in an autopsy series. LANJEWAR *et al.*<sup>6</sup> evaluated the spectrum of hepatic disorders among AIDS patients and detected only one case of PLL among 171 autopsy and biopsy specimens analyzed. Patients with PLL associated with AIDS generally presented "B" symptoms (fever and weight loss), abdominal pain and hepatomegaly with or without jaundice at the time of diagnosis. High-grade, unfavorable histology and bulky tumour volume, as in our patient, are associated with poor prognosis and an estimated median survival of only six months, including those patients who received chemotherapy.

Ultrasonographic and CT scans may be helpful for the diagnosis of focal hepatic lesions of lymphoma not only in patients with AIDS, but no imaging finding is specific for the diagnosis of hepatic lymphoma<sup>9</sup>. RIZZI *et al.*<sup>11</sup> analyzed retrospectively, between 1992 and 1996, the sonograms and CT scan images of 26 patients with diagnosis of AIDS and associated PLL (10 were primary and 16 were secondary neoplasms). For 38% of the patients included in this evaluation (n = 26), PLL was the first manifestation of AIDS, as presented by the patient. The authors observed that multiple lesions were most frequent in both, primary (seven of 10 cases) and secondary (15 of 16 cases) liver lymphomas. Ultrasonographic findings showed hypoechoic lesions in 25 (96.1%) patients. Our case presented three large lesions and all were hypoechoic in the sonographic images. In the same study, CT scans showed that all lesions were hypodense with enhancing-ring contrast in only six (23%) patients.

Image-guided needle fine biopsy of the liver is the best method for the definitive diagnosis of hepatic lymphoma and prevents surgical biopsy<sup>1</sup>.

In some cases, hepatic lymphoma affected patients who were infected by the hepatitis C virus (HCV). Several studies suggested that HCV plays a role on the pathogenesis of both, lymphoma and hepatocarcinoma. BRONOWICKI *et al.*<sup>2</sup> analyzed the clinical and pathological findings of 31 patients with diagnosis of liver lymphoma. All patients were HIV-seronegative. The seroprevalence of HCV infection by reverse transcription polymerase chain reaction (RT-PCR) in this cohort was 21% (six of 28 blood samples). All patients developed a high-grade "B" phenotype NHL, as in the presented patient.

Other study<sup>3</sup> evaluated the association between HCV infection and different malignancies in a Swedish cohort of 27,150 HCV-infected persons during 1990 through 2000. This study demonstrated a statistically significant increased risk of NHL and multiple myeloma, especially in those patients with more than 15 years of HCV infection. Our patient has no serological evidence of HCV or HBV infection.

Finally, we think that liver lymphoma should be included in the differential diagnosis of multiple hypoechoic lesions in the ultrasonographic images in AIDS patients.

## RESUMO

### Linfoma não-Hodgkin primário do fígado em paciente com SIDA

Os linfomas não-Hodgkin (LNH) são as segundas neoplasias mais frequentes nos pacientes com síndrome da imunodeficiência adquirida (SIDA). A maioria dos LNH associados à AIDS envolvem locais extraganglionares, especialmente o trato digestivo e o sistema nervoso central. O linfoma não-Hodgkin primário do fígado (LPF) é uma neoplasia incomum nestes pacientes. A ultrassonografia (US) e a tomografia computadorizada (TC) podem ser úteis no diagnóstico de linfoma não-Hodgkin hepático apresentando-se como lesões multifocais. A biópsia com agulha fina guiada por imagens (US, TC) juntamente com a histopatologia das lesões do fígado constitui o padrão-ouro para o diagnóstico de linfoma hepático. Este trabalho relata um caso de LPF como manifestação inicial de AIDS em um paciente sem infecção prévia pelo vírus da hepatite C e B, que se apresentou como massas hepáticas múltiplas e de grandes dimensões.

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