CASE REPORT

Primary T-cell lymphoma of liver

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SUMMARY

Primary hepatic lymphoma (PHL) is rare and represents approximately 0.016% of all cases of non-Hodgkin's lymphoma (NHL). The majority of these are B-cell NHL of diffuse large B-cell type. Primary T-cell lymphoma constitutes approximately 5–10% of all PHLs arising in the liver, 90% being B-cell type. Peripheral T-cell lymphoma, $\gamma\delta$ hepatosplenic T-cell lymphoma and $\alpha\beta$ hepatosplenic T-cell lymphoma are the common T-cell lymphomas involving hepatic parenchyma. We encountered a case presenting with gross hepatomegaly extending beyond umbilicus, mild ascites, pedal oedema, icterus and dyspnoea. Haemogram showed moderate anaemia with counts. Bone marrow aspiration showed erythroid hyperplasia with dimorphic anaemia. There was no evidence of atypical lymphoid cells in peripheral blood of bone marrow. We present a rare case of primary T-cell lymphoma presenting as primary liver involvement without splenomegaly, lymphadenopathy, bone marrow or peripheral blood involvement.

BACKGROUND

Primary T-cell lymphoma is rare, and few cases have been reported in the literature, particularly from the Indian Subcontinent. Early diagnosis can be made by high suspicion index and by simple screening methods such as fine needle aspiration cytology and serological tests. Primary T-cell lymphoma carries a poor response to therapy, but in our case the patient is in progression-free survival for the last year.

CASE PRESENTATION

A 40-year-old woman, belonging to a low socio-economic group, presented with progressive distension of abdomen primarily in the right hypochondrium for 1 month duration, and for the previous week she had developed progressive icterus, dyspnoea and pedal oedema. She also had mild pain over her right hypochondrium. She had no fever, night sweats, bony pain, bleeding from any site, malaena, altered bowel habits, cough, haemoptysis or nodular swelling elsewhere in body.

On examination, she was looking ill and dyspnoeic. She had massive hepatomegaly which was tender and extended beyond umbilicus. Also, she had mild ascites and pedal oedema. There were no splenomegaly, lymphadenopathy, any other palpable organomegaly or skin lesions. She did not have any significant/relevant medical or family history.

INVESTIGATIONS

Her complete blood count showed haemoglobin of 10.4 g/dl, total leucocyte count of 9000/mm³ with granulocytes constituting 65%. Platelets were 2.5×10^5 /mm³. General blood picture and bone

marrow aspiration/biopsy showed no atypical lymphocytes or infiltration. Her biochemical investigations revealed progressive jaundice (bilirubin went up to 6.7 mg/dl), alanine transaminase 98 IU/l, aspartate aminotransferase 258 IU/l, serum alkaline phosphatase 2513 IU/l and serum lactate dehydrogenase (S-LDH) 688 IU/dl. Serum protein was found to be 4.5 g/dl with albumin being 2.4 g/dl. Serum uric acid was raised to 7.2 mg/dl. α -Fetoprotein was found to be 0.68 ng/ml (normal value <10 ng/ml).

Her viral profile of hepatitis A virus, hepatitis B virus (HBV) and hepatitis C virus (HCV) was negative. There was no contributory evidence of autoimmune hepatitis. Fine needle aspiration of the mass showed sheets of atypical lymphoid cells with moderate pleomorphism (figure 1). There were few small clusters of hepatocytes, showing fatty changes, interspersed within these atypical lymphoid cells. A provisional diagnosis of lymphoma was established. Thorough search for evidence of lymphadenopathy was made both clinically and by imaging studies. Contrast-enhanced CT and plain CT of whole abdomen and thorax showed gross hepatomegaly measuring upto 30 cm in size with well-preserved hepatic architecture, homogeneous parenchyma with normal homogeneous attenuation value. Spleen and lymphnodes were within normal limits.

Histopathological examination revealed disorganised architecture of liver parenchyma with diffuse infiltration of medium-sized round to oval cells mainly concentrating around the biliary ductules and infiltrating the sinusoids (figure 2). The hepatic cells show fatty changes and bile stasis. Immunohistochemistry showed positivity for CD 3, CD 5, T-cell (UCHL1) and it was negative for $\gamma\delta$ T-cell receptors ($\gamma\delta$ -TCRs) and $\alpha\beta$ TCR,

Figure 1 Fine needle aspiration from the liver mass showing pleomorphic lymphoid cells and centrally located hepatocytes showing fatty changes (Leishman-Giemsa $\times 40$).

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Figure 2 Histopathological section showing effaced architecture of liver by diffuse infiltration of pleomorphic lymphoid cells (H&E ×40).

CD20, CD 23, CD 10, CD 30, CD7, CD 56, Bcl2 and cyclin D1 (figures 3 and 4).

DIFFERENTIAL DIAGNOSIS

Hepatocellular carcinoma, metastatic adenocarcinoma to liver and lymphoma of liver were considered.

TREATMENT

The patient was treated with eight cycles of cyclophosphamide, doxorubicin, oncovin (vincristine), prednisolone (CHOP) regimen and has been in progression-free survival for the last 12 months of follow-up.

DISCUSSION

The liver is a common site for malignant lesions of both primary and secondary malignancies. Among the primary lesions, the incidence of hepatocellular carcinoma is increasing, first, because of increasing incidence of HCV/HBV infection and increasing life expectancy of these patients and, second, due to better imaging and diagnostic facilities. Liver parenchyma is an uncommon site for primary haematopoietic malignancies. Approximately 0.4% of all extranodal and 0.016% of all non-Hodgkin's lymphoma (NHL) arise primarily from the liver.^{1–3} These haematopoietic malignancies too are shown to affect HCV/HBV-infected or autoimmune hepatitis individuals and there are various studies establishing the role of HCV

Figure 3 Section from liver showing diffuse positivity for CD3 (IHC ×40).

Figure 4 Section of liver showing CD20 negativity by malignant lymphoid cells (IHC ×40).

infection in the development of primary NHL.⁴ Secondary lymphoma infiltrating the liver is common and as many as 21% of all advanced NHL involves liver parenchyma.

Primary hepatic lymphoma (PHL) is defined according to the Caccamo's criteria as lymphoma with only liver involvement at presentation and no spleen, lymph nodes, peripheral blood, bone marrow or other tissue involvement until at least 6 months after diagnosis.⁵ Majority of these NHLs are of diffuse large B-cell lymphoma.⁶

Clinically, the patient presents most commonly with hepatomegaly (75–100%), abdominal pain (39–70%), general malaise, night sweats, weight loss and occasionally fulminant hepatic failure. Liver function tests are abnormal in upto 70% of cases as was in our case. S-LDH and β 2 microglobulin (prognostic marker) are increased in 30–80% and 90% of times, respectively. There are no specific tumour markers for PHL, but normal levels of alpha foeto protein and carcino-embryonic antigen are found in almost 100% of patients, facilitating the differential diagnosis.

Hepatocellular carcinoma and metastases from gastrointestinal tract have a very similar clinical pattern, are much more common and should be excluded first. PHL may present as solitary liver mass (42%) or multiple focal lesions (50%); diffuse infiltration of the liver is rare in Caucasian (8%) and more common in Asian patients. Diagnosis of PHL requires a liver biopsy compatible with lymphoma and the absence of lymphoproliferative disease outside the liver. Because liver biopsy may not distinguish between PHL and poorly differentiated carcinoma, immunohistochemical typing and flow studies are almost always required. In some cases, a surgical biopsy might be required.

The prognosis of PHL is considered to be very poor with a median survival time of 15 months; however, it varies widely, ranging from 3 to 124 months,⁷ with median survival as low as 6 months for patients treated with chemotherapy alone, and longer for patients treated with a combination.⁸ The following factors have been associated with worse prognosis: massive liver infiltration/replacement, high index of proliferation, advanced age, elevated LDH levels, the presence of underlying liver cirrhosis and elevated levels of β 2-microglobulin.⁹

Stancu *et al* reviewed 14 cases of primary hepatic T-cell lymphoma, with 3 cases representing their own series and 11 previously reported cases. They reported that primary hepatic T-cell lymphoma has a poor prognosis and an aggressive clinical course.¹⁰ In the series reviewed by Miyashita *et al*,¹ 17 of 19

cases showed diffuse liver infiltration, while only the 2 remaining cases showed nodular involvement.

Learning points

- ▶ Primary T-cell lymphoma of liver is very rare, although secondary involvement of liver in lymphoma is very common.
- ▶ Primary T-cell lymphoma of liver can be very aggressive and require early diagnosis and therapeutic intervention.
- ▶ When treated early response may be better than reported in various studies.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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