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PRIMARY NON-HODGKIN LYMPHOMA OF LIVER: AN UNUSUAL PRESENTATION AND REVIEW OF ITS MANAGEMENT.

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Abstract: Primary Non-Hodgkin lymphoma (NHL) of liver is a very rare malignancy. Here, we report a case of 26 years old man who presented with right upper abdomen pain and lump, reduced appetite and progressive weakness of 4 month's duration. Liver functions were deranged but serology was negative for viral markers and α Fetoprotein was within normal range. Ultrasonography and Computed Tomography scan of the abdomen revealed large nodule in right lobe of the liver. USG guided biopsy of liver mass and fluorescence in situ hybridization for CD markers established diagnosis of primary NHL of liver. Extensive investigations including X-ray of chest, whole-body positron-emission tomography scan and bone marrow biopsy showed no involvement of mediastinum, spleen, bone marrow or any other organ or lymph nodes significantly. Having B symptoms disease was staged IV_B, the patient has been treated with 6 cycles of R-CHOP regimen (Rituximab/ Cyclophosphamide – Doxorubicin – Vincristine – Prednisolone) followed by 2 courses of CHOP every three weekly. Response has been excellent and patient is asymptomatic as of now. This case highlights that primary hepatic lymphoma should be considered in the differential diagnosis of space-occupying liver lesions in presence of normal levels of alpha-fetoprotein.

INTRODUCTION

Primary hepatic lymphoma (PHL) is a very rare malignancy.¹ Although the liver contains lymphoid tissue, host factors may make the liver a poor environment for the development of malignant lymphoma.² Here, we present an interesting case of primary non-Hodgkin lymphoma (NHL) of liver. A literature review of clinical features, diagnosis, and management is also provided.

CASE REPORT

This 26 years old man presented to Radiotherapy OPD in August 2013 with right upper abdomen pain and lump, reduced appetite and progressive weakness of 4 month's duration. Patient had occasional fever, night sweats vomiting constipation and weight loss.

The patient's history was also suggested association with lethargy, sleepiness and itching.

Current medications included analgesics, appetizers, liver tonics/ supplements, multivitamins and antacids.

Physical examination was remarkable. Per abdomen examination revealed enlarged, firm and non tender liver spanning in right hypochondriac and epigastric region. Spleen was normal in size.

Blood tests revealed normal counts. Alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and lactate dehydrogenase (LDH) were elevated. Levels of serum alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) were within normal limits. Serology was negative for HIV, hepatitis C (HCV) and hepatitis B (HBV) viruses. Serum calcium was within normal limits.

USG findings (Figure 1) were suggestive of solid mass lesions in the anterior segment of the right lobe and medial segment of the left lobe of liver, largest being 147×127×97 mm³.



Figure 1

CT scan (Figure 2 a, b) of abdomen confirmed irregular hypodense enhancing space occupying lesions in both lobes of the liver; most likely neoplastic. The pancreas, spleen, and biliary tract were normal.

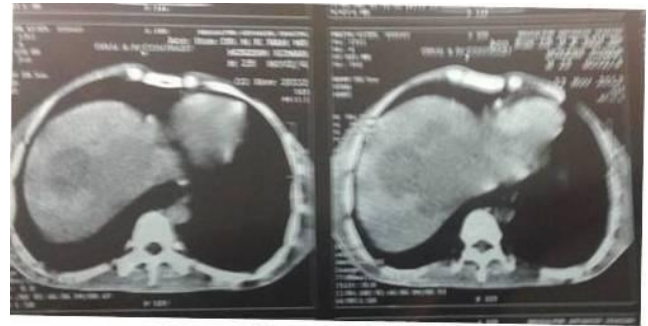


Figure 2 (a)

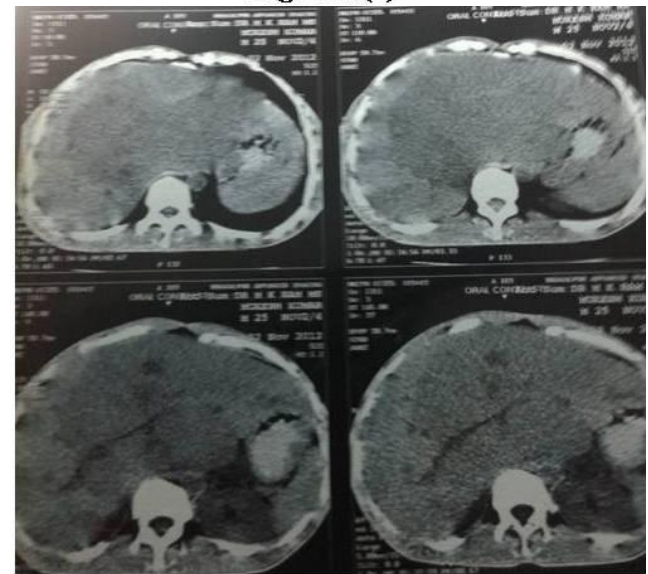


Figure 2 (b)

Chest Radiograph (Figure 3) revealed no mediastinal lymphadenopathy.



Figure 3

Positron-emission tomography (Figure 4) showed hyper-metabolic activity in a single lesion present in the right lobe of the liver.



Figure 4

Histological examination (Figure 5) after ultrasound-guided biopsy of the lesion showed diffuse infiltrates and small-to-intermediate atypical cells. IHC of the tumor cells showed positivity for CD20 & LCA.

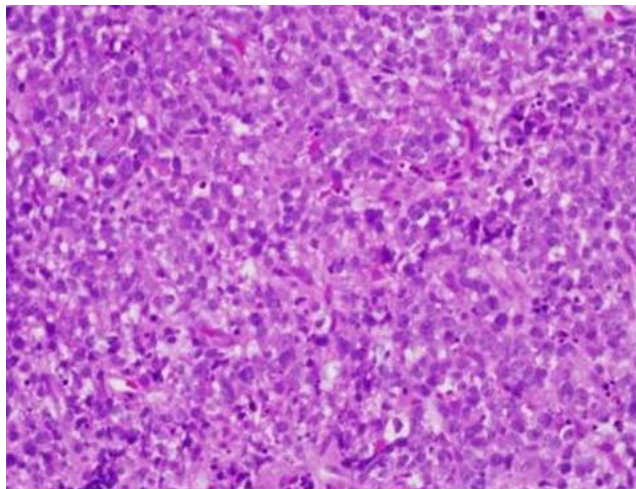


Figure 5

Bone marrow biopsy showed normal cellularity and was free from NHL infiltration. Histological and immunophenotypic evidence of B-cell lymphoma was present.

The patient was diagnosed with primary large B-cell lymphoma (NHL), Stage IV_B of liver. Patient received 6 cycles chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, Prednisone and Rituximab (RCHOP regimen) followed by 2 courses of CHOP only. Patient is on regular follow up and yet shows complete clinical and radiological response and is free from disease symptoms.

DISCUSSION

Primary hepatic non-hodgkin lymphoma (PHNHL) is defined as lymphoma which is either confined to liver or having major liver involvement.³ It represents less than 1% of all extranodal lymphomas.⁴

The exact etiology of PHL is still unknown; however some viruses have been established as causative agents such as HBV, HCV, and Epstein-Barr virus.³ A strong association appears between primary hepatic NHL and HCV.⁵ Hepatitis C is found in 40%–60% of patients with PHL.⁴ Role of HCV, cirrhosis, and therapeutic interferon as causative agents of lymphoma remain a hypothetical possibility⁶; however, this patient was not positive for HCV or HBV.

Primary hepatic lymphoma is two times commoner in men than of women, and the usual age of presentation is about 50 years.³ Presentations vary from incidental discovery of hepatic abnormalities in otherwise asymptomatic patients, to onset of fulminant hepatic failure with rapid progression of encephalopathy to coma and death.⁵ Symptoms are usually nonspecific and vague, with most patients reporting right upper quadrant and epigastric pain and tightness, fatigue, weight loss, fever, anorexia, and nausea. Hepatomegaly is frequent, and jaundice is an occasional finding at physical examination.¹

Based on liver infiltration, PHL can be subdivided into nodular or diffuse types.¹ The pattern of liver infiltration has no prognostic value.⁴ Similarly, the disease may be of either T- or B-cell origin.¹ Most PHL corresponds to a larger cell type and demonstrates a B-cell immunophenotype.⁶ Other histological subtypes of PHL include high-grade tumors (lymphoblastic and Burkett lymphoma, 17%), follicular lymphoma (4%), diffuse histiocytic lymphoma (5%), lymphoma of the mucosa-associated lymphoid tissue type, anaplastic large-cell lymphoma, mantle cell lymphoma, and T-cell-rich B-cell lymphoma.⁷

Patients with PHL characteristically have abnormal liver function tests, with elevated LDH and ALP.⁴ Elevated LDH, with normal AFP and CEA remains an important biologic feature⁶; but in this case, all three markers were negative.

PHL lesions on ultrasonography are hypo-echoic relative to normal liver. CT imaging shows hypo-attenuating lesions and rim enhancement after contrast. Findings on MRI are variable.⁸

Liver biopsy remains the most valuable and specific tool for diagnosis of PHL. If a discrete mass is not visible on imaging for percutaneous liver biopsy (PLB), the transjugular approach may be tried. A recent review indicated that transjugular liver biopsy can be used to obtain adequate tissue samples with similar complications and mortality rates with PLB.³

For PHL diagnosis, tumor must be limited to liver, without involvement of spleen, lymph nodes, bone marrow, or other lymphoid structures.⁷

Almost all patients are treated with chemotherapy, except some physicians practicing a multimodality approach i.e. surgery and radiotherapy.¹⁰

The standard treatment for patients with diffuse large B-cell lymphoma is chemotherapy with CHOP regimen. The addition of Rituximab, a chimeric mouse–human monoclonal antibody targeting the pan-B-cell antigenic marker CD20 to the CHOP regimen augments the complete response rate and prolongs event-free and overall survival in elderly patients with diffuse large B-cell lymphoma, without a clinically increase in toxicity.^{11,12}

Poor prognostic features include advanced age, constitutional symptoms, bulky disease, unfavorable histological subtype, elevated levels of LDH and β_2 -microglobulin, a high proliferation rate, cirrhosis and co-morbid condition of patient.

CONCLUSIONS

Primary hepatic lymphoma should be considered in the differential diagnosis in a patient with space occupying liver lesions and normal levels of alpha-fetoprotein (AFP) and CEA. If the clinical picture is suspicious for PHL, a liver core biopsy should be obtained, because the disease is treatable, and with new therapeutic drugs such as Rituximab a monoclonal antibody, overall survival has improved.

REFERENCES

1. Cameron AM, Truty J, Truell J, et al. Fulminant hepatic failure from primary hepatic lymphoma: successful treatment with orthotopic liver transplantation and chemotherapy. *Transplantation* 2005; 80:993-6.
2. Ryan J, Straus DJ, Lange C, et al. Primary lymphoma of the liver. *Cancer* 1988;61:370-5.
3. Haider FS, Smith R, Khan S. Primary hepatic lymphoma presenting as fulminant hepatic failure with hyperferritinemia: a case report. *J Med Case Reports* 2008; 2:279.
4. Agmon-Levin N, Berger I, Shtalrid M, Schlanger H, Sthoeger ZM. Primary hepatic lymphoma: a case report and review of the literature. *Age Ageing* 2004; 33:637-40.

5. Salmon JS, Thompson MA, Arildsen RC, Greer JP. Non-Hodgkin's lymphoma involving the liver: clinical and therapeutic considerations. *Clin Lymphoma Myeloma* 2006; 6:273-80.
6. Bauduer F, Marty F, Gemain MC, Dulubac E, Bordahandy R. Primary non-Hodgkin's lymphoma of the liver in a patient with hepatitis B, C, hiv infections. *Am J Hematol* 1997; 54:265.
7. Page RD, Romaguera JE, Osborne B, et al. Primary hepatic lymphoma: favorable outcome after combination chemotherapy. *Cancer* 2001; 92:2023-9.
8. Maher MM, McDermott SR, Fenlon HM, et al. Imaging primary non-Hodgkin's lymphoma of the liver. *Clin Radiol* 2001; 56:295-301.
9. Coenegrachts K, Vanbeckevoort D, Deraedt K, Van Steenberghe W. MRI findings in primary non-Hodgkin's lymphoma of the liver. *JBR-BTR* 2005; 88:17-9.
10. Noronha V, Shafi NQ, Obando JA, Kummar S. Primary non-Hodgkin's lymphoma of the liver. *Crit Rev Oncol Hematol* 2005; 53:199-207.
11. Winter MC, Hancock BW. Ten years of Rituximab in NHL. *Expert Opin Drug Saf* 2009; 8:223-35.
12. Coiffier B, Lepage E, Briere J, et al. chop chemotherapy plus rituximab compared with chop alone in elderly patients with diffuse large-B-cell lymphoma. *N Engl J Med* 2002; 346:235-42.
13. Marcus R, Hagenbeek A. The therapeutic use of Rituximab in non-Hodgkin's lymphoma. *Eur J Haematol Suppl* 2007; (67):514.

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