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**CASE REPORT**

# HODGKIN'S LYMPHOMA WITH ATYPICAL PRESENTATION-ONE CASE REPORT AND REVIEW OF LITERATURE

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**ABSTRACT**

A 20-year-old boy presenting daily febrile episodes was suspected to have developed acute hepatic failure. Serologic tests ruled out infectious and autoimmune causes apart from drug toxicity. During clinical examinations, he was found to have generalized enlarged lymph nodes that were then taken biopsy. It was diagnosed as classical Hodgkin's lymphoma based on histological examination of the lymph node. A bone marrow biopsy showed marrow infiltration by Hodgkin's lymphoma with hemophagocytosis and secondary myelofibrosis. A percutaneous liver biopsy demonstrated hepatic involvement of the same disease. After an extensive work-up, the cause of liver failure was figure out to be only attributed to the involvement of the lymphoma. Hodgkin's lymphoma as a cause of hepatic failure is rare and young patients diagnosed as Hodgkin's lymphoma causing hepatic failure has been reported very rarely so far.

**Keywords:** Hodgkin's disease, bone marrow, liver failure, acute.

## 1.INTRODUCTION

Hodgkin's disease, being a lymph node-based disease, is a type of lymphoma, which is a cancer originating from white blood cells called lymphocytes. It usually starts in an area within the lym-phatic system and is characterized by the orderly spread of disease from one lymph node group to another and by the development of systemic symptoms with advanced disease. Acute liver failure caused by hematological malignancies has been reported sporadically. Generally, in lymphoma, liver failure is a feature of end-stage disease. Thus, hepatic involvement usually occurs late in the course of Hodgkin's disease or with advanced-stage disease, but complicating acute liver failure is extremely rare. Previously, in most of the cases, the diagnosis was made upon autopsy only. This report describes a young patient with Hodgkin's disease presenting acute liver failure. This is a very uncommon form of Hodgkin's lymphoma, since acute liver failure was the presenting feature of the disease. To the best of current knowledge, such a case has been seldom described to date.

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## 2.CASE REPORT

A young man, 20 years of age, presented to the emergency department with high grade fever and jaundice. He had a history of intermittent low grade fever for the past 3 months prior to admission, and along with the fever, he had weakness, significant weight loss, anorexia, swelling of legs and face, and progressive jaundice lasting for 15 day. There were no other systemic symptoms. On examination, the patient was conscious and oriented, febrile (temperature 102-104$^{o}$F) and had moderate pallor, jaundice, generalized lymphadenopathy involving the cervical, axillary and inguinal lymph nodes on both sides. The lymph nodes detected were discrete, firm, non-tender, 1-2 cm in size. Mild hepatomegaly and moderate splenomegaly were detected but no evidence of coagulopathy or encephalopathy was found. Enquiry about the lymphadenopathy revealed that the patient had experienced slow progressive enlargement of the lymph nodes in his neck and groin over the past 3 months. He had no history of blood transfusion, jaundice, upper or lower gastrointestinal bleeding, or any surgical procedures or hospitalization. There was no history of alcohol or any other substance abuse or high risk sexual behavior.

Examination results on admission were as follows: hemoglobin 7.2 g/dL, TLC 5.2 × $10^{9}$/L, platelet count 100 ×

$10^9$/L, ESR 100, N84 L12 M4, prothrombin time 16.4 s (control 11.2 s), no malaria parasite being found, negative result of malaria double antigen tests, nothing found in blood and urine cultures, sodium 122 mmol/L, potassium 4.8 mmol/L, total bilirubin 9 mg/dL, conjugated bilirubin 6 mg/dl, ALT 80 U/L, AST 50 U/L, alkaline phosphatase 650 U/L, albumin 2.6 g/dL, globulin 3.0 g/dL, uric acid 2.0 mg/dL, LDH 1100 U/L, serum α-fetoprotein and carcino-embryonic antigen levels within normal limits. Serology for HIV and hepatitis A, B, C and E were negative. Serology for CMV and EBV were IgM and IgG negative. Serologic autoimmune markers like ANA and anti-mitochondrial antibody were negative. Abdominal ultrasound revealed mild hepatosplenomegaly along with multiple enlarged lymph nodes in periportal and peripancreatic regions, a solitary enlarged lymph node near the splenic hilum, mild ascites and normal common bile duct. A computer tomography (CT) scan showed intraabdominal enlarged lymph glands, without focal liver lesions. Chest X-ray findings were normal. Excision biopsy of cervical lymph node showed effacement of lymph node architecture, which was replaced by lymphocytes, histiocytes, plasma cells, mononuclear cells with prominent eosinophilic nucleoli (Hodgkin's cells), and multinucleated cells resembling Reed-Sternberg cells (Fig.1), therefore, the case was diagnosed as Hodgkin's lymphoma. Immunohistochemistry revealed the pattern of disease was consistent with classical Hodgkin's lymphoma with a high load of Reed-Sternberg cells ($CD30^+$, $CD15^+$, $LCA^-$, $CD20^-$, $CD3^-$) and a background rich in T cells.

The patient became afebrile after 7 days of intrave-nous antibiotic therapy, with a decrease in jaundice, but developed severe symptomatic pallor. Investigations re-vealed severe pancytopenia (hemoglobin 3.5 g/dL, TLC 1.0 × $10^9$/L, ANC 0.27 × $10^9$/L, platelets 20 × $10^9$/L) and deterioration of liver function [total bilirubin 8.6 mg/dL (conjugated bilirubin 5.4 mg/dL), ALT 162 U/L, AST 227 U/L, alkaline phosphatase 361 U/L]. He received concentrated RBC transfusion for correction of anemia. He was also found to develop altered sensorium and coagulopathy (prothrombin time prolongation > 4 s). A CT scan of the brain did not detect any abnormality. Supportive treatment consisting of fresh frozen plasma, platelets and red cell transfusion along with intravenous antibiotics resulted in improvement in his sensorium, but his jaundice progressed. The pancytopenia persisted for more than a week and the patient became febrile again. Bone marrow aspiration and trephine biopsy re-vealed polymorphic infiltrate, consisting of lymphoid cells, histiocytes, neutrophils, eosinophils, plasma cells, mononuclear giant cells and Reed-Sternberg cells (Fig.2), focal myelofibrosis (Fig.3), and hemophagocy-tosis. The overall features of the bone marrow detected were consistent with those of bone marrow infiltration by Hodgkin's lymphoma, which presented hemophago-cytosis and secondary myelofibrosis also. Liver biopsy showed infiltration of portal tracts by polymorphic cell population (Fig.4), consisting of lymphocytes, histio-cytes, plasma cells, and occasional Reed-Sternberg cells, and the histology suggested liver involvement by Hodgkin's lymphoma. In spite of intensive supportive management, the patient continued to deteriorate and died after 25 days of hospitalization.

## 3.DISCUSSION

An acute form of Hodgkin's disease, characterized by generalized lymph node involvement with clinically palpable nodes, by a short febrile course, and by fatal consequences has been well documented. In this group of patients, liver involvement is often found in post mor-tem examination. However, there are very few reports as to cases whose liver failure was the predominant clinical feature leading to death. Jackson and Parker,(1944) classi-fied Hodgkin's disease (HD), according to the increased severity of Hodgkin's disease, into 3 clinical and patho-logical types: paragranuloma, granuloma and sarcoma. Paragranuloma involving the internal organs is unusual. In granuloma, the liver is commonly infiltrated, but mas-sive enlargement of the liver is rare. Bile stasis resulting in jaundice is also unusual in these patients. In sarcoma, jaundice is never seen in this group. Liver involvement by HD usually occurs in the late course of the disease and primary presentation about liver involvement is very rare(Chim et al., 2000; Torneo et al., 1998). The most common causes of acute liver failure (ALF) are viral and toxin-induced hepatitis. Malignant infiltration of the liver by malignancies, such as cancer of lung, breast, melanoma, and others often leads to ALF. The most common underlying etiology of ALF is hematological malignancies, including leukemia, Hodg-kin's lymphoma, non-Hodgkin's lymphoma, malignant histiocytosis etc. However, it is undoubtedly unusual for ALF to be the initial clinical presentation of an underly-ing malignant disease(Torneo et al., 1998; Moral et al., 2001; Vardareli et al., 2004). Hepatic infiltration by hema-tological malignancies occurs in 15%-22% of the cases, but very rarely causes ALF(Morali et al., 2001). According to Goia, (1932), the enlarged liver commonly occurs in the late stages of malignant lymphogranulomatosis, usually slight, but in rare circumstances, it is massively increased in size. In both of the case studies reported by Goia,(1932) hepatomegaly was found presenting late in the course of a chronic ill-ness. Post-mortem in this case showed that diffuse liver infiltration by lymphomatous deposits was found, but there was no histological evidence of hepatic necrosis. This, however, is not unusual in acute hepatic failure, as, for example, Reye's syndrome(Mowat, 1979) or acute fatty liver of pregnancy(Sherlock,1981).

Lymphoma cells infiltrating into small intrahepatic bile channels may cause bile duct necrosis, obstruction of hepatic venules, and cholangitis. Vanishing bile duct syndrome is also a well known sequel of hepatic Hodg-kin's disease. On the other hand, tumor infiltration into hepatic parenchyma may lead to hepatocyte destruction and subsequently lead to ALF. After extensive infiltra-tion into the liver producing massive structural and functional decline hepatic failure and jaundice often ensue(Torneo et al., 1998; Moral et al., 2001; Vardareli et al., 2004). Berger and Lehman, (1941) reported that the liver was palpable in 20 out of 54 cases with clinical jaundice in only two patients, and none of the patients presented features of liver failure.

As patients presenting ALF due to hepatic infiltration make diagnosis difficult, determinate diagnosis for HD is usually made at later stage of the disease. However, early diagnosis is

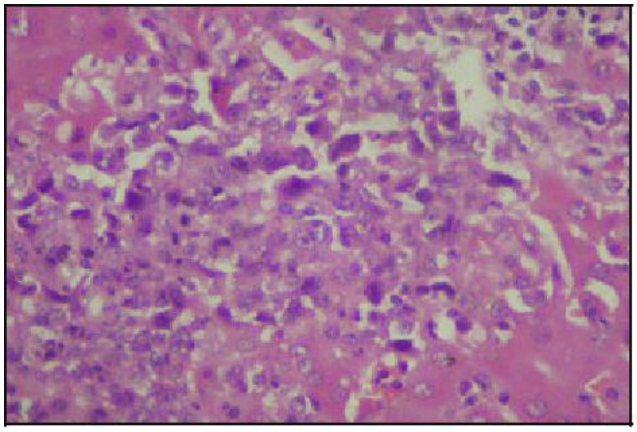

Fig.1. Histopathological examination of cervical lymph node showing effacement of lymph node architecture, replacement by Hodgkin' s cells and multinucleated cells resembling Reed-Sternberg cells.

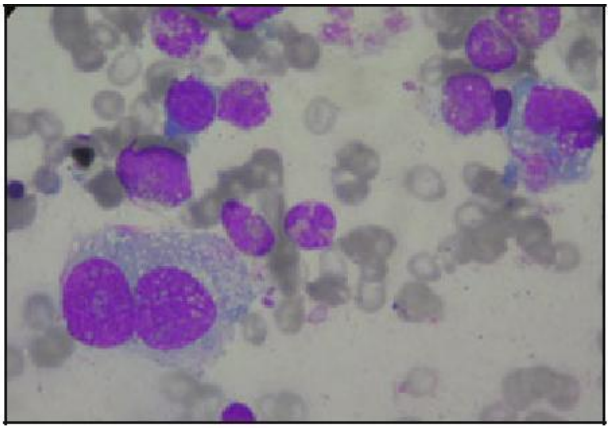

Fig.2. Bone marrow trephine biopsy revealing polymorphic infiltrate and Reed-Sternberg cells.

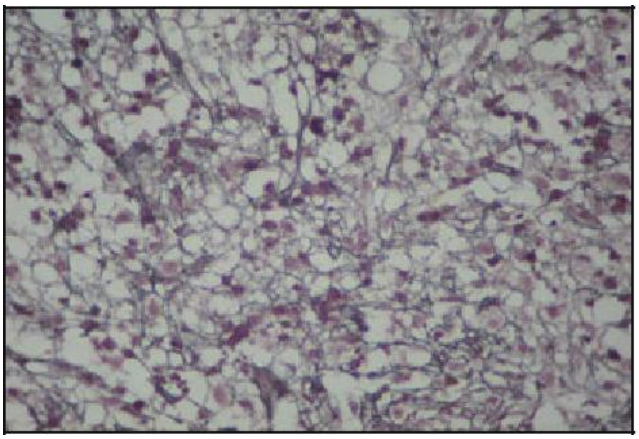

Fig.3. Bone marrow trephine biopsy showing focal fibrosis.

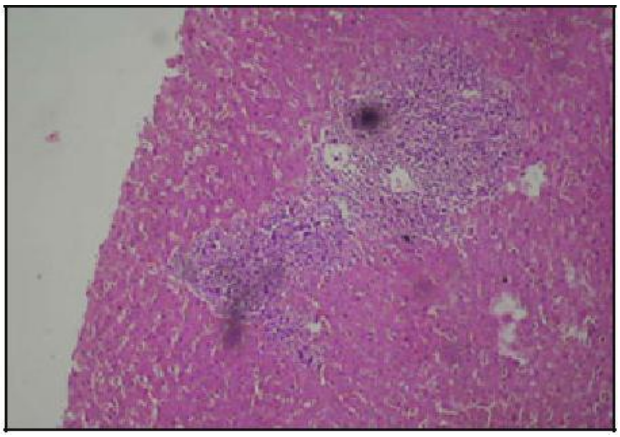

Fig.4. Liver biopsy showing infiltration of portal tracts by polymorphic cell population, mainly Reed-Stemberg cells.

very important because of the fact that quick application of specific chemotherapeutic medica-tions may reverse hepatic pathological changes. Clinical and laboratory findings are not helpful to exclude the other differential diagnoses. A number of primary liver diseases may also manifest in the same way. Radiologi-cal imaging studies like ultrasonography and CT scans are not adequate in diagnosing hepatic lymphoma[5]. If the diagnosis of HD has been established prior to lymph node presenting, the presence of mononuclear variants of RS cells in an appropriate background is sufficient to diagnose hepatic involvement, but classical multinucle-ate RS cells need to be detected, if liver tissue is the only material examined (Chim et al., 2000). As the liver is intolerable to radiotherapy and surgery is only possible for small soli-tary lesion, combined chemotherapy is the choice of the treatment for patients with extensive liver involvement like the patient in this case report (Chim et al., 2000). Patients with relapse of Hodgkin's lymphoma at late stage have shown the highest rate of remission of 75%, compared with that of 55% for early relapse and that of 35% for primary refractory Hodgkin's lymphoma(Cavalieri et al., 2009). This case study depicts that for the patients with lymphomatous liver infiltration, even for patients with evidence of extrahe-patic malignancy, differential diagnosis of ALF is sup-posed to be done and then right modality of treatment is followed accordingly. If generalized lymphadenopathy and hepatosplenomegaly in ALF patients occur, hemato-logical malignancies should be taken into account first, and histopathological examination of the liver and the associated lymph nodes should be performed as early as possible. This is the only way to correctly diagnose the disease and to plan an appropriate chemotherapy regi-men, which can achieve expected outcomes of the treat-ment.

## 4.CONCLUSION:

The patient reported here has shown an unusual clinical presentation of Hodgkin's disease. In fact, he shared few distinctive features with HD, includ-ing: *i*) the initial clinical presentations resembling acute hepatitis, *ii*) the presence of generalized lymphadenopa-thy, along with hepatosplenic involvement. Even in the absence of a massive lesion, young patients diagnosed as hepatosplenic Hodgkin's disease should be explored for an acute hepatic dysfunction, even no clinical and laboratory evidence of infective, toxic, autoimmune or

metabolic liver disease are presented. It is important to pay special attention to the abnormal liver function tests for the patients with no definite signs of liver dysfunc-tion induced by HD prior to chemotherapy.

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