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Gastrointestinal

Primary hepatic mucosa-associated lymphoid tissue lymphoma in a patient with no chronic liver disease: Case report

Cezar I. Betianu MD^{a,*}, Augustin Dima MD^b, Giorgiana Pavaloiu MD^a^aDepartment of Radiology, “Carol Davila” Central Military Emergency University Hospital, Mircea Vulcanescu Street, no.88, Bucharest, Romania, 010825^bDepartment of Surgery, “Carol Davila” Central Military Emergency University Hospital, Bucharest, Romania

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ABSTRACT

Extramarginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) is a non-Hodgkin lymphoma of low-grade malignancy. The most common localization is the stomach, and the common nongastric sites are salivary glands, the skin, orbits, the conjunctiva, the lung, breasts, upper airways, other gastrointestinal sites, and the liver. Primary hepatic MALT lymphoma is a rare disease and the diagnostic can be challenging. The clinical presentation is nonspecific and may range from no symptoms to end-stage liver disease. The radiological aspect of hepatic lymphoma may indicate this diagnosis; however, the final diagnosis is made by hepatic biopsy. We report the case of a 47-year-old woman with no chronic liver disease, incidentally found with a focal liver mass at ultrasound examination. The only clinical symptom was fatigue. The blood tests were normal and tumoral markers were negative. Computed tomography and magnetic resonance imaging were performed. However, because the hepatic lesion was first described as a benign entity and, at second opinion, the suspicion of lymphoma was raised, the patient decided to undergo surgery first, without prior biopsy. The histopathologic analysis confirmed the diagnosis: hepatic MALT lymphoma positive for CD 20 and negative for CD 5, BCL6, cyclin D1, and CD 23. No lymph node involvement was noted and follow-up imaging with positron emission tomography-computed tomography did not show any other site of disease, thus confirming the diagnosis of primary hepatic MALT lymphoma. The aim of this paper was to highlight the imagistic features of primary hepatic lymphoma to contribute to the early diagnosis of this rare disease entity.

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* Corresponding author.

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Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma is a non-Hodgkin lymphoma of low-grade malignancy and was first described in 1965 by Ata and Kamel [1,2]. The most common site for MALT lymphoma is the stomach, and it is usually associated with *Helicobacter pylori* infection. Nongastric sites for primary MALT lymphoma are the salivary glands, the skin, orbits, the conjunctiva, the lung, breasts, upper airways, other gastrointestinal sites, and the liver. Primary hepatic lymphoma (PHL) is a very rare disease that accounts for only 0.016% of all cases of non-Hodgkin lymphoma [3]. The majority of PHLs are diffuse large B-cell lymphomas. MALT lymphoma and other histologies (diffuse mixed small and large cell, lymphoblastic, diffuse immunoblastic, Burkitt lymphoma, etc.) have been described in less than 5% of cases [4]. The imagistic characteristics can be misleading, making PHL a challenging diagnosis; however, there are hallmarks that suggest the malignant nature of the lesion. Therefore, we report the case of a surgically resected primary hepatic MALT lymphoma that was first described as a benign hepatic lesion.

Case report

A 47-year-old woman was referred to our department for an incidentally focal liver mass found on a routine ultrasound examination. The patient had an unremarkable medical history. The only clinical symptom described by the patient was fatigue. The physical examination at presentation did not reveal any abnormalities. The laboratory tests showed the following: alanine aminotransferase: 18 U/L (normal, 14-54 U/L), aspartate transaminase: 22 U/L (normal, 15-41 U/L), gamma-glutamyl

transferase: 29 U/L (normal, 7-50 U/L), alpha-fetoprotein: 8 ng/mL, normal blood cell counts, coagulation, and protein electrophoresis. Serological examinations for HIV and hepatitis B and C viruses were negative. The ultrasound revealed a hypoechoic hepatic lesion in segment IV, without any other abdominal abnormalities.

Imagistic investigations, contrast-enhanced computed tomography (CT) and contrast-enhanced magnetic resonance imaging (MRI) were performed.

Nonenhanced CT showed a slightly hypodense focal mass in segment IVA of the liver, measuring 85/50 mm in diameter (A). On contrast-enhanced CT, there was no enhancement of the lesion on arterial, portal, or delayed phase. The vessels were not invaded; the vessels pass through the mass without having their vascular paths modified, although their caliber was slightly reduced, indicating the infiltrative pattern of the lesion (Fig. 1C, yellow arrows). Based on the clinical and radiological findings, the lesion was first described as a benign entity (focal steatosis or hepatic pseudolesion).

MRI showed a solitary, well-defined focal mass occupying segment IVA, measuring 85/50 mm in diameter, moderately hypointense T1, and hyperintense T2 fat suppressed (Fig. 2). The hepatic lesion showed an intense restriction of diffusion on diffusion-weighted images (Fig. 3). There was no drop of signal on in and out of phase images, which made the diagnosis of focal steatosis unlikely. After contrast administration, the lesion remained hypointense on all phases (Fig. 4). CT and MRI examinations showed that there were no enlarged abdominal lymph nodes and no evidence of intrahepatic or extrahepatic biliary tree dilatation.

The hepatic mass was first described as a benign hepatic lesion, even though, at second opinion, the suspicion of lymphoma was raised. Therefore, the patient decided to undergo surgery first without prior biopsy irrespective of the medical management of the lymphoma. Intraoperative biopsy confirmed

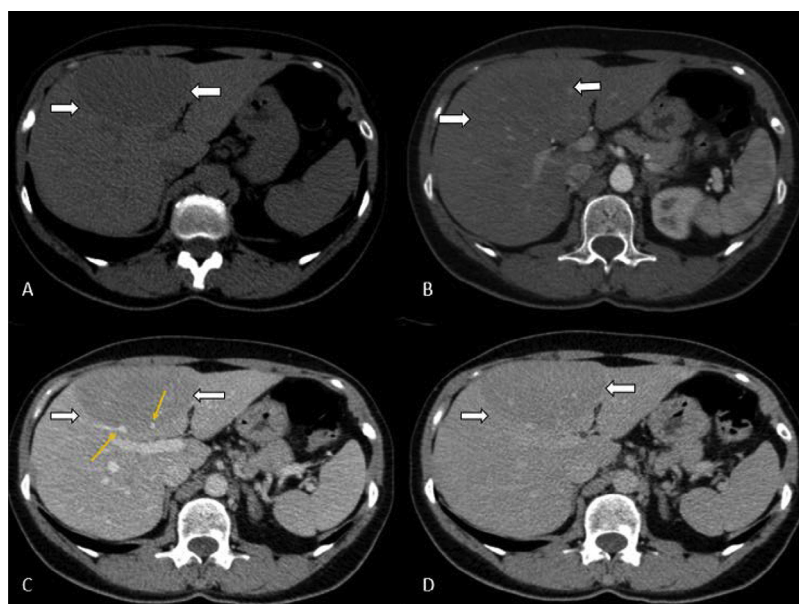


Fig. 1 – Nonenhanced axial computed tomography images show a slightly hypodense focal mass in segment IV A of the liver (A), with no enhancement of the lesion on arterial (B), portal (C), or delayed phases (D).

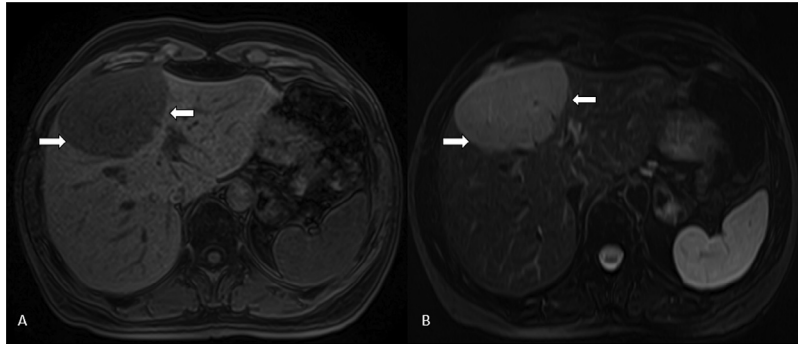


Fig. 2 – Axial magnetic resonance images demonstrate a solitary, well-defined focal mass occupying the segment IVA, measuring 85/50 mm in diameter, moderately hypointense T1 (A) and hyperintense T2 fat suppressed (B).

the diagnosis of lymphoma. The histopathologic and immunohistochemical analyses revealed hepatic MALT lymphoma positive for CD 20 and negative for CD 5, BCL6, cyclin D1, and CD 23. Bone marrow biopsy and gastric endoscopy were normal. The patient underwent R-CHOP-based regimen chemotherapy, which consisted of 6 cycles of rituximab, cyclophosphamide, vincristine, and dexamethasone.

At 6 and 9 months, respectively, after surgery, the contrast-enhanced CT and positron emission tomography-computed tomography (PET-CT) demonstrated no lymph node involvement

confirming the diagnosis of primary hepatic MALT lymphoma (Fig. 5).

Discussion

PHL is a very rare primary liver tumor and a rare type of extranodal non-Hodgkin lymphoma. It is defined as a lymphoma limited to the liver without extrahepatic involvement until at least 6 months after diagnosis [5]. The etiology of PHL

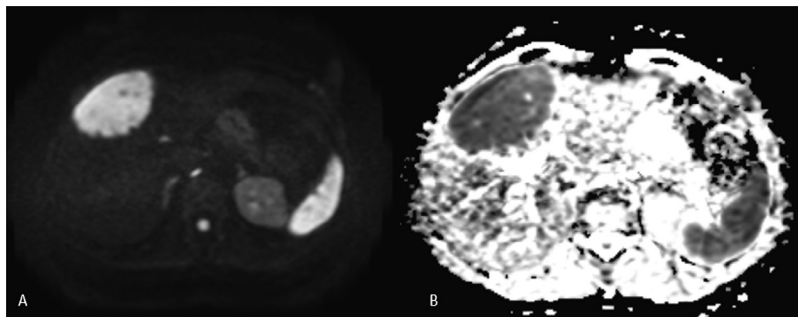


Fig. 3 – Axial magnetic resonance images show an intense restriction of diffusion on diffusion-weighted imaging, similar to the spleen (A) with hypointensity on the apparent diffusion coefficient map (B).

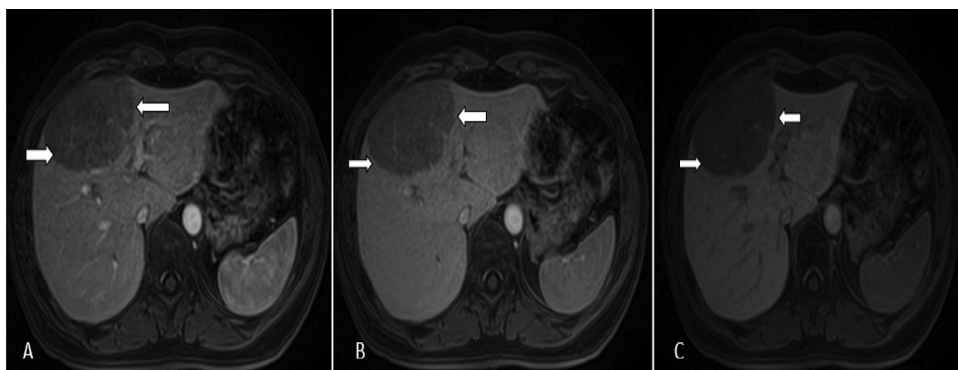


Fig. 4 – Axial contrast-enhanced magnetic resonance images, after gadobenate dimeglumine administration, show that the lesion (white arrows) remains hypointense on all phases: arterial (A), portal (B), and delayed phase (C).

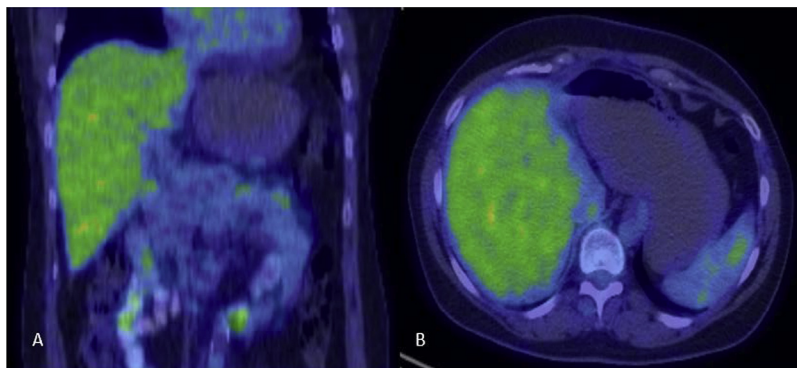


Fig. 5 – Coronal (A) and axial images (B) on positron emission tomography-computed tomography performed at 9 months after surgery and chemotherapy demonstrate no sign of relapse.

is still unclear, even though it has been associated with hepatitis C virus, Epstein-Barr virus, or autoimmune disease [6]. The particularity of our case is that, although PHL has been associated with infection, chronic inflammation, or autoimmune disease, none of these were present in our patient.

As far as we know, there are only 67 cases of primary hepatic MALT lymphoma reported in 39 English literatures to date [7]. Very few cases have been reported in the literature and little is known about the imagistic features of this lesion; therefore, PHL is often diagnosed intra- or postoperatively. Because of its rarity, PHL can be easily mistaken for focal steatosis, cholangiocellular carcinoma [7], or hepatocellular carcinoma [8–10].

As far as the imagistic characteristics of PHL, there are certain features that indicate the nature of the lesion. Primary liver tumors usually have a heterogeneous appearance on ultrasound and at CT scan show an intense arterial enhancement with washout on portal or delayed phases. In opposition, lymphoma has a homogenous hypoechoic aspect on ultrasound and is hypoattenuating on CT scan, with no or minimal peripheral enhancement.

To date, there are no characteristic radiological findings of PHL. Three different aspects of PHL have been described: as a solitary lesion, as multiple lesions in the liver, or as a diffuse infiltration of the liver. In more than 50% of cases, PHL presents as a solitary lesion, as in our case. On ultrasound, PHL is usually a hypoechoic lesion. After contrast administration, more than 50% of PHLs show no enhancement. In about 30% of cases, there is a patchy enhancement and 15% show a ring enhancement. On MRI, PHL is usually hypo- or isointense on T1 and hyperintense on T2 [4]. Similarly, in our case, PHL was a solitary lesion, hypoechoic at ultrasound, hypoattenuating at CT scan, and showed no enhancement on CT or MRI scan. Unfortunately, we did not have access to the ultrasound images, but in the report, PHL was described as a hypoechoic lesion. The infiltrative pattern of the lesions with no distortion of vessels traversing the mass and the intense restriction of diffusion on DWI, similar to the spleen, raised the suspicion of a hepatic lymphoma at further evaluation. It is true that diffusion restriction may be seen in other benign entities, such as hepatic hemangioma or hepatic abscess. However, none of these benign entities correlated with the other radiological and clinical findings in our patient. All these features, along with

the hypoechoic appearance at the ultrasound, raised the suspicion of PHL at second opinion.

Even though the diagnosis of PHL can be suggested by the imagistic features, this entity cannot be diagnosed definitely without histologic analysis. Therefore, hepatic lymphoma must be confirmed by liver biopsy. In our case, the liver biopsy was not performed due to the following reasons: (1) the imagistic findings were inconclusive; therefore, the patient decided not to undergo a biopsy due to the risk of a potential needle dissemination, in case of a malignant lesion; (2) the hepatic lesion was considered resectable. Therefore, the patient underwent surgical resection followed by chemotherapy. Staging evaluations with CT and PET-CT at 6 and 9 months, respectively, after diagnosis confirmed the diagnosis of primary MALT lymphoma.

As far as we know, there is no consensus regarding the optimal treatment of nongastric MALT lymphomas. The recommendations of the National Comprehensive Cancer Network for nongastric MALT lymphomas include radiation therapy, surgery, rituximab, or observation in selected cases. R-CHOP-based regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) is an effective treatment of choice for B-cell lymphoma [11,12]. Rituximab, which is an anti-CD 20 monoclonal antibody, is efficient in MALT lymphoma and is given alone or in combination with other chemotherapy regimens [13,14].

As far as the role of surgery in PHL is concerned, there are studies that report better outcomes in terms of survival in patients treated with surgery and postoperative chemotherapy for PHL [15–17]. In our case, surgery was performed because the patient was confused about the interpretation of the imaging findings and considered surgery as the optimal treatment. In PHL, surgery is performed to reduce the volume of the tumor before chemotherapy; surgery alone does not appear to be a sufficient treatment as extrahepatic recurrences can appear [8]. However, surgical resection of a primary liver lymphoma requires a normal function of the liver and the absence of comorbidities.

Close follow-up of patients with liver MALT lymphoma is mandatory as extranodal recurrences may occur. Recurrences in the lungs, the parotid glands, and the liver have been reported [8]. In our case, the patient underwent CT scan and PET-CT at 6 and 9 months after chemotherapy. The role of PET-CT in the follow-up of MALT lymphoma is controversial with

studies suggesting that the role of PET in MALT lymphomas is limited due to their low or non-FDG avidity and studies reporting that the 18-fluorodeoxyglucose (FDG) avidity correlates with lesion location and histologic features [18]. A more recent article indicates that the 18-FDG avidity in extragastric MALT lymphomas correlates with Ki-67 proliferation [19]. According to the study, patients with a Ki-67 of >15% had FDG-avid lesions. These findings require further investigations but indicate that PET-CT might be a useful tool for staging and follow-up in patients with MALT lymphoma. In our case, the Ki-67% index was <10%; because the controversy regarding the FDG avidity of MALT lymphoma was under debate at that time, the patient underwent PET-CT at 9 months after the diagnosis, which demonstrated no sign of relapse.

In summary, even though the diagnosis of PHL is made by hepatic biopsy, the imagistic findings can help indicate this diagnosis. Also, it is of utmost importance to correlate all the characteristics of the lesion at ultrasound, CT, and MRI, along with the clinical data of the patient.

Conclusion

Even though PHL, including MALT lymphoma, is a rare primary tumor of the liver, it is a diagnosis the radiologist should keep in mind as lymphoma is a great disease mimicker. It is important to recognize early the imagistic features of such lesions as primary extranodal marginal lymphoma of the liver is a potentially curable malignancy.

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