HSPI The Open Access Publisher

ACR ARCHIVES OF CASE REPORTS
ISSN 2637-3793

Case Report

Hepatic Pseudolymphoma Mimicking Neoplasia in Primary Biliary Cholangitis: A Case Report

Jeremy Hassoun[1], Aurélie Bornand[2], Alexis Ricoeur[3], Giulia Magini[1], Nicolas Goossens[1] and Laurent Spahr[1]*

[1]Gastroenterology and Hepatology, University Hospitals and Faculty of Medicine, Geneva, Switzerland
[2]Clinical Pathology, University Hospitals and Faculty of Medicine, Geneva, Switzerland
[3]Radiology, University Hospitals and Faculty of Medicine, Geneva, Switzerland

Abstract

Visualizing a nodule in the liver parenchyma of a patient with chronic liver disease raises the suspicion of hepatic malignancy. We report here the case of a 63-year-old female with primary biliary cholangitis (PBC) in whom a hepatic pseudolymphoma (HPL) was incidentally detected. This fairly rare lesion mimics primary liver cancer, has no specific radiological features, and requires histology for a definite diagnosis. This tumor-like lymphoid liver proliferation has been reported in clinical situations with immune-mediated inflammation including PBC. It can be observed in many organs but very rarely in the liver. The diagnosis of HPL should be considered when detecting a liver nodule in a patient with this particular chronic cholestatic liver disease.

More Information

***Address for correspondence:** Laurent Spahr, Professor, Department of Gastroenterology/ Hepatology, University Hospitals and Faculty of Medicine, 4 Rue Gabrielle Perret-Gentil, Floor P, CH-1205Geneva, Switzerland,
Email: laurent.spahr@hug.ch

https://orcid.org/0000-0001-8407-2463

Submitted: December 04, 2024
Approved: December 18, 2024
Published: December 19, 2024

How to cite this article: Hassoun J, Bornand A, Ricoeur A, Magini G, Goossens N, Spahr L. Hepatic Pseudolymphoma Mimicking Neoplasia in Primary Biliary Cholangitis: A Case Report. Arch Case Rep. 2024; 8(3): 152-155. Available from: https://dx.doi.org/10.29328/journal.acr.1001115

Keywords: Hepatic malignancy; Chronic liver disease; Chronic cholestatic liver disease; Lymphoid liver proliferation

Abbreviations: PBC: Primary Biliary Cholangitis; HPL: Hepatic Pseudolymphoma

Introduction

Pseudolymphoma, also named reactive lymphoid hyperplasia or nodular lymphoid lesion, is characterized by a dense proliferation of polyclonal lymphocytes organized in follicles. Such lymphoid lesion is associated with chronic inflammation as HPL has been observed in various conditions including autoimmune diseases and cancers. Anatomical sites in which HPL has been described include the gastrointestinal tract, lung, or skin, but only rarely the liver. Although accepted as a benign lesion without risk of malignant transformation, making a definite diagnosis is a major challenge, as the distinction between hepatocellular carcinoma and HPL may be difficult using radiological features only, and histopathological examination is therefore required.

The present case of HPL illustrates the difficulty in characterizing this focal liver lesion in spite of dedicated radiological methods and multidisciplinary team discussion. Histopathological examination of a biopsy targeting the lesion allowed a definite diagnosis. This clinical observation underlines the decisive role of histology when facing a nodule in a non-cirrhotic liver.

Case presentation

A 63-year-old woman with PBC was referred to our multidisciplinary team meeting at our institution on August 25, 2023, for further investigations following the discovery of a liver nodule on a routine abdominal echography. She had been diagnosed with PBC 7 years earlier based on moderately elevated alkaline phosphatase and gamma-glutamyl transferase serum levels together with positive type 2 anti-mitochondrial antibodies at a 1/160 titer. She was prescribed ursodeoxycholic acid at a 15 mg/kg daily dose, qualified as a responder at one year based on Paris II criteria [1], and thus remained at this dosage since. However, transient elastography was not performed at this time. She was otherwise healthy, without alcohol consumption, and reported no family history of cancer. On clinical examination, there was no stigmata of chronic liver disease, no xanthelasma and the edge of the liver was unremarkable at abdominal palpation. Laboratory tests were as follows: normal blood count and coagulation time, platelets 229 G/L (N: 150-350), serum creatinine 64 umol/l, AST 26 IU/L (N: <35), ALT 31 IU/L (N:<35), GGT 28 IU/L (N: < 40), alkaline phosphatase 118 IU/L (N: 35-104), serum bilirubin 10.8 umol/L (N: < 21), albumin 42 gr/L (N: 35-46). Tumor markers including alpha-

foetoprotein, carcinoembryonic antigen, and CA 19-9 serum levels were normal. At abdominal ultrasonography, the liver was slightly dysmorphic and a single poorly demarcated subcapsular hypoechoic lesion of 16 mm in diameter was seen at the junction of segments VI and VII (Figure 1), which didn't demonstrate arterial phase enhancement on injected computed tomography (CT scan), and motivated an MRI scan to get a full characterization of this liver nodule. On this particular imaging technique, the lesion demonstrated low intensity on T1-weighted images, slightly higher intensity on T2-weighted sequences with a restricted-diffusion pattern, and no uptake following injection of gadoxetic acid (Gd-EOB-DTPA), the most efficient radiological method to characterize a focal liver lesion. Because these imaging findings could not exclude hepatic neoplasia, our multidisciplinary group proposed an image-guided liver biopsy targeting the nodule and the non-tumoral liver. This procedure was performed under light sedation on September 15, 2023, and the patient left the hospital on the same day without any relevant complications.

At histology, the non-tumoral liver showed moderate peri-portal fibrosis and inflammation around bile ducts consistent with Scheuer stage 2 PBC lesions [2]. Examination of the nodule (Figure 2) demonstrated small mature lymphocytes without atypical features, intermixed with non-necrotizing histiocytic granulomatous reaction, focal fibrosis, and polyclonal plasmocytic infiltration. As lymphoma was suspected, we decided to perform immunohistochemical studies on the biopsy, in order to differentiate between benign and malignant infiltration of the liver. Both CD3 and CD20 are commonly used as specific markers of T and B cells, respectively. Thus, the biopsy sections were stained using anti-CD3 and anti-CD20 monoclonal antibodies, followed by a careful manual count of cells that demonstrated immunoreactivity for these two markers. Results showed a heterogeneous pattern of distribution with both T lymphocyte CD3 + and B lymphocyte CD20 + forming occasional lymphoid follicles together with a focal dendritic network. All these histological characteristics were consistent with the diagnosis of HPL. The risk of lymphoma in PBC is estimated at <1%

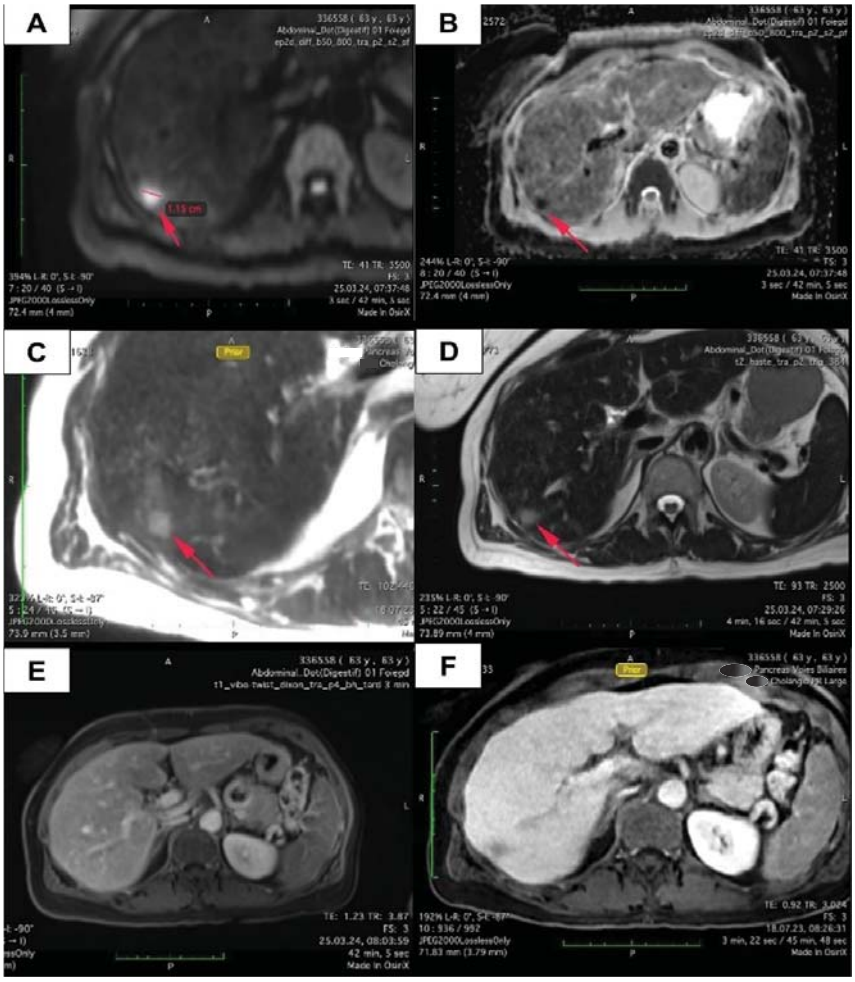

Figure 1: Radiological images
The liver MRI scan demonstrates an 11 mm round-shaped nodule in segment VI of the liver with hypersignal on diffusion-weighted imaging sequences and high restriction of diffusion (panels A and B), hypersignal on T2-weighted images (panels C and D). The lesion also shows homogeneous arterial enhancement with a washout at the venous phase on gadolinium-enhanced T1-weighted images (panels E and F).

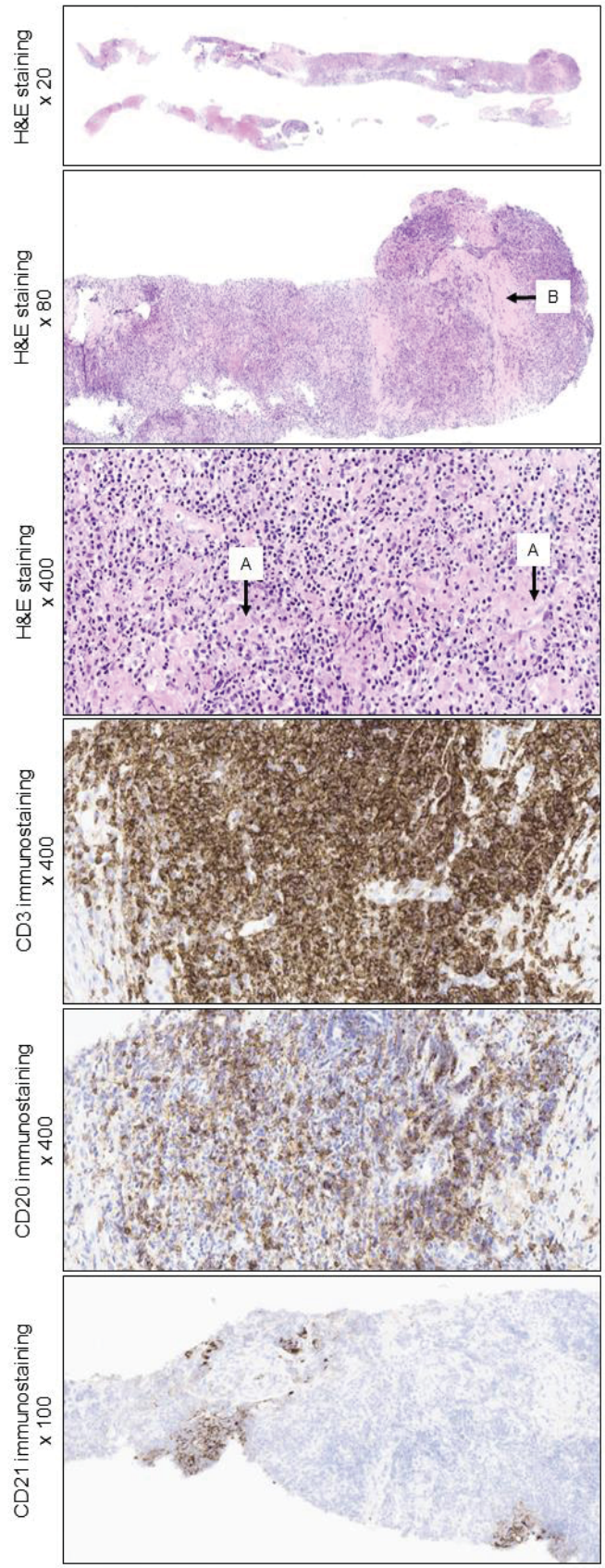

Figure 2: Histological examination
Histological examination of the liver nodule (H&E: haematoxylin-eosin staining) shows a dense cellular infiltration with mature hyperplastic lymphocytes intermixed with non-necrotizing histiocytic granulomatous reaction (A), focal fibrosis (B) and polyclonal plasma cells aggregates. Immunostaining revealed T CD3+ and B CD20+ lymphocytes forming occasional lymphoid follicles with focal follicular dendritic CD21+ network.

[3], and malignant transformation of HPL into lymphoma is anecdotal [4]. At a follow-up consultation on May 5, 2024, the patient was informed that both biological values and transient elastography will be proposed annually in the setting of PBC surveillance, but a liver cancer surveillance program would not be implemented in this chronic non-cirrhotic liver disease.

Discussion

Primary biliary cholangitis is a chronic cholestatic liver disease that may progress to cirrhosis and its potentially associated complications include hepatocellular carcinoma (HCC). The risk of developing HCC at a pre-cirrhotic stage is low [5]. However, the incidence is significantly higher compared to age-matched individuals in a recent large population-based study [6]. Still, international guidelines recommend HCC surveillance in patients with PBC at a cirrhotic stage [7].

In our patient with non-cirrhotic PBC, it was difficult to minimize the signification of this liver nodule as radiological features including a faint enhancement in T2 images, no uptake by the liver-specific contrast agent, and a restricted diffusion pattern couldn't formerly exclude a developing primary liver neoplasia. Thus, the histopathological diagnosis of HPL was unexpected, although anecdotal reports have described this lesion in various clinical situations [8] including PBC [4,9,10].

Making a diagnosis of HPL is challenging. In a recent series of 80 HPL, lesions were predominant in females, unique, and less than 2 cm in size [9]. In a retrospective study from China, the HPL lesions varied from 0.5 cm to 3 cm in size [11]. Due to the variable radiodynamic aspects of the lesions (either hypo- or hypervascular) suggesting a primary or metastatic liver cancer, almost eight out of ten patients in the report by Inoue, et al. [9] were initially misdiagnosed, and histopathological analysis was necessary to confirm the diagnosis.

Hepatic pseudolymphoma is uncommon, and most reported cases demonstrate PBC as a coexistent liver disease [4,9,10,12]. The chronic inflammation that characterizes this cholestatic liver disease and the associated sustained immune response may participate in the development of HPL [4].

In conclusion, we present here in detail a case of a liver nodule in the setting of a chronic liver disease that mimics primary liver cancer. In spite of well-conducted contrast CT and MRI imaging studies, the diagnosis of HPL may remain elusive and often requires histological examination for confirmation of diagnosis. This clinical observation underlines the decisive role of histology when facing a nodule in a non cirrhotic liver The diagnosis of HPL should be considered when detecting a liver nodule in a patient with PBC.

With regards to the limited number of reported cases and the anecdotal risk of malignant transformation of HPL [13], detailed information on long-term follow-up of patients who didn't undergo surgical resection would be helpful for selecting patients who may require surveillance.

Acknowledgment

We would like to acknowledge the contribution of the general practitioner who provided us with the patient's clinical and biological data that were important to report in detail this valuable clinical observation.

Consent

A written informed consent was obtained from the patient for publication of this case report. A copy of this document is available for review by the journal editorial board upon request.

Authors' contribution

JH: conception and writing of the manuscript; AB: detailed description of pathological findings, review of literature, writing and critical revision of the manuscript; AR: performed all radiological images and liver biopsy, drafting and critical review of the manuscript; GM: writing and critical revision of the manuscript; NG: writing and critical revision of the manuscript; LS: conception of the work, design, writing of the manuscript and review of literature, response to reviewers. All authors approved the final version of the manuscript.

References

1. Jones DE, Bassendine MF. Primary biliary cirrhosis. J Intern Med 1997; 241:345-8. Available from: https://doi.org/10.1016/s0168-8278(99)80097-x
2. Wendum D, Boelle PY, Bedossa P, Zafrani ES, Charlotte F, Saint-Paul MC, et al. Primary biliary cirrhosis: proposal for a new simple histological scoring system. Liver Int 2015;35:652-9. Available from: https://doi.org/10.1111/liv.12620
3. Panjala C, Talwalkar JA, Lindor KD. Risk of lymphoma in primary biliary cirrhosis. Clin Gastroenterol Hepatol 2007;5:761-4. Available from: https://doi.org/10.1016/j.cgh.2007.02.020
4. Okada T, Mibayashi H, Hasatani K, Hayashi Y, Tsuji S, Kaneko Y, et al. Pseudolymphoma of the liver associated with primary biliary cirrhosis: a case report and review of literature. World J Gastroenterol 2009;15:4587-92. Available from: https://doi.org/10.3748/wjg.15.4587
5. Jones DE, Metcalf JV, Collier JD, Bassendine MF, James OF. Hepatocellular carcinoma in primary biliary cirrhosis and its impact on outcomes. Hepatology 1997;26:1138-42. Available from: https://doi.org/10.1002/hep.510260508
6. Schonau JWASJH, H. Risk of cancer and subsequent mortality in primary biliary cholangitis: a population-based cohort study of 3052 patients. Gastro Hep Advances 2023;2:879-888. Available from: https://doi.org/10.1016/j.gastha.2023.05.004
7. Natarajan Y, Tansel A, Patel P, Emologu K, Shukla R, Qureshi Z, et al. Incidence of Hepatocellular Carcinoma in Primary Biliary Cholangitis: A Systematic Review and Meta-Analysis. Dig Dis Sci 2021;66:2439-2451. Available from: https://doi.org/10.1007/s10620-020-06498-7
8. Kwon YK, Jha RC, Etesami K, Fishbein TM, Ozdemirli M, Desai CS. Pseudolymphoma (reactive lymphoid hyperplasia) of the liver: A clinical challenge. World J Hepatol 2015;7:2696-702. Available from: https://doi.org/10.4254/wjh.v7.i26.2696
9. Inoue M, Tanemura M, Yuba T, Miyamoto T, Yamaguchi M, Irei T, et al. A case of hepatic pseudolymphoma in a patient with primary biliary cirrhosis. Clin Case Rep 2019;7:1863-1869. Available from: https://doi.org/10.1002/ccr3.2378
10. Sim KK, Fernando T, Tarquinio L, Navadgi S. Hepatic reactive lymphoid hyperplasia-associated primary biliary cholangitis masquerading as a neoplastic liver lesion. BMJ Case Rep 2023;16. Available from: https://doi.org/10.1136/bcr-2023-254963
11. Jiang W, Wu D, Li Q, Liu CH, Zeng Q, Chen E, et al. Clinical features, natural history and outcomes of pseudolymphoma of liver: A case-series and systematic review. Asian J Surg 2023;46:841-849. Available from: https://doi.org/10.1016/j.asjsur.2022.08.113
12. Fukuo Y, Shibuya T, Fukumura Y, Mizui T, Sai JK, Nagahara A, et al. Reactive lymphoid hyperplasia of the liver associated with primary biliary cirrhosis. Med Sci Monit 2010;16:CS81-6. Available from: https://pubmed.ncbi.nlm.nih.gov/20581780/
13. Sato S, Masuda T, Oikawa H, Satoh T, Suzuki Y, Takikawa Y, et al. Primary hepatic lymphoma associated with primary biliary cirrhosis. Am J Gastroenterol 1999;94:1669-73. Available from: https://doi.org/10.1111/j.1572-0241.1999.01160.x