

# Acute Liver Failure With Malignant Ascites: An Unusual Presentation Of Hepatosplenic T Cell Lymphoma.

S Chowdhury, R Chakraborty, B Seligman, T Bashir

## Citation

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## Abstract

Hepatosplenic T cell lymphoma is a rare neoplasm accounting for less than 1 percent of non-Hodgkin lymphomas. It most commonly presents in young men with a median age at diagnosis of 35 years. Ten to 20 percent of patients have a history of chronic immune suppression related to treatment for solid organ transplantation, lymphoma, or inflammatory bowel disease. Most patients with HSTCL present with marked hepatosplenomegaly and thrombocytopenia without lymphadenopathy. Liver involvement is usually characterized by infiltration of dilated sinusoids by atypical lymphoid cells, with portal tracts and hepatocytes generally remaining uninvolved. Our patient presented with severe obstructive jaundice, impending hepatic failure and malignant ascites. He was refractory to steroid and radiation and biliary stenting had to be performed for severe hyperbilirubinemia.

## INTRODUCTION

Hepatosplenic T cell lymphoma is a rare neoplasm accounting for less than 1 percent of non-Hodgkin lymphomas. It most commonly presents in young men with a median age at diagnosis of 35 years. Ten to 20 percent of patients have a history of chronic immune suppression related to treatment for solid organ transplantation, lymphoma, or inflammatory bowel disease. Most patients with HSTCL present with marked hepatosplenomegaly and thrombocytopenia without lymphadenopathy. Liver involvement is usually characterized by infiltration of dilated sinusoids by atypical lymphoid cells, with portal tracts and hepatocytes generally remaining uninvolved. Our patient presented with severe obstructive jaundice, impending hepatic failure and malignant ascites. He was refractory to steroid and radiation and biliary stenting had to be performed for severe hyperbilirubinemia.

## CASE REPORT

This is a 29 y/o male from Indonesia with no past medical history, who came with fever, weakness and cough with yellow sputum for a few days. He worked in a cruise ship and had initial evaluation done by a cruise ship physician. Review of systems was positive for jaundice, mild abdominal pain, diarrhea, loss of appetite and subjective weight loss since one month. On physical examination, there was conjunctival pallor, scleral icterus, dry oral mucosa,

crackles in bilateral lung bases, nontender hepatomegaly with distended abdomen and two small palpable left supraclavicular lymph nodes. Prior to admission in our hospital, patient was sent to another hospital by the cruise ship physician, where ultrasound of right upper quadrant of abdomen was done. A 7cm hepatic mass was revealed, which was drained with radiological guidance and minimal blood tinged fluid was obtained. Culture of the drained fluid was negative and screening for malaria, HIV, Hepatitis B and Dengue was also negative. The initial impression was hepatic abscess, either amoebic or bacterial. He was given metronidazole and levofloxacin and discharged subsequently.

Initial labs in our hospital showed grossly deranged hepatic function panel with alkaline phosphatase 649 U/L, AST 322 U/L, ALT 89U/L, GGT 398 U/L, LDH 1549U/L, total bilirubin 15.54 mg/dl, conjugated bilirubin 9.11 mg/dl and albumin of 1.7 g/dl. CBC was significant for pancytopenia with WBC of  $2.2 \times 10^9/l$ , Platelets of  $115 \times 10^9/l$  and RBC of  $4.45 \times 10^{12}/l$ . Hemoglobin was 10.6 g/dl and Prothrombin time was slightly prolonged at 15.3 seconds. In the interim, CT scan of chest, abdomen and pelvis was done which revealed bilateral multilobar atelectasis in lungs, large right and moderate left pleural effusions, a mass measuring 6.8 x 7.8 x 7.7 cm in the inferior right lobe of liver with a satellite lesion posterolateral to the mass, intrahepatic biliary dilatation, porta hepatis adenopathy, a round lesion

measuring 2.3 x 2.1 cm in the superior subcapsular aspect of spleen, retrocrural and retroperitoneal lymphadenopathy and large amount of ascitic fluid, predominantly in the pelvis(Figure 1).

Figure 1-CT scan of abdomen showing hypo dense lesion in liver.

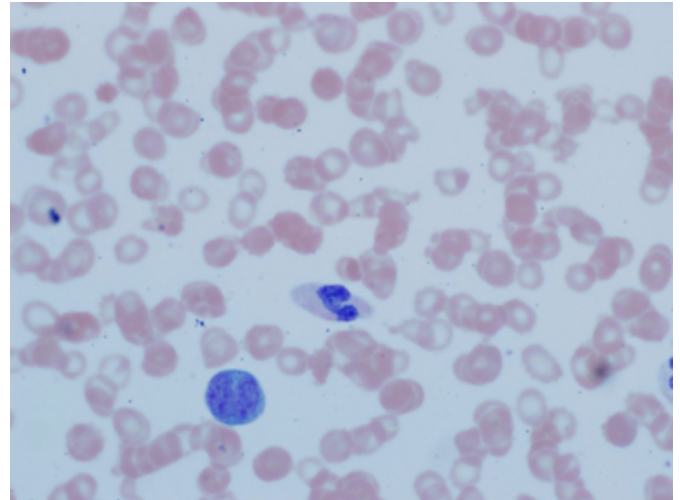
Based upon the radiologic findings, suspicion of metastatic tumor was very high. In the interim, a meticulous workup was also done to rule out an infectious etiology. Biopsy of liver lesions was postponed at this time due to deranged coagulation profile and ascites which implied a high risk of bleeding. Serological workup for Echinococcus, Histoplasma, E. histolytica, Cryptococcus, Leishmania, Leptospira, HTLV I/II and syphilis was negative. There was positive IgG antibody against EBV and CMV.

Subsequently, Thoracentesis was done and 700 ml of blood tinged yellow fluid was removed, which was exudative as per Light's criteria. Gram stain and culture was negative, acid fast bacilli were absent on special stains, culture for AFB was negative and fungal culture was negative. On cytopathology, some atypical cells were seen, origin of which was uncertain due to paucicellularity. Alpha fetoprotein in the serum was negative. He was also placed on broad spectrum antibiotic coverage with Ciprofloxacin, Vancomycin, Metronidazole and Piperacillin-tazobactam as he was neutropenic, febrile and infectious etiology was not entirely ruled out.

Hematology/Oncology service was consulted for increasing suspicion of malignancy. The peripheral blood smear was reviewed and it revealed an atypical lymphoid cell with high nucleocytoplasmic ratio and indented nuclear membrane (Figure 2).

### Figure 1

Figure 2-Peripheral smear showing immature lymphocytes with indented nucleus and high nucleocytoplasmic ratio.



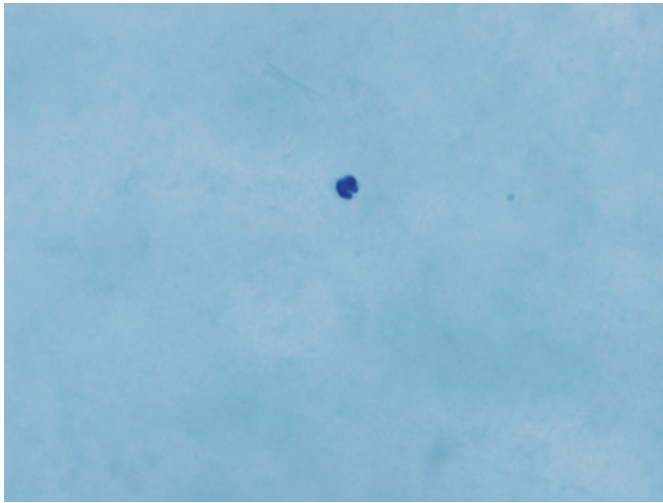
They performed a bone marrow aspiration and biopsy to investigate the cause of pancytopenia. Bone marrow aspirate slides revealed normal hematopoiesis. Bone marrow biopsy revealed hypercellular marrow with increased megakaryocytes, adequate maturation of erythroid and myeloid series, moderate to marked plasmacytosis, approximately 20-30%, increased reticulin fibers(3+), decreased iron, no evidence of tumor, granuloma, lymphoma, viral inclusions or parasites, with overall picture suggestive of hypersplenism and chronic inflammation.

On day 4 of hospital stay, it was decided to perform IR guided liver biopsy. However, after consultation with the gastroenterologist and interventional radiologist, plan was made to perform large volume paracentesis via pelvic catheter prior to biopsy for reducing the volume of ascitic fluid, which would reduce the risk of bleeding after liver biopsy. Abdominal paracentesis was done after administration of fresh frozen plasma and cryoprecipitate to reduce the risk of bleeding. The cytology of ascitic fluid(Figure 3) was reviewed which revealed large atypical cells with high nucleocytoplasmic ratio, indented nuclear membrane and scanty basophilic cytoplasm, which were very similar to the cells seen in peripheral smear of patients with hepatosplenic T cell lymphoma. Due to grossly abnormal liver chemistries, patient was not a candidate for chemotherapy at that time.

Figure 1-Ascitic fluid cytology showing immature lymphoid cells with indented nucleus and high nucleocytoplasmic ratio

**Figure 2**

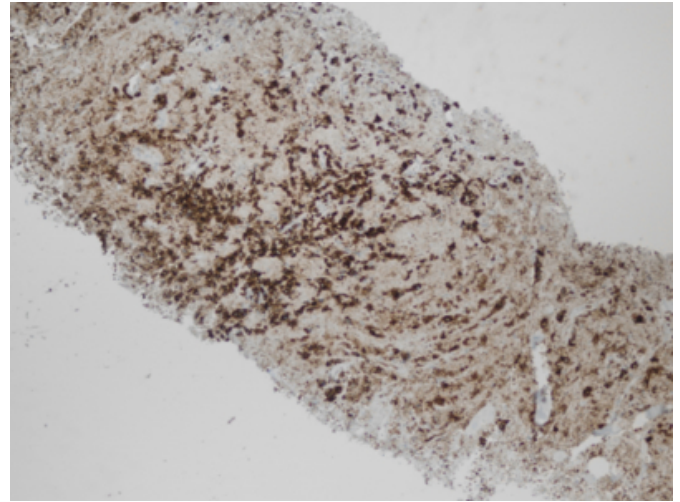
Figure 3-Ascitic fluid cytology showing immature lymphoid cells with indented nucleus and high nucleo cytoplasmic ratio



Finally, on day 6, CT guided liver biopsy was done for tissue diagnosis. After extensive discussion among multiple sub specialties involved in the care, consensus was to proceed with palliative radiation therapy to porta-hepatic region for ameliorating hyperbilirubinemia and jaundice. Meanwhile, the pathologist was called for a preliminary report of liver biopsy. Due to the presence of extensive necrotic tissue, it was difficult to distinguish between lymphoma and hepatoma. Immunostains were pending at this point. Palliative radiation therapy was started along with prednisone 100 mg daily and allopurinol 300 mg daily. However, he did not respond and after three treatments of radiation therapy to the porta hepatis region, LFTs continued to deteriorate with total bilirubin trending up to 25.3 mg/dl and conjugated bilirubin to 13.06 mg/dl. At this point, it was decided to perform surgical decompression of biliary tract by biliary stent placement for palliation of jaundice and patient was transferred to a higher center for ERCP and stenting of biliary tract. Subsequently, final report of liver biopsy was obtained. Tissue sample showed extensive necrotic tissue with atypical cells, positive for CD 45 and CD 3, negative for CD 20, PAX 5 and screening cytokeratins AE1/AE3, suggestive of malignant T cell lymphoma (Figure 4).

**Figure 3**

Figure 4-Immunostaining of liver biopsy specimen showing positivity for CD3



Our patient underwent ERCP with successful biliary stenting for palliation. Subsequently, he refused any further chemotherapy, after being explained the natural history of the disease and opted for comfort care.

## DISCUSSION

Hepatosplenic T cell lymphoma was first described in 1990 as an aggressive illness with B symptoms and organomegaly in young adult males (1) It has been described in patients with solid organ transplant and Crohn's disease (2). The median age is 29-35 years and patients have splenomegaly (98%), hepatomegaly (80%), minimal to no lymphadenopathy, anemia (84%) and severe thrombocytopenia (85%)(3, 4). In contrast to B-cell post-transplant lymphoproliferative disorder, Epstein Barr Virus can be detected in a minority of HSTL cases and may have a pathogenic role by stimulating and expanding  $\gamma$  T-cells(5). Antibodies against EBV were positive in the serum of our index case.

Hepatosplenic T cell lymphoma is usually a diagnostic challenge for clinicians. Apart from hepatosplenomegaly, anemia and thrombocytopenia, bone marrow involvement is almost constant at diagnosis(3,6) and circulating neoplastic lymphocytes are present in peripheral blood in 50-80% of cases(7). There has been one case report of autoimmune hemolytic anemia being associated with HSTCL (8). In our patient, bone marrow aspirate and biopsy did not show any evidence of disease and a diagnostic paracentesis showed classical neoplastic cells in ascitic fluid, which are usually seen in peripheral blood smear of these patients. The atypical lymphoid cells seen in the ascitic fluid of our patient had a

high nucleocytoplasmic ratio, indented nuclear membrane and scanty basophilic cytoplasm. To the best of our knowledge, malignant ascites has never been documented in literature in association with hepatosplenic T cell lymphoma. There has been one case report of this disorder being diagnosed by ultrasound guided FNAC of spleen in a 60 year old female patient presenting with fever and heaviness of left upper abdomen(9).

Various case series of HSTCL have revealed that the incidence of bone marrow involvement differs in different regions. A case series by Chang-li Lu et al in China found bone marrow involvement only in 53% of their patients, much lower than that cited in most literatures (10). Trepine biopsy commonly shows a hypercellular marrow with sinusoids containing variable amounts of tumoral cells, whose detection is greatly facilitated by immunohistochemical techniques. With progression, the pattern of bone-marrow involvement becomes increasingly interstitial and shows a shift toward larger blastic cells (11). Erythrophagocytosis is also not uncommon in bone marrow biopsy and there can be a full blown hemophagocytic syndrome in some cases.

Our patient also had pleural effusion, more on the right side with cytology showing some atypical cells, which could not be typed due to paucicellularity. It is possible that he might have developed capillary leak syndrome secondary to hypercytokinemia, giving rise to ascites and pleural effusion. Capillary leak syndrome has been shown to be associated with ALK+ anaplastic large cell lymphoma at diagnosis in a case report (12).

Abnormalities of liver function tests at presentation are usually present in half of the cases, with mild elevation of AST, ALT and Alkaline phosphatase and marked elevation of LDH. In our patient, Alkaline Phosphatase and GGT was significantly elevated with severe hyperbilirubinemia secondary to anatomic location of the tumor. The total bilirubin level trended up to 25 mg /dl despite steroids and radiotherapy and patient had to be transferred to a higher center for palliative biliary stenting. Since the patient had fever and diarrhea at presentation in the setting of extensive travel history, infectious etiology was high in the list of differential diagnosis initially. There has been one case report in the past of acute hepatic failure and death in a patient with new onset T cell lymphoma (13). Furthermore, our patient had supraclavicular lymphadenopathy, which is unusual in HSTCL.

Thus, our patient had an atypical presentation with acute hepatic failure secondary to obstruction of biliary tree, malignant ascites and absence of bone marrow involvement. Ascitic fluid cytology and peripheral blood smear were helpful in making a preliminary diagnosis, which was confirmed later by liver biopsy.

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**Author Information**

**Shahinur Chowdhury, MD**  
Queens Hospital Center

**Rajshekhar Chakraborty, MD**  
Queens Hospital Center

**Barbara Seligman, MD**  
Queens Hospital Center

**Tayyaba Bashir, MD**  
Queens Hospital Center