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Case Report

Primary Hepatic Burkitt Lymphoma

João Kleber de Almeida Gentile [1, *], Beatriz Renesto [1], Luis Fernando Alves Miléo [1], André Cosme de Oliveira [2], Rosely Antunes Patzina [3], César Cilento Ponce [3], Walter Moises Tobias Braga [4]

[1] General Surgeon at the Emilio Ribas Infectious Diseases Institute, São Paulo, SP, Brazil.
[2] Director of the General Surgery at the Emilio Ribas Infectious Diseases Institute, São Paulo, SP, Brazil.
[3] Pathologist at the Emílio Ribas Infectious Diseases Institute, São Paulo, SP, Brazil.
[4] Hematologist, Instituto de Infectologia Emílio Ribas, São Paulo, SP, Brazil.

* Correspondence: joaokleberg@gmail.com.

Abstract: The liver is an uncommon primary site for lymphoma, comprising only 0.4% of extranodal lymphomas, and liver involvement is almost always secondary to systemic lymphoma. Primary hepatic lymphoma has been reported to occur more frequently in immunosuppressed patients, especially with chronic hepatitis C infection, and may be associated with hepatitis B infection and the Epstein-Barr virus. Patients usually present with pain or a mass in the right upper quadrant, with or without jaundice, and it is more common in middle-aged males. The diagnosis of extranodal lymphoma or primary hepatic lymphoma can be difficult, especially in people living with human immunodeficiency virus (HIV) positivity or acquired immunodeficiency syndrome (AIDS). Due to its rarity, it is often overlooked as a possible differential diagnosis, with nonspecific imaging findings and a definitive diagnosis made only after anatomopathological and immunocytochemical examination. We present a rare case of Burkitt's lymphoma presenting as liver masses.

Keywords: AIDS-Related Lymphoma; Burkitt's Lymphoma; Liver Neoplasms.

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1. Introduction

The gastrointestinal tract is the extranodal site most frequently affected by lymphoproliferative diseases, accounting for 5-20% of all cases and is usually secondary to systemic nodal diseases. However, primary gastrointestinal lymphoma is a very rare condition, making up only around 1-4% of all gastrointestinal malignant tumors [1]. Primary hepatic Burkitt's lymphoma is an extremely rare condition, with only a few cases reported in the literature to date. Given the rarity of its occurrence, the epidemiology and exact etiology still remain uncertain. Burkitt's lymphoma is an undifferentiated malignant neoplasm of B lymphocytes. Primary hepatic lymphoma is defined as an extranodal lymphoma restricted to the liver, representing only 0.4% of all extra-nodal lymphomas [2, 3]. Due to its rarity, it is often overlooked as a possible differential diagnosis, with nonspecific imaging findings and a definitive diagnosis made only after anatomopathological and immunocytochemical examination. We present a rare case of Burkitt's lymphoma presenting as liver masses.

2. Case Report

A 39-year-old white man with human immunodeficiency virus (HIV), recently diagnosed (less than 6 months) and a CD4 count of 34/μL, presented to the emergency department with marked weight loss (approximately 30 kg in 2 months) for no apparent reason, associated with mild epigastric pain, fatigue and a decline in general condition. Initial

tests showed an HIV viral load of more than 1.5 million/copy while taking antiretroviral therapy and liver profile tests were initially normal, with only alterations in the canalicular enzymes, GGT: 1039 mg/dL (VR: 9-36 mg/dL) and FA: 1190 mg/dL (VR: 40-150 mg/dL) with initially unchanged tumor markers. An abdominal computed tomography scan showed a small amount of free fluid in the abdominal and pelvic cavity associated with the presence of multiple solid, heterogeneous focal liver lesions affecting a large part of the right and left lobes, some of which were confluent, the largest measuring around 13 cm in diameter in the right lobe (Figure 1).

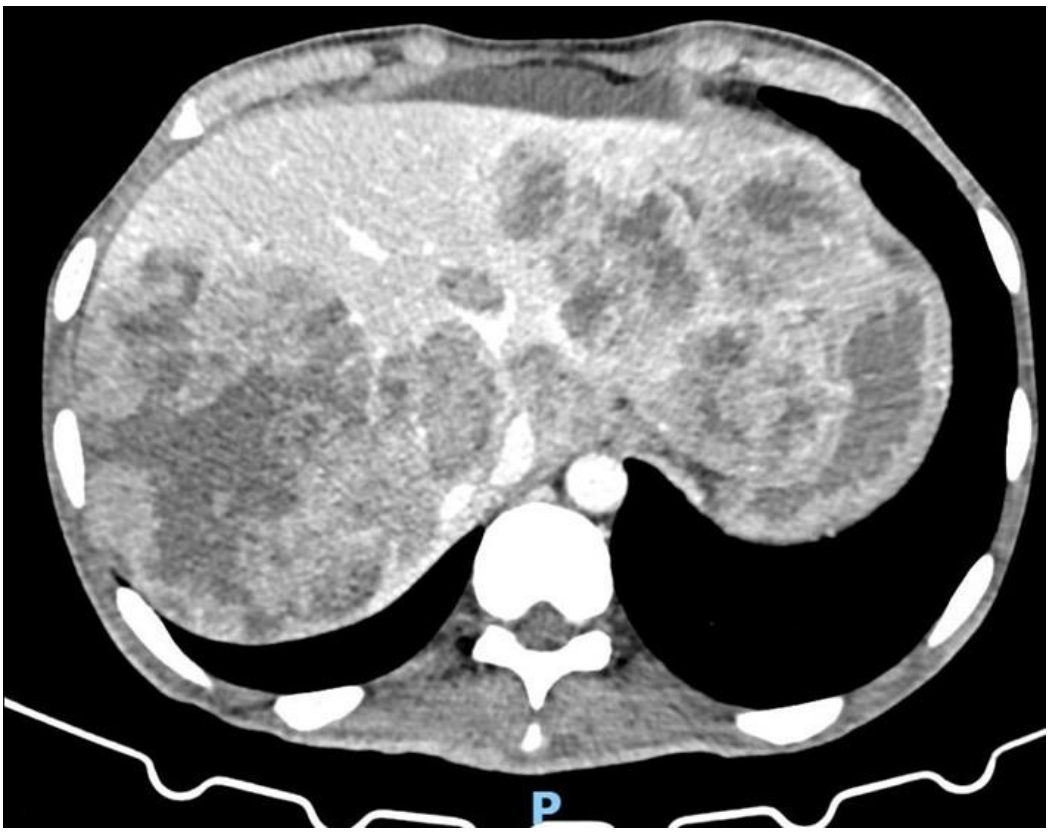

Figure 1. CT of the abdomen with intravenous contrast in the late phase showing the presence of multiple solid and heterogeneous focal lesions affecting a large part of the parenchyma of the right and left hepatic lobes, sometimes with a confluent aspect.

There was also a nodular implant 1 cm in diameter in the retroperitoneum, posterior to the left renal store, and nodular lesions with a lytic behavior in the left iliac wing next to the lesser trochanter of the homolateral femur. In view of the tomographic findings, the infectology team requested a laparotomic liver biopsy using a 16G tru cut needle. The anatomopathological examination showed a histological picture compatible with lymphoproliferative disease with high-grade undifferentiated malignant neoplasia (Figure 2) and immunohistochemistry showed a panel compatible with hepatic infiltration by Burkitt's lymphoma, the panel of which is shown in Table 1.

After diagnosis, he was accompanied by the hematology and clinical oncology team and received treatment with Cyclophosphamide 1000mg, Vincristine 2mg on D1 and prednisone 100mg/day from D1-D5 with weekly clinical follow-up and radiological follow-up at 30 days with evidence of disease control and current remission of the disease.

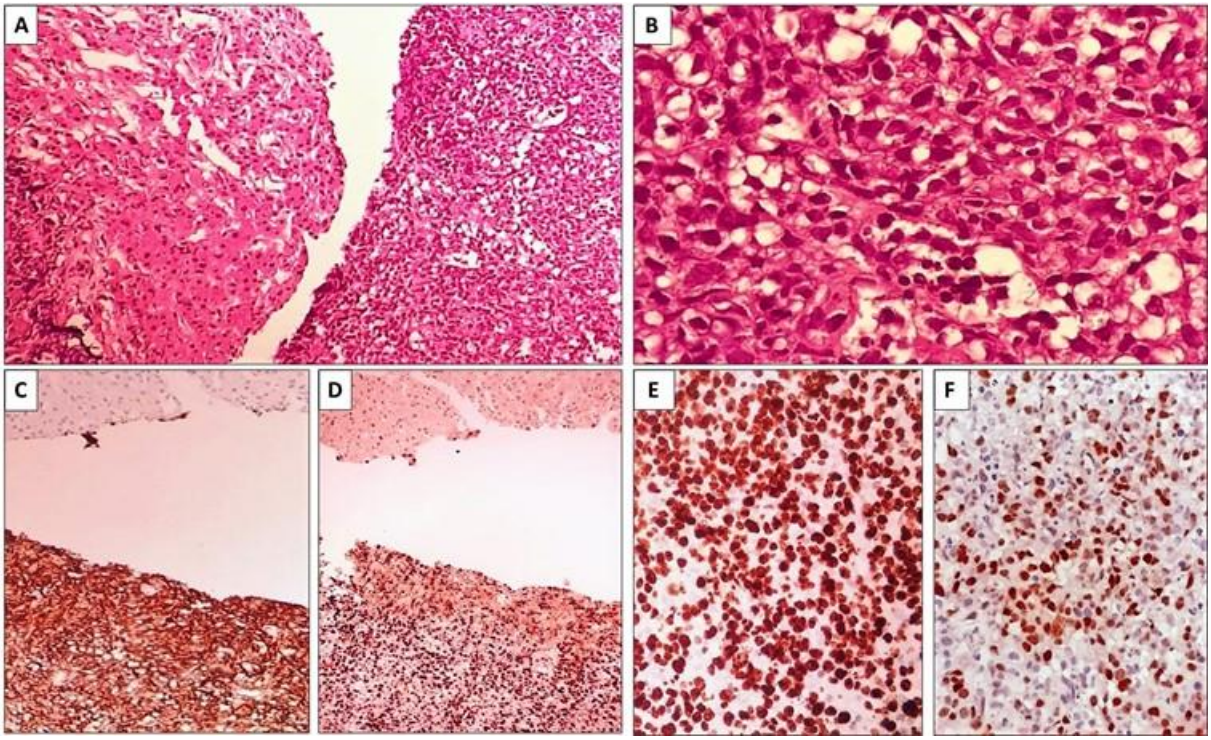

Figure 2. A. Burkitt's lymphoma involving liver parenchyma (H&E, 100X); B. Intermediate-sized cells with abundant basophilic cytoplasm, round to oval nuclei containing nucleoli, a monotonous appearance, and numerous mitosis figures (H&E, 400X); C. Burkitt's lymphoma cells express B-cell antigens (IHC CD20, 100X); D. Bcl6 is a marker of germinal center differentiation (IHC Bcl6, 100x); E. More than 95% of the cells are positive for the proliferation marker protein Ki-67, which reflects the tumor's high proliferation rate (IHC Ki-67, 200X); F. t(8;14) common in AIDS-related Burkitt's lymphomas (IHC c-myc, 200X). H&E: hematoxylin and eosin staining; IHQ: immunohistochemistry.

Table 1. Immunohistochemistry panel.

CD3	NEGATIVE
CD 20	POSITIVE
Bc12	NEGATIVE
Bc16	POSITIVE
CD10	POSITIVE
MUM-1	NEGATIVE
Ki-67	POSITIVE > 95% CELLS
C.MYC	POSITIVE
AE1/AE3	NEGATIVE

3. Discussion and conclusion

Current literature describes an incidence of non-Hodgkin's lymphoma of around 12.2 cases per 100,000 inhabitants, of which approximately 30% present an extranodal primary site, and of these, only 0.4% manifest as primary hepatic lymphomas [4]. B-cell non-Hodgkin's lymphoma is the most common, accounting for around 60% of liver lymphomas, compared to T-cell non-Hodgkin's lymphoma, which accounts for only 30% of cases [4]. The pathophysiology of hepatic lymphoma remains unknown, but chronic antigenic stimulation seems to play a key role in the development of this entity. Some known risk factors

are infection with hepatotropic viruses such as C virus and B virus, as well as HIV and Epstein-Barr virus [4]. Primary hepatic lymphoma has been observed in solid organ transplant recipients, presenting in up to 4% of cases [4].

In 2011, Fwu et al. presented a cohort of patients with primary hepatic lymphoma where they found a rate of 3.18 cases per 100,000 pregnant women with positive hepatitis B virus surface antigen compared to 1.23 cases per 100,000 women with negative hepatitis B virus antigen [5]. A meta-analysis conducted by Hartridge-Lambert et al showed that hepatitis C virus surface antigen positive patients with primary hepatic lymphoma can respond to treatment with pegylated interferon alfa-2a associated with ribavirin, without the need for surgical treatment [6].

Primary hepatic lymphoma usually presents in the fifth decade of life and is more common in men. Symptoms are generally vague and general, although 70% of patients present with abdominal pain and less than 10% with B symptoms. The most notable finding on physical examination is hepatomegaly, present in 50% of patients. The progression of the disease to fulminant acute liver failure fortunately occurs in less than 1% of patients with hepatic lymphoma [7]. In a retrospective study by Dias et al, a total of 36 patients with hepatic lymphoma were identified, with a mean age of 56.6 years and a predominance of males (58%). There were also three patients with primary liver lymphoma (8.3%) and 33 with secondary hepatic lymphoma (91.7%). The most common histological type in the study was diffuse large B-cell lymphoma (33.3%). The most common clinical manifestations included fever, lymphadenopathy, weight loss, night sweats and abdominal discomfort. Night sweats and abdominal discomfort; three patients (11.1%) were asymptomatic. Computed tomography revealed heterogeneous radiological patterns, including a single nodule (26.5%), multiple nodules (41.2%) or diffuse infiltration (32.4%). The mortality rate during follow-up was 55.6%. Higher levels of C-reactive protein ($p=0.031$) and lack of response to treatment ($p<0.001$) seemed to be associated with higher mortality [8].

Laboratory investigation can show multiple alterations, the most frequent being the presence of altered liver enzymes with a cholestatic pattern, although it can also be liver-predominant, as well as increased LDH and B2-microglobulin. Three-phase abdominal computed tomography reveals heterogeneous hypodense lesions with obvious annular enhancement in the arterial phase, as in our case. The finding of calcifications and necrosis is less common and can be difficult to visualize [9].

Abdominal MRI reveals hypo- or isointense lesions on T1-weighted images, with enhancement on T2-weighted images. Gallamini and Borra described the usefulness of positron emission tomography-computed tomography (PET-CT) in staging, as it is more accurate in detecting nodal and extranodal involvement and provides useful information for treatment [10]. Despite the above, our patient's laboratory tests did not reveal any major abnormalities, apart from canalicular enzymes, and only the CT scan led to the suspicion of a diagnosis. In the current literature, there is no consensus on the use of diagnostic criteria, with histopathology being essential for the diagnosis and typing of hepatic lymphoma [6].

The treatment of this type of tumor is quite controversial, with standard chemotherapy treatment regimens for non-Hodgkin's lymphomas generally being used and surgery rarely being indicated in specific cases of obstructive biliary complications [5]. It is clear that the treatment of hepatic lymphoma should involve a multidisciplinary team including a hematologist, hepatologist, infectious disease specialist and liver surgeon in order to optimize the differences between therapeutic approaches with the aim of increasing the survival of these patients.

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Conflicts of Interest: None.

Supplementary Materials: None.

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