



An infant with significant elevation of alanine aminotransferase and elevated serum creatinine: autoimmune hepatitis or not?

Mitra Ahmadi^{1,2}, Hazhir Javaherizadeh^{1,2*}, Seyed Mohsen Dehghani³, Parisa Amoori⁴, Marjaneh Khalighi²

¹Alimentary Tract Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

²Department of Pediatric Gastroenterology, Abuzar Children's Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

³Gastroenterohepatology Research Center, Nemazee Teaching Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

⁴Department of Pediatric Nephrology, Abuzar Children's Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

*Correspondence to

Hazhir Javaherizadeh Email:

Hazhirja@yahoo.com,

Hazhirja@ajums.ac.ir

Received 20 Dec. 2021

Accepted: 10 Feb. 2022

Published online 18 Feb. 2022

Keywords: Creatinine, Hepatitis, Liver

Key point

A one-year-old boy with significantly elevated aminotransferase elevated creatinine and hepatomegaly was admitted to our hospital. Autoimmune hepatitis may have different presentations. Autoimmune hepatitis associated with a rise of blood urea nitrogen and creatinine level was not reported. We report this case with the probable diagnosis of autoimmune hepatitis with elevated blood urea nitrogen and serum creatinine.

Citation: Ahmadi M, Javaherizadeh H, Dehghani SM, Amoori P, Khalighi M. An infant with significant elevation of alanine aminotransferase and elevated serum creatinine: autoimmune hepatitis or not? *Immunopathol Persa.* 2022;x(x):e31340. DOI:10.34172/ipp.2022.31340.

Autoimmune hepatitis is an inflammatory liver disorder with a wide clinical spectrum ranging between isolated liver enzyme elevation to acute or chronic liver failure, which leads to liver transplantation (1). Autoimmune hepatitis is one of the liver diseases leading to liver transplantation in children (2). Prompt diagnosis and treatment are very important to avoid more complications.

In the literature, elevated creatinine was not reported as the manifestation of autoimmune hepatitis. In this report, we present a patient with elevated blood urea nitrogen and serum creatinine and hepatomegaly at the initial visit.

A one-year-old boy was admitted to the hospital due to a rise in blood urea nitrogen and creatinine. The patient also showed a significant rise of alanine aminotransferase and aspartate aminotransferase (ALT=1872 U/L, AST=1554 U/L). Summary of laboratory findings were shown in Box 1.

The result for hepatitis A infection (IgM anti HAV) was negative. The patient underwent bone marrow examination to exclude hematologic or oncologic disease. The result of bone marrow examination was normal. Indirect fluorescent antibody for Kala-azar was negative.

Echocardiography was done. Pleural effusion was not present. Left ventricular and

right ventricular function was normal.

Liver sonography was done. Gallbladder was normal. Mild increased cortical parenchymal echogenicity with no sign of stone, stasis or perinephric collection was seen in the kidney evaluation during sonography. Increased echogenicity of the liver cortex was noted in sonography which was done in the workup.

Liver size is larger than normal (span = 115 mm) with increased parenchymal echogenicity. Normal intra- and extra-biliary tract. An abnormal portal vein was seen. Cavernous transformation was seen starting from distal of splenic vein. Evidence suggests previous portal vein thrombosis. Bilirubin decreased during follow-up period.

Box 1. Laboratory data of the case during the initial visit and follow-up period

Total bilirubin: 2.4 mg/dL
 Direct bilirubin: 2.1 mg/dL
 AST: 1554, 149, 87,97 and 104 U/L
 ALT: 1872, 3592,1133,310,211 and 127 U/L
 Blood urea nitrogen (BUN): 65,75,50,45 and 20 mg/dL
 Creatinine: 3,7,2.3,3.8 and 1.7 mg/dL
 Amylase: 29 U/L
 Lipase: 52 U/L
 Epstein-Barr virus ((EBV) IgG: 0.05 (Normal)
 EBV IgM: 0.02(Normal)
 Metabolic panel: NL



Bilirubin total: 0.7 mg/dL
 Bilirubin direct: 0.3 mg/dL
 ALT and AST were 75 IU/L and 65 IU/L respectively.
 Total protein: 8.1 g/dL
 Albumin: 5.1 g/dL
 Globulin: 3.0 g/dL
 ANA: 0.2 (<1.0 negative)
 Anti LKM: NL
 Anti-smooth muscle antibody: positive (NL: up to 1/100)
 Pt: 12.0 seconds
 INR:1.0

Liver biopsy was conducted under a sonographic guide. Report of pathology was as the following: About 16 portal tracts and portal expansion with short fibrous septa infiltrated with mild chronic inflammatory cells and a prominent number of eosinophils. No bile duct lesion, proliferation, or granuloma. Mild interface hepatitis is seen without lobular inflammation, cholestasis, or ground-glass hepatocytes. About 20% steatosis was seen with ballooned hepatocytes.

After two months of follow-up and treatment with azathioprine and prednisolone, AST was 57 IU/L, ALT=41 IU/L. Total protein was 7.5g/dL. Serum albumin was 4.8g/dL. Recently, Total and direct bilirubin was 0.8mg/dL and 0.3 mg/dL respectively. AST and ALT were 41 and 38 IU/L. ASMA (anti-smooth muscle antibody) was 1.8 UI/mL (normal<15).

The patient showed significant improvement during treatment with azathioprine and prednisolone. In the follow-up period ALT, AST, and other laboratory examinations were normal. Follow-up sonography was normal. After tapering of prednisolone, ALT and AST showed elevation. Azathioprine and prednisolone dose was modified again. ALT and AST were normal after increased dose of azathioprine and prednisolone. Endoscopy was done to evaluate esophageal varices. Esophageal varices were not seen.

Autoimmune hepatitis may be seronegative (3). ANA and/or ASMA are almost requisites for diagnosis of type I AIH (4). In children, ASMA \geq 1/20 UI/mL was considered clinically significant (5). Our patient had ASMA \geq 1/100 UI/mL in the initial presentation. In the follow-up period after treatment with prednisolone and azathioprine, ASMA level was decreased.

Our patient had evidence of previous portal vein thrombosis. In patients with autoimmune hepatitis, there is increased risk of portal vein thrombosis (6). According to simplified diagnostic criteria for autoimmune hepatitis, our case had probable diagnosis (ASMA positive, interface hepatitis and viral hepatitis absent). Interface hepatitis

is hallmark of autoimmune hepatitis. Eosinophils may present. Interface hepatitis and eosinophil was reported by a pathologist. In the current report, age of the case was one year. In the study by Sogo et al, autoimmune hepatitis was reported in children aged 3 months (7). Our patient was followed 5 years after the initial presentation. Autoimmune hepatitis should be considered in children with unusual presentation of liver disease.

Authors' contribution

MA, HJ, SMD, PA, MK had the role in diagnosis, management and follow up the patient. SMD revised the draft of manuscript. HJ is responsible for revising the manuscript. All of the authors read and approved the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient gave the consent to publish as epidemiology and prevention article.

Funding/Support

No funding was received .

References

1. Krawitt EL. Clinical features and management of autoimmune hepatitis. *World J Gastroenterol.* 2008;14(21):3301-5. doi: 10.3748/wjg.14.3301.
2. Haghghat M, Mardani S, Dehghani SM, Javaherizadeh H. Clinical and laboratory data in pediatric autoimmune hepatitis: study from referral center in Iran. *Rev Gastroenterol Peru.* 2020;40:149-54.
3. Maggiore G, Socie G, Sciveres M, Roque-Afonso AM, Nastasio S, Johanet C, et al. Seronegative autoimmune hepatitis in children: spectrum of disorders. *Dig Liver Dis.* 2016;48:785-91. doi: 10.1016/j.dld.2016.03.015.
4. Manns MP, Strassburg CP. Autoimmune hepatitis: clinical challenges. *Gastroenterology.* 2001;120:1502-17. doi: 10.1053/gast.2001.24227.
5. Vergani D, Alvarez F, Bianchi FB, Cançado EL, Mackay IR, Manns MP, et al. Liver autoimmune serology: a consensus statement from the committee for autoimmune serology of the International Autoimmune Hepatitis Group. *J Hepatol.* 2004;41:677-83. doi: 10.1016/j.jhep.2004.08.002.
6. Ruiz P, Sastre L, Crespo G, Blasi A, Colmenero J, García-Valdecasas JC, et al. Increased risk of portal vein thrombosis in patients with autoimmune hepatitis on the liver transplantation waiting list. *Clin Transplant.* 2017;31:e13001. doi: 10.1111/ctr.13001.
7. Sogo T, Takahashi A, Inui A, Fujisawa T, Ohira H, Takikawa H. Clinical features of pediatric autoimmune hepatitis in Japan: a nationwide survey. *Hepatol Res.* 2018;48:286-94. doi: 10.1111/hepr.12998.