CASE REPORT

DOI: 10.5336/caserep.2023-95926

A Rare Case of Hepatic MALT Lymphoma with Coexistence of Hepatitis B Virus and Echinococcus Infection

Ceyda ASLAN[a], Esra TERZİ DEMİRSOY[b], Mehmet ASLAN[c], Gökhan DİNDAR[d]

[a]Department of Hematology, University of Health Sciences Derince Training and Research Hospital, Kocaeli, Türkiye
[b]Department of Hematology, Kocaeli University Faculty of Medicine, Kocaeli, Türkiye
[c]Department of Surgical Oncology, VM Medical Park Kocaeli Hospital, Kocaeli, Türkiye
[d]Department of Gastroenterology, University of Health Sciences Derince Training and Research Hospital, Kocaeli, Türkiye

ABSTRACT Primary hepatic extranodal mucosa-associated lymphoid tissue (MALT) lymphoma is seen extremely rare compromising 0,016% among non-Hodgkin lymphomas. Association of chronic inflammatory conditions or infectious processes mostly hepatitis B virus (HBV) infection has been reported by scarce number of case presentations. Whereas MALT lymphoma accompanied by echinococcus granulosus infection was described only in one primary pulmonary lymphoma case. We herein present a primary hepatic MALT lymphoma case with both HBV carrier state and liver hydatid cyst history. A 86 years old male patient referred to our clinic with a sole liver mass and was diagnosed with primary hepatic MALT lymphoma by core biopsy. Positron emission tomography detected increased uptake in the liver lesion without any other uptake site. He was successfully treated with rituximab-chemotherapy, tenofovir and albendazole. By adding one more case to the literature we aimed to emphasize the probable etiologic causative role of echinococcus infection in MALT lymphoma.

Keywords: Hepatic marginal zone lymphoma; hepatitis B virus; hydatid disease

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) represents 7-8% of all non-Hodgkin lymphomas (NHL) in western countries. Sites of occurrence include mostly stomach, infrequently salivary gland, lung, thyroid, ocular adnexa, and skin.[1,2] Whereas primary hepatic MALT lymphoma is seen extremely rare compromising 0.016% within all NHLs and 2-4% among MALT lymphomas.[3,4] MALT lymphomas have been associated with chronic inflammatory conditions such as an infectious or autoimmune process. The role of hepatitis B virus (HBV), hepatitis C virus (HCV), non-alcoholic steatohepatitis and alcoholic liver disease, primary biliary cholangitis, also autoimmune hepatitis in development of hepatic MALT lymphoma was highlighted with low number of cases.[5,6] To the best of our knowledge hepatic hydatid disease (HD) in primary hepatic MALT lymphoma has not been reported yet. Here we present a primary hepatic MALT lymphoma case with HBV carrier state and history of surgical procedure for liver cyst HD.

CASE REPORT

A 86-year old male patient with an isolated liver mass was examined by surgical oncologist with preliminary diagnosis of hepatocellular carcinoma or liver metastasis and referred us after diagnosed with extranodal marginal zone lymphoma by core biopsy. He had a history of type 2 diabetes, hypertension, and peripheral vascular disease. He also stated having an operation for liver cyst HD about 20 years ago. Physical examination was unremarkable except for non-pitting lower extremity edema and right-sided subcostal incision scar. The routine clinical laboratory parameters were as follows: Complete blood count, biochemistry results including liver and renal function tests were within normal ranges. Erythrocyte

Correspondence: Ceyda ASLAN
Department of Hematology, University of Health Sciences Derince Training and Research Hospital, Kocaeli, Türkiye
E-mail: ceyda-beray82@hotmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 02 Feb 2023 ***Accepted:*** 03 Apr 2023 ***Available online:*** 04 Apr 2023

sedimentation rate revealed with 70 mm/hour, beta-2 microglobulin level was 4.01 mcg/mL. Tumor markers such as CA19-9, AFP and CEA were unremarkable. Patients serological tests was seronegative for HCV and human immunodeficiency virus but was seropositive for HBsAg, Anti-HBs, Anti-HBc IgG. HBV DNA was: 52I U/mL (1 IU/mL=4.5 copies/mL) and HBe antigen was negative. The patient was considered as HBV carrier according to normal liver function tests and absence of liver failure clinic features. Indirect hemagglutination (IHA) test for cyst hydatid was performed and found 1/2560 positive.

No malignant lesion was observed in esophagogastroduodenoscopy and colonoscopy. Abdominal ultrasonography (USG) showed a 4.5 cm hypoechoic homogeneous mass in between segment 4 and 8. As imagining magnetic resonance imaging (MRI) and 18F-fluorodeoxyglucose (FDG)-positron emission tomography-computed tomography (PET-CT) were performed. In the MRI a 44mm sized with T1 hypo intensity and T2 hyper intensity round mass located in the right anterior segment of liver was observed. PET-CT revealed a sole 4 cm sized mass with high 18 F-FDG uptake (SUVmax 6.1) in liver segment 8 (Figure 1).

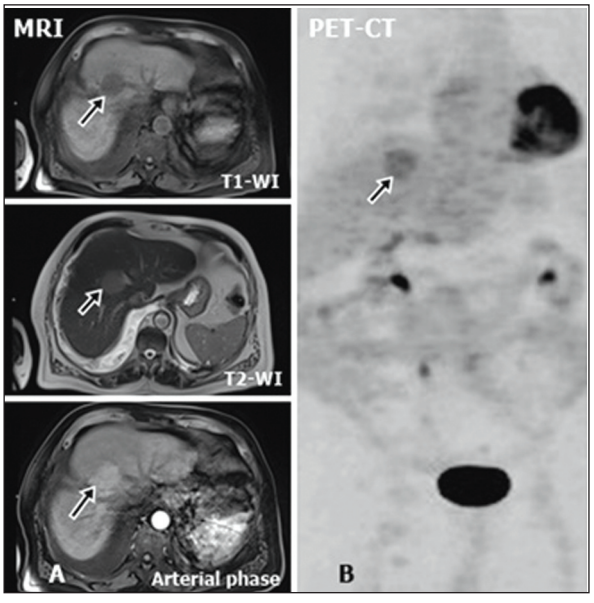

FIGURE 1: The magnetic resonance imagining shows a hypo intense in T1 and T2 and arterial enhancing mass lesion in the eight segment of liver (arrows). (b) The PET CT shows hyper metabolic mass at the same location as MRI with maximum standardized uptake value 6.1 (arrow).
PET-CT: Positron emission tomography-computed tomography; MRI: Magnetic resonance imaging.

Liver specimen obtained by percutaneous USG-guided core biopsy showed that in the neoplastic area there were 45-50% infiltration of small atypical lymphoid cells with narrow cytoplasm and 10-15% plasma cells monotypic for kappa. In the immunohistochemistry studies neoplastic lymphoid cells showed irregular nuclear contour with dense chromatin, and moderately abundant pale cytoplasm, all of which were supporting malignant lymphoma involvement. These cells were CD20+, CD79A+, CD10-, CD5-, BCL1-, BCL6- and BCL2+, were showing a Ki-67 labeling index of 25%. Pancytokeratin staining was negative in the neoplastic area. Non-tumoral parenchymal liver tissue was consistent with normal liver histological features without fibrosis. Based on the immune-pathologic features and imagining studies, the patient was diagnosed with Ann Arbor stage IE primary hepatic MALT lymphoma. The patient was scheduled to receive rituximab, cyclophosphamide, vincristine and prednisolone (R-CVP) chemotherapy. Standard doses were 25% reduced considering patient's older age. Oral tenofovir alafenamide was started to prevent HBV reactivation. He completed the treatment without complication and achieved complete metabolic response which was confirmed via PET-CT imaging. Owing to concerns about possible drug interactions albendazole treatment for HD was initiated after lymphoma treatment completion. Three cycles of oral albendazole 400 mg twice daily were given. Control IHA value was measured as the same level as before therapy. No mass in favor of recurrence was detected in the USG at the first year after chemo-immuno therapy. Informed consent was obtained from the patient in this report.

DISCUSSION

Primary hepatic extranodal MALT lymphoma is an extremely rare subtype of MALT lymphomas.[4] Via chronic antigenic stimulation; infections like *Borrelia burgdorferi* for skin, *Helicobacter pylori* for gastric, *Campylobacter jejuni* for small intestine, *Chlamydophila psittaci* for ocular adnexa and *Achromobacter xylosoxidans* for lung and also longstanding inflammation are important etiologic factors of MALT lymphoma development.

Primary hepatic MALT lymphoma pathogenesis is still unclear and given the rare incidence only case reports and literature reviews provide limited data.[5-9] HBV virus and HCV infections, alcoholic liver disease, non-alcoholic steatohepatitis, primary biliary cholangitis (PBC) and autoimmune hepatitis have been reported to be associated with hepatic MALT lymphoma.[5-8] Xie et al. reported the collective data of 47 primary hepatic MALT lymphoma cases in the literature. In their report 26 of 47 patients had concomitant liver diseases including HBV in 11, HCV in 7, PBC in 2, hepatocellular carcinoma in 2 and other liver diseases in 4 patients.[5] Our patient had HBV carrier state without active liver disease. Tenofovir alafenamide was started to prevent HBV reactivation as the planned R-CVP therapy protocol contained rituximab and prednisolone.

Our case had a history of surgery for liver cyst HD presenting with a sole hepatic cystic lesion. Positivity of IHA test was supporting the past *Echinococcus* infection. HD is an infection of the larval stages of taeniid cestodes of the genus *Echinococcus.* Most common sites of Echinococcal cysts are liver (>65%) then lungs (20%). The diagnosis is made by imagining studies and serological tests most commonly with IHA assay which detects antibodies against *Echinococcus granulosus.*[10] Even after surgical excision of the cyst or proper medication antibody titer may remain positive for years.[11] Hence, differentiation of past inactive disease from present active disease is challenging with existing serologic assays. Based on this we gave 3 cycles of albendazole treatment to our patient. However pre and post-therapy IHA titers resulted with same levels.

To our knowledge, only one case report representing MALT lymphoma and Echinococcosis is present in the literature which is by Göya et al. reporting the co-occurrence of pulmonary hydatid cyst and primary pulmonary MALT lymphoma.[12] However primary hepatic MALT lymphoma with HD has not been reported yet. In our case even if it is not possible to attribute Echinococcal infection as the sole etiological reason of MALT lymphoma considering the HBV coexistence, here we aimed to emphasize the probable causative role of Echinococcal infection in the development of primary hepatic MALT lymphoma.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ceyda Aslan;* ***Design:*** *Esra Terzi Demirsoy;* ***Control/Supervision:*** *Ceyda Aslan;* ***Data Collection and/or Processing:*** *Mehmet Aslan;* ***Analysis and/or Interpretation:*** *Esra Terzi Demirsoy;* ***Literature Review:*** *Gökhan Dindar;* ***Writing the Article:*** *Ceyda Aslan;* ***Critical Review:*** *Gökhan Dindar;* ***References and Fundings:*** *Mehmet Aslan;* ***Materials:*** *Mehmet Aslan.*

REFERENCES

1. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IBO, Berti E, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(7): 1720-48. [PubMed] [PMC]
2. Schreuder MI, van den Brand M, Hebeda KM, Groenen PJTA, van Krieken JH, Scheijen B. Novel developments in the pathogenesis and diagnosis of extranodal marginal zone lymphoma. J Hematop. 2017;10(3-4):91-107. [Crossref] [PubMed] [PMC]
3. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer. 1972;29(1):252-60. [PubMed]
4. El-Fattah MA. Non-Hodgkin lymphoma of the liver: A US population-based analysis. J Clin Transl Hepatol. 2017;5(2):83-91. [PubMed] [PMC]
5. Xie H, Lv J, Ji Y, Du X, Yang X. Primary hepatic mucosa-associated lymphoid tissue lymphoma: a case report and literature review. Medicine (Baltimore). 2019;98(13):e15034. [Crossref] [PubMed] [PMC]
6. Yamashita Y, Joshita S, Kobayashi H, Wakabayashi SI, Sugiura A, Yamazaki T, et al. Primary hepatic extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue in a patient with chronic hepatitis B virus infection: case report and summary of the literature. Medicina (Kaunas). 2021;57(3):280. [Crossref] [PubMed] [PMC]
7. Choi S, Kim JH, Kim K, Kim M, Choi HJ, Kim YM, et al. Primary hepatic extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue. J Pathol Transl Med. 2020;54(4):340-5. [Crossref] [PubMed] [PMC]
8. Dong S, Chen L, Chen Y, Chen X. Primary hepatic extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type: a case report and literature review. Medicine (Baltimore). 2017;96(13):e6305. [Crossref] [PubMed] [PMC]
9. Fu Z, Wu L, Chen J, Zheng Q, Li P, Zhang L, et al. Primary hepatic mucosa-associated lymphoid tissue lymphoma: case report and literature review. Int J Clin Exp Pathol. 2021;14(3):375-82. [PubMed] [PMC]
10. Guidelines for treatment of cystic and alveolar echinococcosis in humans. WHO Informal Working Group on Echinococcosis. Bull World Health Organ. 1996;74(3):231-42. [PubMed] [PMC]
11. Riganò R, Ioppolo S, Ortona E, Margutti P, Profumo E, Ali MD, et al. Long-term serological evaluation of patients with cystic echinococcosis treated with benzimidazole carbamates. Clin Exp Immunol. 2002;129(3):485-92. [Crossref] [PubMed] [PMC]
12. Göya C, Hamidi C, Cetinçakmak MG, Hattapoğlu S, Teke M. Primary pulmonary mucosa-associated lymphoid tissue lymphoma accompanied by a hydatid cyst. Respir Care. 2014;59(11):e186-9. [Crossref] [PubMed]