Acute autoimmune hepatitis mimicking metastatic liver disease: A case report

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Abstract

We report progressive painless jaundice in a 39 year old female with a suspicion of metastatic liver disease on ultrasound and computed tomography scan of the abdomen. Although the most frequent liver lesions are liver metastasis because of dual blood supply of the liver and the impact of hormones, the index case proved to have acute autoimmune hepatitis (AIH) after liver biopsy was undertaken. AIH, an unresolving inflammation of liver, occurs predominantly among females worldwide. It may present acutely and even fulminant hepatitis has been described. The index case had a dramatic response to steroid treatment with total recovery and complete resolution of liver lesions. She is clinically fine and has been regularly attending our clinic for the last year. To our knowledge from a Medline search, this is the first report where AIH was seen to mimic metastatic liver disease.

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Key words: Metastatic liver disease; Auto immune hepatitis; Jaundice; Liver biopsy

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INTRODUCTION

Focal liver lesions are more often discovered with widespread use of diagnostic imaging modalities. Despite tremendous advancements in the field of radiology, radiological features are not definite. Difficulties may occur in differentiating atypical hemangiomas and focal nodular hyperplasia. Even differentiation of granulomatous lesions of the liver from primary benign or malignant lesions is also difficult. Liver biopsy becomes an indispensable tool to identify these lesions in a given case. The index case, with multiple liver lesions on radiography, proved to have acute auto immune hepatitis on liver biopsy. The etiopathogenesis of acute auto immune hepatitis (AIH) is unknown and is a diagnosis of exclusion. Multiple factors that trigger autoimmune phenomenon include infectious agents, drugs and toxins[1]. There can be a long time lag between exposure of a triggering agent and the disease[2] and, in time, steroid treatment determines the prognosis. Any treatment delay may result in irreversible liver cell damage.

CASE REPORT

A 39 year old female presented to our clinic at King Fahad Medical City, Riyadh with a history of progressive painless jaundice of 2 wk duration without any viral prodrome or offending drug intake. The patient is a non al-
coholic and denied a history of drug abuse. On examination
she was conscious, oriented and icteric. Her vitals were stable.
Her physical examination was unremarkable. Laboratory
tests showed normal hemogram but erythrocyte sedimentation
rate was raised at 52 mm/H (normal, 0-20 mm/H). She
had an elevated INR 2.7 s (N = 0.9-1.2 s). Her liver function
tests revealed predominantly conjugated hyper bilirubinemia [Bilirubin 43.9 umol/L (N = 0.17.1 umol/L)] with
elevated liver enzymes (aspartate aminotransferase: 818
U/L and alanine aminotransferase: 514 U/L). Serum
alkaline phosphatase levels were also elevated at 327 IU/L
(N = 50-136 U/L). An ultrasound examination (Figure 1)
showed a heterogeneous echo pattern of the liver with in-
filttrative hyper echoic areas, suggesting liver metastasis.
Common bile duct was normal and no intra or extra he-
patic biliary ductal dilatation was noted. The intra hepatic
veins and portal vein was normal. The gall bladder was
also normal. An abdominal computed tomography (Fig-
ure 2) showed diffuse enlargement of the liver with mul-
tiple hypo dense lesions with no vascular invasion in both
lobes of liver. No visceral mass lesion was seen in the
computed tomography (CT) scan. Tumor markers CA
19-9 levels were elevated at 114.8 KU/L (N = 0.37 KU/
L) and AFP levels were also elevated [15.5 µg/L (N = 0-10
µg/L)]. However, CEA and CA-125 levels were within
normal range. She underwent upper and lower endos-
copy, which were within normal limits. Mammography
revealed no abnormality. Her ANA, ASMA and ALKLM
levels were normal and viral markers (HBsAg, Anti-HCV,
IgM HEN, IgM HAV, IgM EBV and HSV) were negative.
Her celiac profile and HIV serology were also negative.
Further evaluation revealed normal serum ceruloplasmin
levels and normal iron studies. However, she had elevated
immunoglobin levels; IgG 0.27-4.2 mL/L) 4.4 pmol/L
(N = 0.4-2.3 g/L). Thyroid func-
tion tests were suggestive of hypothyroidism [TSH 17.93
mIU/L (N = 0.27-4.2 mL/L), T3 4.40 pmol/L (N =
0.3-1.68 pmol/L)]. She was started on Tab. Thyroxin 50
µg once daily and supportive treatment. She underwent
liver biopsy after transfusion of 4 units of fresh frozen
plasma. The liver biopsy revealed extensive hepatocellu-
lar necrosis with cholestasis. There was no evidence of
granuloma or malignancy. Keeping in mind hyper gam-
maglobulinemia and the absence of malignancy, autoim-
une hepatitis was considered as a diagnosis of exclusion
and an AIH score of 17 was calculated. She was started
on prednisolone (40 mg tablets) once daily. Liver cell
function tests were monitored. She showed progressive
improvement in her liver cell functions and her coagula-
tion parameters improved over a period of 6 wk. Repeat
ultrasound examination after a period of 9 mo (Figure 3)
showed a normal hepatobiliary system and clearance of
previous lesions. The patient has been followed up at our
clinic for the last year, with normal liver function tests.

**DISCUSSION**

The index case had diffuse liver lesions on radiology (ul-
trasound and CT scan abdomen) and various disorders
giving rise to such a radiological picture include lym-
phoma, metastasis from carcinoma, breast, lung or mela-
noma. Her tumor markers were elevated; hence, it was
prudent to rule out an internal malignancy. **However, no**
malignancy was found on evaluation and liver biopsy was
undertaken to evaluate the liver lesions. Liver biopsy re-
vealed the absence of any malignancy and instead bridg-
ing necrosis was seen. Keeping in mind hyper gamma
globulinemia and a negative etiological workup, she was
managed as acute auto immune hepatitis and started on
steroids (1 mg/kg). She responded to this treatment and
there was an improvement in her liver function tests. All
her liver lesions disappeared on ultrasound (Figure 3)
after 9 mo. Liver histology proved to be a key investiga-
tion in the index case. The histological patterns can be
variable in acute auto immune hepatitis. **It may resemble**
acute viral hepatitis or drug induced hepatitis, even
centrilobular or perivenular patterns resembling acute
toxic injury have been described\(^4\). It is very important
to differentiate drug induced liver injury from AIH on

![Figure 1](image1.png)

Figure 1 Ultrasound liver showing multiple hypo echoic lesions in liver.

![Figure 2](image2.png)

Figure 2 Computed tomography scan abdomen showing multiple hypo
dense liver lesions suspicious of liver metastasis.
histology as the treatment modalities are diagonal. Suzuki et al[8] compared Ishak scores, prominent inflammatory cell types in 35 cases of drug induced liver injury with 28 cases of AIH. The authors observed that interface hepatitis, focal necrosis and portal inflammation were more severe in AIH and also Ishak inflammation scores were more severe in AIH than in drug induced liver injury. In contrast, drug induced liver injury was characterized predominantly by hepatocellular cholestasis and portal neutrophils. The authors in this study were of the opinion that the pattern of injury could be used to differentiate drug induced liver injury from AIH.

Auto immune hepatitis presenting as acute hepatitis is known to occur in 25% of patients[9]. The AIH scoring system based on clinical and histological features proposed by international AIH group[10] is widely used to manage AIH. However, acute onset AIH is one of the conditions which may not fulfill these criteria[11], warranting an alert clinical attitude. The clinical suspicion of acute AIH needs to be high as the disease has an excellent response to steroids and, in time, treatment can prevent fatality, which otherwise can occur to the tune of 40% over a six month period in an untreated case[12]. The classical auto antibodies ANA and ASMA are usually supportive in making the diagnosis but ANA negativity has been described up to 56% of patients[13], as in the index case. Fujiwara et al[14] observed that immunoglobulin levels correlated with increased disease activity on histology and in their series of 39 patients of auto immune hepatitis, 7 (37%) patients had normal IgG levels. Immunoglobulin levels in the index case were elevated and she had extensive hepatic necrosis on histology. There are no morphological features that are pathognomonic of acute AIH, but the characteristic histological picture is that of an interface hepatitis with predominantly lympho plasmacytic necroinflammatory infiltrates, with or without lobular involvement and bridging necrosis, often with the formation of liver cell rosettes[15]. There are only a few reports on the histological features of acute-onset AIH. Lefkowitch et al[16] first reported AIH cases presenting histologically as acute hepatitis. Data from Japan showed features of acute hepatitis occurring in 5.6% of patients on histological examination[17].

In conclusion, it may be said that the present case brings to the fore the role of liver biopsy in suspected metastatic liver disease when investigations do not reveal any primary source. Furthermore, despite negative auto antibodies, the possibility of acute AIH must be borne in mind while evaluating acute hepatitis of unknown etiology as the response to steroids is excellent and life saving.

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