Case Report

Autoimmiune Hepatitis in Children: Two Case Report

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Abstract

Autoimmune hepatitis (AIH) is the disease of immune mediated inflammation of liver. Presentation of AIH in children is variable, ranging from acute hepatitis to cirrhosis of liver and also as only asymptomatic raised ALT. AIH can present at any age and female are more affected. Here we are presenting two cases. Case 1 presented with jaundice and H/O epistaxis, having cutaneous echymosis, hepato-splenomegaly and ascites. Case 2 was a diagnosed case of Systemic Lupus Erythematosus (SLE) presented with only persistent raised of serum ALT. Both were diagnosed as autoimmune hepatitis on the basis of positive auto antibodies, histopathology of liver tissues and exclusion of all other causes of acute and chronic hepatitis.

Keywords: *Autoimmune hepatitis, children, auto antibodies*

INTRODUCTION

Autoimmune hepatitis (AIH) is one of the prototype of autoimmune liver disease, it was first described in the 1950.[1-3] AIH is characterized by progressive inflammatory tissue damage as a result of the loss of self-tolerance.[4] AIH is more common in women; ratio of 3.6/1.0.[5] The prevalence of AIH is in Scandinavia is 1 to 2 cases /100,000 populations / year with a point prevalence of 11 to 17 cases / year.[6,7] In Canadian cohort, an annual incidence of pediatric AIH of 0.23 case /100,000 children.[8] In Bangladesh, Benzamin et al found that, about 8% of children with chronic liver disease with hepatomegaly and or splenomegaly are due to AIH. [9]

Autoimmune hepatitis (AIH) is characterized biochemically by increased transaminase levels, and serologically by circulating autoantibodies and high immunoglobulin G (IgG) levels, histologically by interface hepatitis, in absence of known etiology. Autoimmune hepatitis can present at any age and in all ethnic groups, the peak incidence occurs at the ages of 16 to 30 years. [5-7,10,11]

On the basis of autoantibody AIH classified as type 1 and type 2.

a. Type 1: Antinuclear antibody (ANA) and or anti Smooth muscle antibody (SMA). It presents at puberty & accounts for two third of cases.

b. Type 2: Anti liver kidney microsomal (LKM1) and or anti liver cytosol 1(LC1) antibody. It usually occurs in younger age & during infancy. [12,13]

Autoimmune hepatitis always suspected when all cause of acute and chronic hepatitis is excluded.[14]

CASE REPORTS

Case 1

Choity, 8½ years old immunized girl, 1st issue of non-consanguineous parents, presented with jaundice for 1 month along with anorexia, nausea, weakness and gradual abdominal distension. She also developed bleeding from nose for last 7days. There was no H/O abdominal pain, altered sleep pattern, abnormal behavior, any GI bleeding, rash, arthralgia, H/O of blood transfusion, any surgical procedure, any autoimmune diseases or family history of such type of illness and no H/O offending drug exposure. She had past H/O jaundice and ascites 1 ½ years back. On examination, she was moderately pale, icteric (fig 1), skin survey revealed multiple echymosis. Vitals were within

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normal limit. Anthropometrically she was well thriving. Abdominal exam revealed, hepato-splenomegaly and ascites evidenced by shifting dullness. Other systemic examinations revealed normal findings.

Investigation showed- moderate anaemia (Hb 9.6 gm/dl), Leucopenia (WBC 3400/mm^3), Thrombocytopenia (53000/mm3), serum bilirubin increased (6mg/dl), prolong prothrombin time (26.6 sec, INR: 2.38), serum ALT was mildly raised (102 U/L), hypoalbuminemia (20 gm/l), ultrasonography of whole abdomen showed hepatomegaly with coarse parenchyma with increased parenchymal echogenicity and splenomegaly and moderate ascites. Investigations for HBV, HCV and Wilson disease were negative. For Autoimmune hepatitis, ANA was negative, Anti- LKM1 was positive, Total IgG: 28 g/l increase (normal 7-16 g/l), Tissue Trans-glutaminase- Ig A was negative, thyroid function test was normal and anti -Thyroglobulin Ab were negative. Endoscopy of upper GIT showed Grade III esophageal varices and histopathology of liver tissue revealed moderate chronic hepatitis, consistent with autoimmune hepatitis (table 1). So finally we diagnosed the case as chronic liver disease with portal hypertension with coagulopathy due to autoimmune hepatitis with grade III esophageal varices. We treated the child with Tab. Prednisolone 2 mg/kg /day and tab. Azathioprine (1-2mg/kg/day) added 2 weeks later of prednisolone started. Tablet. Propranolol (1mg/kg/day) was given as primary prophylaxis for portal hypertension.

Case 2

Bristy, a 10 ½ years old immunized girl, 3rd issue of non consanguineous parents, diagnosed case of Systemic Lupus Erythematosus (SLE) for last 1 year and on treatment with tab. prednisolone (0.6 mg/kg/day) along with tab. hydroxychloroquine. She was referred to us with the complaints of persistent raised S.ALT for last six months. She had no H/O anorexia, nausea, vomiting, abdominal pain, headache, weight loss, any gastrointestinal bleeding, H/O of blood transfusion, any surgical procedure, family history of such type of illness and no H/O offending drug exposure. She had H/O jaundice 2 years back. On examination she was anicteric, mildly pale, vital signs were within normal limit, anthropometrically well thriving, no feature of steroid toxicity, bed side urine albumin (BSUA) was nil and abdominal examination revealed no organomegaly. Investigation shows- mildly anaemic (Hb 11.4 gm/dl), S. bilirubin and prothrombin time normal, S. ALT raised (1027 U/L), Investigations for HBV, HCV, HAV, HEV and Wilson disease were negative. For Autoimmune hepatitis- Anti- LKM1: positive, anti SMA: positive, comb's test (direct and indirect) : negative. Histopathology of liver tissue was highly suggestive of autoimmune hepatitis. (table 1) So finally we diagnosed the case as Systemic Lupus Erythematosus (SLE) with Autoimmune hepatitis. We treated the child with tab. Prednisolone 2 mg/kg /day, tab. hydroxychloroquine and tab. Azathioprine (1-2mg/kg/day) added 2 weeks later of prednisolone started.

Table 1 : Investigation profile of case-1 (Choity) and case-2 (Bristy)

Investigations	Case 1	Case 2
Hb	9.6 gm/dl	11.4 gm/dl
WBC	3600/mm3	9000/mm3
Platelate	53000/mm3	2,20000/mm3
S. bilirubin	6mg/dl ↑	0.6mg/dl
PT	26.6 sec↑	13.4 sec
INR	2.38 ↑	1.04
S. ALT	102 U/L ↑	1027 U/L ↑
S. Albumin	20 gm/L ↓	43gm/L
USG of whole abdomen	Liver- enlarged. Coarse parenchyma with parenchymal echogenicity increased and splenomegaly. vascular dilatations around splenic hilar region. Moderate Ascites present.	Mild hepatomegaly with heterogenous echogenicity and splenomegaly.

Table 1

Investigations	Case 1	Case 2
HBs Ag-	Negative	Negative
Anti HCV	Negative	Negative
Anti HAV IgM	Not done	Negative
Anti HEV IgM	Not done	Negative
S. Ceruloplasmin:	22mg/dl	41 mg/dl
24 h urinary copper	58.5 µgm / day	42.77 µgm / day
Slit lamp examination of eye	No K-F ring found	No K-F ring found
ANA	Negative	Positive
Anti- LKM1	Positive	Positive
Total IgG	28 g/l ↑	Not done
Anti SMA	Not done	Positive
S.F T4	9.94 µg/dl (N)	7.4 µg/dl (N)
TSH	0.81µIU/mL (N)	2.1µIU/mL (N)
Thyroglobulin Ab	<20.0 IU/ml (N)	<20.0 IU/ml (N)
Endoscopy of upper	Grade III esophageal	Not done
GIT	varices seen	
Histopathology of Liver biopsy tissue	Portal area revealed a moderate number of chronic inflammatory cells. Marked piecemeal necrosis and mild lobular necrosis present. Bridging fibrosis is also seen. Comments- Moderate chronic hepatitis in consistent with autoimmune Hepatitis.	Portal area show moderate fibrosis and many number of chronic inflammatory cells. Marked interface hepatitis and mild lobular degeneration are present. Bridging fibrosis is also seen. Comments- highly suggestive of autoimmune hepatitis. (fig 2)

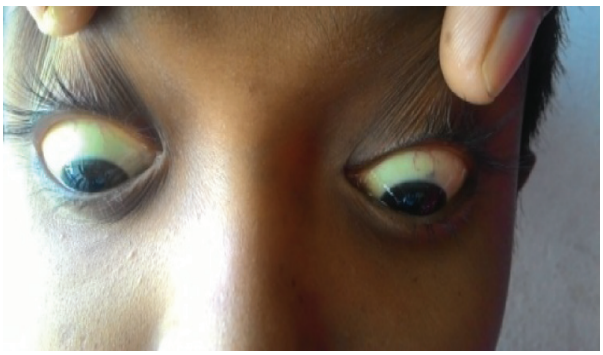

Fig.-1: Jaundice (case 1)

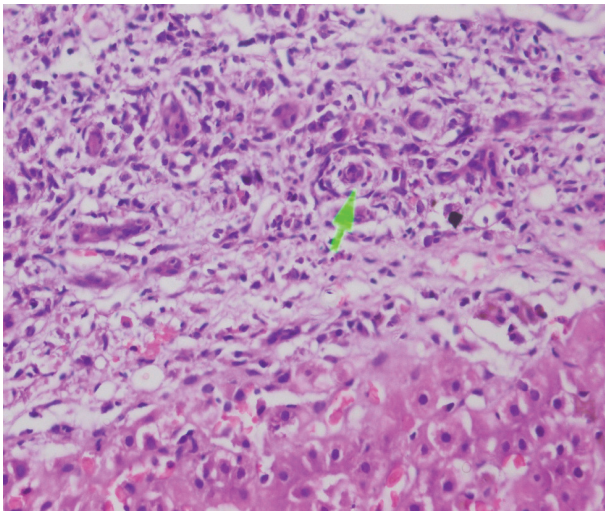

Fig.-2: H&E, 200x: Section of liver tissue showing plasma cell rich Portal inflammation, Interface hepatitis and Hepatocyte rosette formation (Marked with arrow).

DISCUSSION

AIH has variable clinical presentation which include followings- acute presentation like viral hepatitis with malaise, nausea, anorexia, vomiting, joint pain, abdominal pain, followed by jaundice, dark urine, pale stool

(40-50%), fulminant hepatic failure or chronic liver disease, complication of cirrhosis and portal hypertension without history of previous liver disease and jaundice. Non specific symptoms like progressive fatigue, relapsing jaundice, amenorrhea, headache, anorexia, joint pain, abdominal pain, diarrhea, weight loss, this symptom may last for 6 month to few years before diagnosis. Incidental finding of raised ALT without sign symptoms is another presentation of AIH. [8,15-20] Our case 1 presented with jaundice, anorexia, nausea, weakness and hepato-splenomegaly, ascites and bleeding manifestation in the form of epistaxis and echymosis. Case 2 presented with raised ALT without sign symptom.

AIH can present at any age and in all ethnic groups, but it has female predominance. [5,6,10,11] Our both cases are female.

Family history of autoimmune disease (40%) is frequent in AIH.[14] But in our both case there is no family history of autoimmune disease.

Diagnosis of AIH is made by combination of clinical, biochemical, immunological and histological features and exclusion of other liver diseases (like hepatitis B, C, E, Wilson disease, non alcoholic steatohepatitis (NASH) and drug induced liver disease. [5,14,21]

The key of diagnosis of AIH is the presence of auto antibody. Following are consider for diagnosis of AIH- Raised IgG level and auto antibody found like Antinuclear antibody (ANA), anti Smooth muscle antibody (SMA), anti liver kidney microsomal (LKM1) antibody, anti liver cytosol (LC1) antibody, anti mitochondrial antibody (AMA). [12-14] Our case 1 also had Anti- LKM1- positive, raised Total IgG and case 2 had ANA positive, Anti-LKM1: positive, anti SMA positive.

Histological features of AIH consist of: Interface hepatitis characterized by infiltration of lymphocytes, plasma cells; which cross the limiting plate and invade the surrounding parenchyma. Connective tissue collapse resulting from hepatocyte death and expanding from the portal area into the lobule ("bridging collapse"). Hepatic regeneration with "rosette" formation.[22-27] Our case 1's histtopathology of liver tissue showed portal area with a moderate number of chronic inflammatory cells, marked piecemeal necrosis and mild lobular necrosis and bridging fibrosis present. Case 2's histtopathology of liver tissue showed portal area with moderate fibrosis and many number of chronic inflammatory cells, marked interface hepatitis, mild lobular degeneration and bridging fibrosis present.

Twenty percent (20%) of AIH patients have other autoimmune diseases at diagnosis or developed during follow up. Autoimmune thyroiditis with hypothyroidism (8-23%), inflammatory bowel disease (18%), celiac disease (5-10%), hemolytic anemia, vitiligo, diabetes mellitus, urticaria pigmentosa, sjogren syndrome (SJS), SLE, glomerulonephritis, idiopathic thrombocytopenia, addison disease.[14,15,17,28] Our case 1 had no autoimmune disease but case 2 was a diagnosed case of Systemic Lupus Erythematosus (SLE).

Final diagnosis of AIH was done after exclusion of liver disease (like hepatitis B, C, E, Wilson disease, NASH and drug induced liver disease) that may share serological and histological features with autoimmune hepatitis.[14] We exclude HAV,HBV,HCV , Wilson disease, NASH in both case 1& 2.

After diagnosis, prompt treatment should be started. AIH is responsive to immunosuppressive drug. Treatment consists of two parts- induction of remission and maintenance phase.

Conventional treatment include prednisolone 2mg/kg/day (maximum 60 mg/day) and azathioprine. Prednisolone dose decreases in parallel to decline of ALT over a period of 4 to 8 weeks, maintenance dose of prednisolone will be 2.5 to 5 gm/day. For adjustment of prednisolone dose, liver function tests should be done frequently, preferably weekly. Azathioprine (AZ) is added 0.5 to 2 mg/kg/day, 2 weeks after starting prednisolone.[5,14,21,29-31] In both case we started treatment with prednisolone 2mg/kg/day. Azathioprine (AZ) is added 0.5 to 2 mg/kg/day, 2 weeks after starting prednisolone. Azathioprine will be continued in maintenance phase.

CONCLUSIONS

AIH has various spectrum of clinical manifestations like asymptomatic raised ALT to jaundice, ascites, hepato-splenomegaly etc. So AIH should be put in differential diagnosis of any liver disease in children. Auto antibodies and liver biopsy are the gold standard for diagnosis of AIH. Other autoimmune diseases may be associated with AIH. Long term treatment and meticulous follow up is needed for preventing disease progression.

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