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Case Report **Biochemistry**

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A RARE CASE OF AUTOIMMUNE CHOLANGITIS

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ABSTRACT

Autoimmune cholangitis has recently been described as a rare, chronic cholestatic liver disease with clinical, biochemical, and immunological features of both primary and autoimmune hepatitis (CAH) and cholestasis with raised Ig G4 levels. In autoimmunecholangitis, increased levels ofγ- glutamyl transferase (GGT) and alkaline phophatase (AP) are disproportionate in comparison with the elevation in transaminases (AST/ALT), suggesting cholestatic liverdisease.We present a 34 year old female who presented with features of chronic hepatitis with pruritus which turned out to be Auto immune cholangitis (AIC).

KEY WORDS: **Cholestasis, chronic hepatitis, autoimmune cholangitis.**

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CASE DISCUSSION

The patient was a 32 year old female with 2 months of high colored urine, clay colored stools for initial 2-3 days followed by normal stools; with pruritus. She had no abdominal pain and was afebrile. She had no history of chronic drug or alcohol use. No recurrent episodes in the past. No involuntary movements and no altered sensorium seen. No family history of similar complaints. No previous history any connective tissue diseases. Patient had taken native treatment for one and a half months but the jaundice didn't improve, hence she presented to our medical office. On clinical examination: Patient was icteric, afebrile, not pale, noKayser–Fleischer ring seen on slit lamp examination of her eyes. She had no hyper pigmentation of skin. No thyromegaly, rash or scratch marks found.Per Abdomen she had a non-tender hepatomegaly felt that was palpable upto4 cm below the right costal margin without splenomegaly and a scites.

Her liver functions were deranged. Her total bilirubin levels increased from 2 on 10/10/2013 to 4.2 (direct3.8) on 26/10/2013.Her complete liver function test done on 18/11/2013 revealed

Total bilirubin	**13.5 mg/dl**
Direct	7 mg/dl
Indirect	6.5mg/dl
SGOT	316 IU/L
SGPT	222IU/L
Serum Alkaline Phosphatase	306 IU/L
Total protein	7.2 g/dl
Albumin	3.4g/dl
GGT	26 IU/L

Complete blood counts showed mild anemia (Hemoglobin 10.5 g/dl, normocytic in nature) and with an elevated ESRof 40mm at half hour and 80 mm after an hour.

PT	**18.9 seconds**
INR	1.45
Blood urea	12.1 mg/dl
Creatinine	0.59 mg/dl

She was evaluated for viral hepatitis. HBsAg was negative on 2 separate occasions; anti-HAV IgM and Anti-HCV were negative. Ultra sonogram study of her abdomen showed a gall bladder showing a hyper echoic content within it-sludge/concentrated bile. She was evaluated for other causes for hepatitis like autoimmune hepatitis, primary biliary cirrhosis and Wilson's disease.

1. Serum ceruloplasmin : 36.4mg/dl (normal:22-58mg/dl)
2. Anti- LKM1 : negative
3. Anti- SLA/LP : negative
4. Anti- LC 1 : negative
5. Anti AMA-M2: : negative

ANA : positive (1:100 Dilution) 2+
Pattern: granular nucleoplasm with distinct nucleoli
IgM : 126 mg/dl
IgG : 3200 mg/dl
ASMA : POSITIVE

She was subjected to an Upper Gastrointestinal scopy to rule out biliary obstruction which showed free bile flow with just a few antral erosions.

Multiline CT plain-whole abdomen showed (Figure 1)

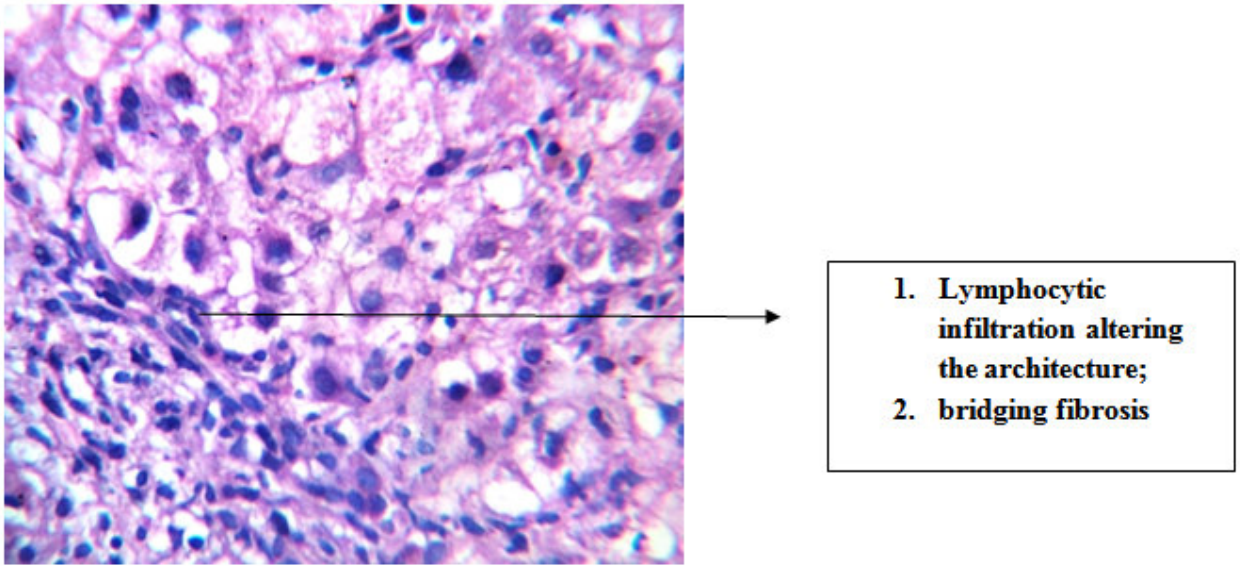
Transient hepatic attenuation difference in left lobe of liver.

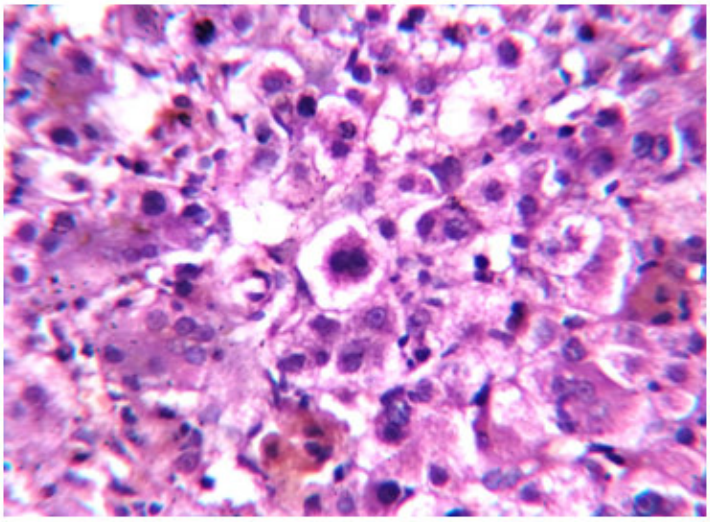
Magnetic resonance cholangiopancreatography showed

1. No significant abnormalities except incidental pancreatic divisum

2. Left lobe of liver showing altered signal intensity- possible focal inflammation.

A differential diagnosis of chronic hepatitis probably autoimmune in nature was made. She was planned to have a liver biopsy done to make a definitive diagnosis. Liver biopsy was done with all the necessary precautions and sent for analysis which revealed (interface hepatitis).





1. Portal tracts infiltrated by lymphocytes
2. Bile stasis(feathery degeneration)

1. *Liver tissue with overall maintenance of architecture.*
2. *Portal areas showing lymphocytic infiltrates.*
3. *Minimal portal creeping inflammation*
4. *Hepatocytes showing focal necrosis and regeneration*
5. *Focal areas of bile plugs and feathery degeneration suggestive of bile stasis*
6. *Sinusoids appearing normal*
7. *Central hepatocytes were normal.*

A diagnosis of autoimmune hepatitis type 1 with help of simplified scoring system which includes variables like

1. auto-antibodies,
2. raised immuno-globulin levels,
3. histological findings,
4. absence of evidence of viral hepatitis and
5. response to immunosuppressive therapy

But due to the disproportionately high IgG levels and both clinical and histopathological features of cholestasis we came to the conclusion that this patient did not have pure autoimmune hepatitis but autoimmune hepatitis with cholestatic features probably 'Autoimmune cholangitis'. The patient was started on oral prednisolone 20 mg with resolution of symptoms of jaundice and near normalization of liver functions within 2 weeks and normalization after a month after which the steroids were tapered to 10 mg once a day and later stopped. Meanwhile patient was started on immunosuppressant drug azathioprine 50mg which was continued.

DISCUSSION

Auto immune Hepatitis can be in the form with AIH-PBC or AIH-PSC but there can also be another variant with cholestatic features which is classified as a separate entity called 'auto-immune cholangiopathy'. In a report from the Mayo Clinic[7], for example, 225 patients with either type I autoimmune hepatitis, primary biliary cirrhosis, or primary sclerosing cholangitis (162, 37, and 26 patients, respectively) defined by standard criteria, were analyzed for serologic and clinical features suggesting variant forms of autoimmune hepatitis. Among these patients, 18 percent had diseases with overlapping features including:

- 7 percent with autoimmune hepatitis/primary biliary cirrhosis
- 6 percent with autoimmune hepatitis/primary sclerosing cholangitis
- 11 percent with autoimmune hepatitis/autoimmune cholangitis

Patients with AIH-(PSC) overlap have serologic features of autoimmune hepatitis but have cholangiographic abnormalities characteristic of primary sclerosingcholangitis. We suspected AIH-PSC overlap in our patient with small duct obstruction but there were no features of bile duct injury in histopathology. In autoimmune cholangitis, increased levels of γ- glutamyl transferase (GGT) and alkaline phophatase (AP) are disproportionate in comparison with the elevation in transaminases (AST/ALT), suggesting cholestatic liver disease. Although the histological changes are similar to those in PBC, anti-mitochondrial antibodies (AMA), the serological hallmark of PBC, are not detectable. However, as in type-1 autoimmune hepatitis, high titers of anti-nuclear (ANA) and smooth muscle antibodies (ASMA) are features of autoimmune cholangitis. The diagnostic differentiation between PBC, CAH (chronic active hepatitis), and autoimmune cholangitis is important because of the different therapeutic strategies. The name "immune cholangitis" was introduced first by Brunner[2] et al to describe a condition seen in three women (two were mother and daughter) who had liver disease which clinically, biochemically, and histologically seemed to be typical of primary biliary cirrhosis, except that the serumant mitochondrial antibody (AMA) test was negative in all three; all three were antinuclear antibody (ANA) positive. Examinations of the bile ducts via endoscopic Retrogradecholangio pancreatography (ERCP) disclosed no abnormalities. Treatment with prednisolone and azathioprine was said to be "successful.

Certain features distinguished the AMApositive and negative cases: the serum IgM concentrations were significantly lower in the AMA negative patients, and all had serum Positive for ANA (often at high titers (1:160-1:1280)) whereas only three of the AMA positive patients were ANApositive. Similarly, more of the AMA negative cases were also SMA positive (seven of 17) compared with the AMApositive cases (one of 17). Aside from the ANA tests and IgM concentrations, these AMA positive and negative patients could not be distinguished. Their symptoms were comparable, the prevalence of other autoimmune diseases was no different, and their liver histology on needle biopsy (read by two independent pathologists blinded to AMA Status) was indistinguishable. They hence coined the phrase "autoimmunecholangitis" to describe what is likely simply AMAnegative primary biliary cirrhosis. Patients with autoimmune cholangitis were distinguished from patients with PBC by having higher serum levels of AST (Aspartate transaminase) and bilirubin, and lower serum concentrations of immunoglobulin M. They also had SMA and/or ANA more frequently and a higher mean composite score for AIH. Patients with autoimmune cholangitis differed from those with PSC by their female predominance, lower serum alkaline phosphatase levels, and higher frequency of concurrent Sero-positivity for SMA and ANA, and greater overall occurrence of auto-antibodies. Importantly, the range of laboratory findings was wide foremost indices in patients with autoimmune cholangitis, and individuals could not be distinguished by an isolated test result. We came to a diagnosis of Auto-immune cholangitis in our patient because she was AMA negative without features of bile tract injury with features of cholestasis and a high Ig G4 levels.

CONCLUSION

Hence autoimmune cholangitis is a new and relatively less understood entity. It is rarely diagnosed as there is no clear cut demarcations from closely related diseases like autoimmune hepatitis and primary biliary cirrhosis. This case report is presented here as this presentation is rare with clinical and biochemical and immunological features of primary and autoimmune hepatitis.

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