

## Primary non-Hodgkin's lymphoma of liver

Daniel Vasilev Kostov, Georgi Leonidov Kobakov, Daniel Veselov Yankov

### CASE REPORT

A 65-year-old male was presented his primary care physician with a two-month history of constipation, upper right abdominal pain and occasional right groin pain. His past medical history included hypertension and hepatitis B from which he had recovered (HBsAg negative). The biochemical analyses revealed alanine transaminase 35 U/L, aspartate transaminase 38 U/L and bilirubin level 26 mmol/L with normal blood count. The result of quantitative HBV DNA revealed an undetectable viral load which is generally lower than 300 copies/mL. Magnetic resonance imaging (MRI) scan of the abdomen showed a mass in the right lobe of the liver with a diameter of 10 cm, located on the right hemiliver (Figure 1A). The tumors markers CA19-9 was 57.3 IU/mL (normal range <27 IU/mL), carcinoma antigen 15-3 was 29.6 IU/mL (normal range <5 IU/mL), and CA125 was 72.4 IU/mL (normal range <35 IU/mL). Alpha-fetoprotein and carcinoembryonic antigen were within normal range. Liver biopsy confirmed non-Hodgkin's lymphoma, staining positive for CD20 lymphocytes.

The patient was diagnosed with primary large B cell lymphoma of the liver stage IE (stage I), given that no additional foci of lymphoma were found anywhere else in the body. A decision was made that the patient had to undergo an operation. Intraoperative findings showed a large tumor mass with a diameter of 10 cm in the right hemiliver which necessitated a right hemihepatectomy (Figure 1B–C). A histomorphological examination of the resected specimen showed large lymphoid cells varying in shape from oval to round vesicular nuclei containing fine chromatin (Figure 2A). The immunohistochemical findings were positive for the pan-B cell marker CD20, as well as LCA, and CD43. Immunostaining of the liver lesion showed reactivity for CD3, CD5, CD10, CD138, MUM1, bcl6, and bcl2 (Figure 2B). Ki67 (MIB-1) immunostaining detected a high proliferation fraction of lymphoid cells. A highly malignant B cell non-Hodgkin's lymphoma diagnosis was given. A liver resection was followed by

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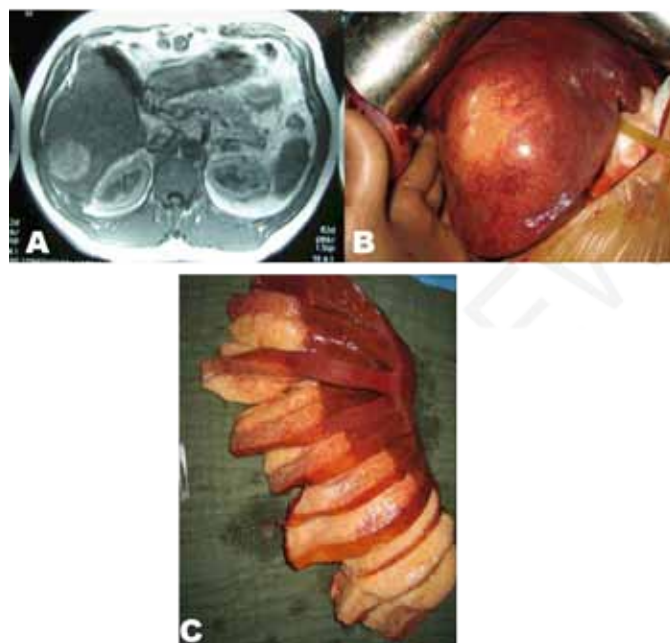


Figure 1: (A) Magnetic resonance imaging scan of abdomen showing a tumor in the right lobe of the liver, (B) Intraoperative view of the lesion, (C) A primary hepatic lymphoma specimen after a right hemihepatectomy.

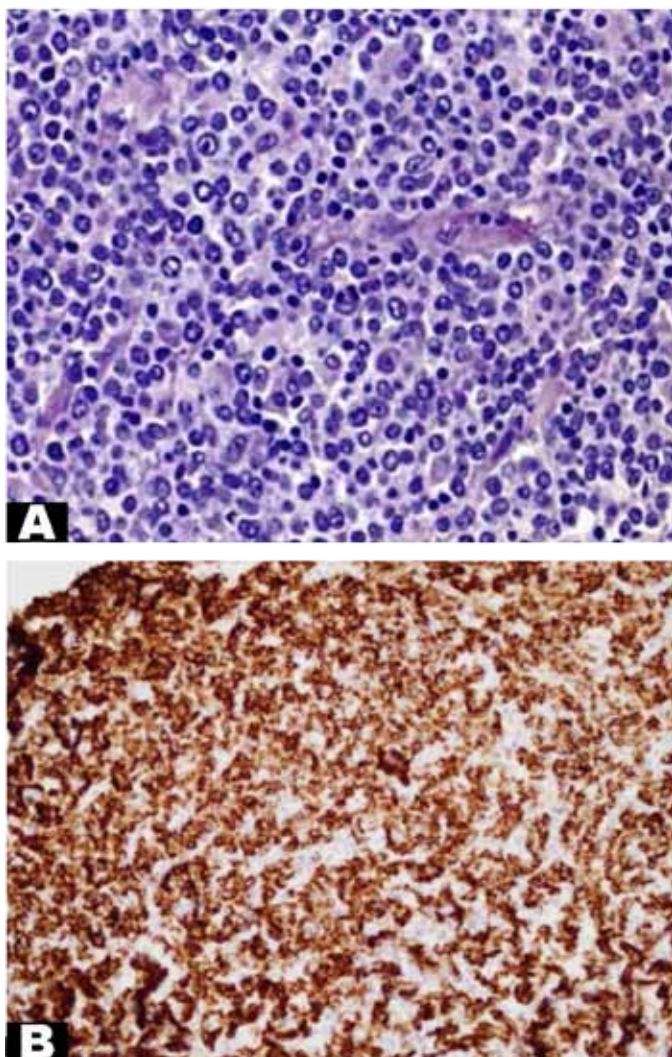


Figure 2: (A) Infiltration of large lymphoid cells (H&E stain, ×400), (B) A photomicrograph showing tumor cells positive for CD20, proving B cell lineage (immunohistochemical stain, ×400).

four cycles of chemotherapy with cyclophosphamide 750 mg/m<sup>2</sup>, doxorubicin 50 mg/m<sup>2</sup>, vincristine 1.4 mg/m<sup>2</sup>, prednisone 100 mg/day, rituximab 375 mg/m<sup>2</sup> (CHOP-R). One year postoperatively, the patient is in good clinical condition without a recurrence of the lymphoma.

## DISCUSSION

Primary hepatic lymphoma (PHL) constitutes about 0.4% of the cases of extra nodal non-Hodgkin’s lymphoma, and only about 0.016% of all cases of non-Hodgkin’s lymphoma [1]. While the pathogenesis of PHL is currently unclear there is evidence that it has been associated with Epstein–Barr virus, hepatitis C virus, human immunodeficiency virus, or human

T-lymphotropic virus infections, liver cirrhosis, systemic lupus erythematosus, and immunosuppressive therapy [2]. The tumor arises from lymphoid elements in the liver, and it is defined by the following clinical criteria (Table 1):

- (i) No evidence of palpable superficial lymphadenopathy and no enlargement of mediastinal nodes.
- (ii) A normal leukocyte count.
- (iii) At surgery, the liver mass predominates with involved lymph nodes confined to the perihepatic region and no splenic involvement.

Extranodal lymphoma is classified as secondary if there is involvement of lymph nodes, except for those of an adjacent primary organ or with more than one extra nodal site. The diffused large B cell is the most common type of non-Hodgkin’s lymphoma, and more than 50% of patients have some extra-nodal lesions [3]. To diagnose a PHL it is necessary for the liver biopsy to coincident with lymphoma and an absence of a lymphoproliferative disease outside the liver. Late diagnosis, however, or failure to make a diagnosis can end up in fulminant hepatic failure and ultimately death. The optimal treatment for PHL has not yet been defined. Many reports have suggested that surgical resection followed by adjuvant chemotherapy and/or radiation results in better prognosis [4]. The current indications that necessitate a surgery are cases of patients with a localized disease

Table 1: Differences between PLL and secondary involvement

Primary lymphoma of the liver	Secondary involvement
No evidence of palpable superficial lymphadenopathy	Evidence of palpable superficial lymphadenopathy
No enlargement of mediastinal nodes	Enlargement of mediastinal nodes
Normal leukocyte count	High leukocyte count
At surgery, the liver mass predominates, with involved lymph nodes confined to the perihepatic region.	Involved paraaortic and mesenterial lymph nodes
No splenic involvement	Splenic involvement
Primary hepatic lymphoma is defined according to Caccamo criteria as lymphoma confined only to the liver without the involvement of any other organ like spleen, bone marrow, lymph nodes, peripheral blood, or other tissues until at least six months after diagnosis.	

that can undergo radical liver resection or if there is presence of a persistent respectable disease followed by chemotherapy [5]. Chemotherapy with CHOP-R based regimens is the gold standard [6].

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## CONCLUSION

Primary non-Hodgkin's lymphoma of the liver is a rare variation of lymphoma and making a precise diagnosis presents a challenge in clinical practice. Magnetic resonance imaging findings of primary and secondary lymphoma may not be sufficient to render a specific diagnosis, especially when liver involvement is the first or only finding. Rather, other parameters must be considered, including a liver biopsy with a histopathological examination.

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## Author Contributions

Daniel Vasilev Kostov – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Georgi Leonidov Kobakov – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

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## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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