Primary Liver Sinusoidal Non-Hodgkin's Lymphoma Presenting as Acute Liver Failure

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We describe a case of a middle-aged woman, who presented to us with fever, anorexia, abdominal distension from a massive hepatomegaly, low hemoglobin, and acute liver failure. A liver biopsy revealed B cell non-Hodgkin's lymphoma predominantly in the sinusoids with CD10, CD20, and Bcl-2 positive on immunohistochemistry. She initially responded well to chemotherapy but succumbed 6 months later to the recurrence of disease. Sinusoidal non-Hodgkin's lymphoma of the liver should be considered in the differential diagnosis of a patient with large hepatomegaly presenting with acute liver failure. (J CLIN EXP HEPATOL 2015;5:341–343)

Malignancies of the liver are known to rarely cause acute liver failure.^{1,2} We describe a rare primary malignancy of the liver presenting with acute liver failure.

A 53-year-old housewife presented with history of fever, anorexia, and abdominal distension of 2 weeks duration. She was well prior to the onset of these symptoms. She gave history of being treated for carcinoma breast (infiltrating ductal carcinoma of the breast) five years back with surgery (modified radical mastectomy) and chemotherapy (Paclitaxel-based regimen with Tamoxifen). She denied any chest pain, abdominal pain, vomiting, and diarrhea, blood in stools, night sweats and weight loss. Clinically she had pallor and massive firm hepatomegaly, palpable up to the right iliac fossa. There was no evidence of lymphadenopathy or stigmata of chronic liver disease.

Her complete blood count showed hemoglobin of 5.6 g %, WBC count of 4970/cmm and platelet count of 1,70,000/mm. Her liver profile showed bilirubin of 2.5 mg/dl, ALT and AST of 165 and 186 U/L respectively, alkaline phosphatase of 217 U/L (normal range 30–150), serum albumin of 3.8 g/dl, INR of 1.7 with normal creatinine and serum electrolytes. Her HBsAg, anti-HCV,

anti-EBV IgM and HIV serology were negative. Serum AFP was normal. Contrast enhanced computed tomography (CT) showed massive hepatomegaly with no focal lesions, splenomegaly with minimal bilateral pleural effusion and minimal fluid in the pelvis.

On the second day of admission, she developed altered sensorium and drowsiness with high arterial ammonia of 140 μ mol/L (normal range 9–33).

A percutaneous liver biopsy was performed under cover of fresh frozen plasma. Her liver biopsy revealed hepatic sinusoidal B cell non-Hodgkin's lymphoma, which on immunochemistry showed CD10 and CD20 positivity (implying lymphocyte germinal center origin) and Bcl 2 positivity (implying B cell origin) (Figures 1–3). The cyto keratin (CK) marker on immunohistochemistry was negative thereby ruling out metastases from the previous breast cancer. Bone marrow aspiration did not show any involvement by the lymphoma.

She received cyclophosphamide, adriamycin, vincristine, and prednisolone (CHOP) regimen with supportive care including anti-coma measures, hydration and blood products. Within 48 h of initiation of treatment, she showed improvement in sensorium and regression of liver span by 5 cm. She had a drop in her leukocyte count after 5 days, which recovered with administration of growth factors. PET CT done 4 days later showed no evidence of disease activity with reduction in liver size. She was given 6 cycles of chemotherapy, which she tolerated well. She however presented 6 months later with recurrence of disease in the bone marrow in the form of pancytopenia to which she succumbed, as the family were not keen on any further chemotherapy.

DISCUSSION

Non-Hodgkin's lymphoma primarily involving the liver is a rare malignancy and constitutes about 0.016% of all cases of primary NHL.³ Liver involvement in non-Hodgkin's

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Abbreviations: AFP: alpha feto protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; Bcl 2: B cell lymphoma 2; CD: cluster differentiation; CECT: contrast enhanced computed tomography; CHOP: cyclophosphamide hydroxydaunorubicin (adriamycin) oncovin (vincristine) prednisolone; CK: cyto keratin; HBsAg: hepatitis B surface antigen; HCV: hepatitis C virus; HIV: human immunodeficiency virus; IgM: immunoglobulin M; NHL: non-Hodgkins lymphoma; PET CT: positron emission tomography-computed tomography; WBC: white blood cells
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Figure 1 The neoplastic lymphoid cells infiltrating the sinusoids of liver (arrows pointing sinusoids). [H&E, 20X].

lymphoma is more often secondary with its involvement usually seen in the late stages. Primary liver involvement represents <1% of all extra nodal lymphomas. Fewer than 100 cases have been reported.⁴⁻⁶ Liver contains lymphoid tissue but host factors may make the liver a poor environment for the development of malignant lymphomas.⁷

Primary non-Hodgkin's lymphoma of the liver usually presents in the elderly population in their fifties as was in our patient but with twice higher incidence in males than females.⁸

Hepatitis B, Hepatitis C, and Epstein Barr viruses have been implicated as probable causes, though our patient was negative for these viral markers. There appears to be a strong association between primary hepatic NHL and hepatitis C virus infection^{9,10} with hepatitis C being implicated in 40-60% of patients with primary hepatic lymphoma.⁸ Most lymphomas arise from lymphocytes in the liver parenchyma. However, the site of the lymphoma was predominantly the sinusoids in our patient, which

Figure 2 The neoplastic lymphoid cells are large and mitotically active (arrows pointing mitoses). [H&E, 40X].

Figure 3 The neoplastic lymphoid cells expressing a pan-B cell marker CD20 on immunohistochemistry. [IHC, 20X].

made it a very rare case and has not been previously described in literature. Majority of NHL lymphomas have B-cell immunophenotype of large cell type, as was found in our case too.¹¹

The presentation of primary NHL of the liver is right quadrant pain, fatigue, anorexia, weight loss and nausea. Our patient was mainly symptomatic from her hepatomegaly and anemia. Jaundice is an occasional finding at physical examination but hepatomegaly is seen in most of the cases including ours, which was massive.¹²

Our patient did not have any focal lesions but a diffuse liver involvement thereby making the diagnosis more difficult.

Liver biopsy remains the most valuable tool for diagnosis as was seen in our case, where the diagnosis was clinched with the histopathology and immunohistochemistry, which not only helped in clinching the diagnosis of a lymphoma but also ruled recurrent breast carcinoma.

The treatment primarily consists of chemotherapy with CHOP regimen but nowadays combination chemotherapy with addition of Rituximab a monoclonal antibody against CD20 is being used with increased remission rates, less side effects, and less relapse rates.¹³ Our patient was not given Rituximab though CD20 positive due to cost constraints. She responded well to chemotherapy initially and was asymptomatic with normalization of her liver profile.

Our case reiterates the fact that when a patient with a large hepatomegaly presents with acute liver failure, an infiltrative disorder like a lymphoma should be considered. Also, this is the first description of a primary non-Hodgkin's lymphoma of the liver arising predominantly in the sinusoids of the liver and presenting as acute liver failure.

CONFLICTS OF INTEREST

The authors have none to declare.

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