Journal of Liver
ISSN: 2167-0889

Dabiri et al., J Liver 2013, 2:4
DOI: 10.4172/2167-0889.1000130

Case Report Open Access

Detection of Undiagnosed Wilson's Disease after Hepatitis A Virus Infection

Reza Dabiri, Ali Bastani and Amir Houshang Mohammad Alizadeh*

Gastroenterology and Liver Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Introduction: Some reports have considered hepatitis A as a possible factor in the development of acute decompensation in patients with Wilson's disease. Here we report the case of a delayed diagnosis of Wilson's disease in the end of the third decade of life in a patient infected with hepatitis A.

Case report: The patient was a 26 year old woman with complaints of nausea and vomiting, anorexia, ichter, fever and epigastric pain since a week before admission. She had not any history of previous disease in herself and her families. Considering an increase in liver enzymes, serum bilirubin levels, serum IgM HAV antibody positivity and symptoms suggestive of hepatitis A associated with autoimmune hepatitis considered and patient was treated and then discharged.

The patient returned two weeks later and symptoms such as ichter, fatigue and edema of the lower extremities were still present. Wilson's disease is suspected, laboratory testing and ophthalmologic examination was performed and diagnosis was confirmed. The patient was treated with D-penicillamin, pyridoxine, and zinc sulfate. On re-examination, the patient's symptoms largely resolved and in the following experiments response to treatment was appropriate.

Conclusion: Hepatitis A can be considered as a factor for acute decompensation in undiagnosed patients with Wilson's disease.

Keyword: Wilson's disease; Hepatitis A; Copper; Coruloplasmine

Introduction

Wilson disease is an autosomal recessive disorder of copper metabolism in the liver and causes degenerative changes in various organs such as the brain, liver and other organ involvement such as Kayser–Fleischer ring in eyes [1,2]. The relative prevalence of this disorder is one in one hundred thousand to one in five hundred thousand at live births [3,4]. In this disease, copper accumulates, as the result of mutation of ATP7B gene located on chromosome 13, and causes damage to the liver and other organs, such as brain and kidneys [2,5].

Wilson's disease can have several manifestations. Classic findings include liver disease, kidney disease, and nerve problems. Liver involvement may be includes asymptomatic hepatomegaly (with or without splenomegaly), sub-acute or chronic hepatitis or fulminant hepatic failure. Due to hepatic dysfunction patients may be at risk for delay in puberty or coagulopathy. Arthritis and glandular disorders are unusual manifestations in these patients [5].

Changes in the basal ganglia that are seen on MRI are diagnostic for the disease [6]. Neurological and psychological symptoms appear much later in life [4].

Early diagnose of this disease, prevents the damaging effects of the accumulation of copper in various organs and also provides possibility of screening of disorder in the patient's family [7]. More than 80% of patients with early signs of the disease will develop in the first three decades of their life, but even disease has also been reported in later decades of life [2]. Iran is among the countries where hepatitis A infection is endemic and high prevalence rate in 6 months to 1.9 year children have been reported (61.5%) [8]. Increases in incidence has been reported with age between 85 to 99% in different part of the country [9]. Some reports have been considered hepatitis A infection as a possible factor in the development of acute decompensation in unknown patients with Wilson's disease [10]. Here we report the case of a delayed diagnosis of Wilson's disease in the end of the third decade of life in a patient infected with hepatitis A.

Case Report

The patient was a 26 year old woman with complaints of nausea and vomiting, anorexia, ichter, fever and epigastric pain since a week before admission in our center. She had not any history of previous disease in herself and her families. She had a history of medicinal use of Senna for constipation since 12 years ago. In physical examination she was ichteric, had mild epigastric tenderness and 38˚C fever which fever resolved after 48 hours. There was not any sign of encephalopathy. Increase in liver enzymes, serum bilirubin levels, and serum IgM HAV antibody positivity was seen in primary laboratory test. Initial laboratory tests are presented in Table 1 and 2.

Abdominal ultrasound was performed on the patient's liver, gallbladder and spleen was normal. Bone marrow aspiration was performed in the patient and showed erythroid hyperplasia. Results of the patient's laboratory tests in the second and seventh day and second

***Corresponding author:** Mohammad Alizadeh AH, Shahid Beheshti University of Medical Sciences, Taleghani Hospital, Parvaneh Ave, Tabnak Str., Evin, Tehran, Iran-19857, P.O.Box: 19835-178, Tel: 0098-21-22432521; Fax: 0098-21-22432517; E-mail: ahmaliver@yahoo.com

Received September 21, 2013; **Accepted** October 18, 2013; **Published** October 26, 2013

Citation: Dabiri R, Bastani A, Alizadeh AHM (2013) Detection of Undiagnosed Wilson's Disease after Hepatitis A Virus Infection. J Liver 2: 130. doi:10.4172/2167-0889.1000130

CBC: 3.4 K/µL	ALT: 207 IU/L	Alb: 3 gr/dl	TIBC: 300 mcg/dl	Anti LKM: Neg
Hb: 10.9 gr/dl	AST: 92 IU/L	Total Pro: 5.5 gr/dl	Ferritin: 824 ng/ml	
MCV: 85.3 fL	Alk Ph: 173 IU/L	INR: 1.5 Min	HBS Ag: Neg	
Plt: 121 K/µL	Bil Total: 44.8 mg/dl	PTT: 40 Sec	HCV Ab: Neg	
ESR: 34 mm/h	Bil Direct: 22.8 mg/dl	LDH: 387 IU/L	Anti HAV IgM (+)	
BUN: 8 mg/dl	Choles: 75 mg/dl	CPK: 38 IU/L	ANA: 1/40	
Cr: 0.5 mg/dl	Tg: 176 mg/dl	Fe: 123 mcg/dl	ASMA: 1/100	

Table 1: Laboratory data of patient in admission.

Fractions	%	% Normal	gr/dl	(gr/dl) Normal
Albumin	51.0	54-66	2.7	3.2-5.3
$Alpha_1$	2.7	1.4-2.8	0.1	0.1-0.2
$Alpha_2$	5.7	9.1-13.8	0.3	0.6-1.1
Beta	11.2	8.7-14.4	0.6	0.5-1.2
Gamma	29.4	10.6-19.2	1.5	0.6-1.5

Table 2: Patient's Serum Protein electrophoresis.

and third weeks after admission is shown in Table 3 which did not showed any much change.

Core needle liver biopsy was performed in patient that results are as follows; swollen and pale changes with accumulation of numerous inflammatory cells in parenchyma, infavor of postnecrotic collapse and early fibrosis of viral hepatitis. Due to the decrease in serum bilirubin levels, improve in the general situation and the lack of signs and symptoms of hepatic encephalopathy and no increase in the PT and INR during admission patient was discharged with a hepatitis A plus autoimmune hepatitis diagnosis. 10 mg/day prednisone was administered and advised for came back after 2 weeks after doing laboratory tests for follow up.

The patient returned two weeks later and symptoms such as ichter, fatigue and edema of the lower extremities were still present. She was ichteric and had +2 lower extremities edema. Results of the patient's laboratory tests in follow up evaluation are shown in Table 4. Due to clinical sign and laboratory findings Wilson's disease is suspected and laboratory test were requested and the results were as follow: serum coruloplasmine was 13 mg/dl, serum copper level and unbounded serum copper level were 170 micgr/dl (normal value:) and 129.5 micgr/dl (normal value:) respectively and finally copper level in 24 hour urine was 476 micgr (normal value:). To confirm the diagnosis of Wilson's disease ophthalmologic examination was performed and typical Kayser–Fleischer ring in eyes was confirmed. The patient was treated with D-penicillamin, pyridoxine, and zinc sulfate. Trend of patient's laboratory test in second admission is showed in Table 5.

On re-examination, the patient's symptoms largely resolved and in the following experiments one month after treatment the response to treatment were appropriate. The last patient's laboratory results is showed in Table 6.

Discussion

We report a case of delayed diagnosis of Wilson's disease in a 26-year-old woman after Super infection with hepatitis A. In this disease, copper accumulates, as the result of mutation of ATP7B gene located on chromosome 13, and causes damage to the liver and other organs, such as brain and kidneys [2,5].

The natural balance of the copper in the body is done through biliary excretion of copper by the liver Lysozymes. Most copper is excreted in the bile as a non-absorbable. Impairment in biliary excretion of copper in Wilson's disease causes liver damage. Gradual accumulation of copper in the liver exceeds the capacity of the liver and by leaving it leads damage in the other organs, especially in the brain and kidneys [2,6].

Histological changes in liver tissue are not specific for Wilson. The earliest microscopic findings are abnormal deposition of glycogen and fat, varying degrees of fibrosis, nucleic vacuolization, active hepatitis and cirrhosis may be outdated. Nodular cirrhosis is the most common abnormality. Liver involvement may be in the form of acute hepatitis, fulminant hepatitis, chronic active hepatitis or cirrhosis with portal hypertension [11]. Non-specific symptoms may cause diagnostic confusion with other chronic and acute liver diseases such as viral and autoimmune hepatitis [12]. Pathologic findings in our patient largely were consistent with viral and autoimmune hepatitis.

Sometimes the symptoms in patients even in one family depending on various factors, and different range in severity may occur [7]. Mak et al. [7] reported a case of Wilson's disease which diagnosed after 18 years in one boy which had a confirmed symptomatic Wilson's disease in his sibling which had not been diagnosed despite screening in previous years and he was given the diagnosis after genetic evaluation after 18 years. While obvious symptoms of the disease did not occur in this patient unlike his sister. Accordingly, authors said only rely on the biochemical screening, particularly among families with Wilson disease is not correct and recommends made genetics screening in these cases.

Czlonkowska et al. [1] reports two Wilson's cases in 30 and 33 years old women who were presented with HELLP syndrome in pregnancy and Wilson disease confirmed in them in postpartum period.

Day	INR	ALT/AST	ALPH	BILI (T&D)
2	1.5	207/92	173	44.8/22.8
7	1	165/112	167	32.9/17.5
14	1	236/125	145	26.6/17.4
21	1.37	189/200	254	24.2/16.1

Table 3: Laboratory data trend of patient in one month after admission.

CBC: 4.6 K/µL	ALT: 144 IU/L	Alb: 2.5 gr/dl
Hb: 11.8 gr/dl	AST: 163 IU/L	Total Pro: 5.0 gr/dl
MCV: 92.5 fL	Alk Ph: 273 IU/L	INR: 1.29 Min
Plt: 109 K/µL	Bil Total: 23.2 mg/dl	PTT: 40 Sec
ESR: 13 mm/h	Bil Direct: 14.6 mg/dl	LDH: 624 IU/L
BUN: 8 mg/dl	CRP: 22 mg/L	ANA: 1/40
Cr: 0.5 mg/dl		ASMA: 1/100

Table 4: Laboratory data of patient in second admission.

Day	ALT	AST	ALkPh	BILI (T&D)	INR	WBC	HB	PLT
1	144	163	273	23.2 (14.6)	1.29	4600	11.8	109
2	102	128	230	17(7)	1.4	3900	10.7	85
5	102	109	247	13.9 (8.7)	1.2	3500	10.8	134
10	94	104	270	11.8 (7.3)	1.3	3.6	10.4	110
14	79	95	388	7.5 (3.3)	1.2	5000	11.3	130

Table 5: Trend of laboratory findings of patient in two week after second admission.

CBC: 3.87 K/µL	ALT: 51 IU/L	Alb: 3.4 gr/dl
Hb: 13.1 gr/dl	AST: 64 IU/L	Total Pro: 7.7 gr/dl
LDH: 403 IU/L	Alk Ph: 576 IU/L	
Plt: 117 K/µL	Bil Total: 4.7 mg/dl	
INR: 1.4 Min	Bil Direct: 2.88 mg/dl	
Cr: 0.8 mg/dl	Urine Zinc Copper: 684 mcgr/24 hr	

Table 6: Last patient's Laboratory data one month after Wilson's disease treatment.

Researchers listed the factors such as ApoE, MURR1 and copper content of the diet as effective factors on delay in Wilson's disease sign and symptoms presentation [7,13,14], In our patient, this can also be considered. Hepatitis A and E infection in patients with chronic liver disease has been reported as a cause for decompensation of the underlying liver diseases and increased mortality in these patients and accordingly hepatitis A vaccination is recommended in these patients [10,15,16]. Sallie, et al. [16] reported a six year old girl with fulminant hepatic failure resulting from hepatitis E and coexistent Wilson's disease. In addition, chronic liver disease may exacerbate by drugs, the addition of sepsis, gastrointestinal bleeding, hepatic and portal vein thrombosis and hepatocellular carcinoma [15].

Our patient also presented with signs of liver failure without history of liver disease and the reason for this were determined super infection of hepatitis A on Wilson's disease after performing diagnostic tests. Due to the nonspecific nature of the symptoms of Wilson's disease which is well seen in our patient, the diagnosis may be delayed and often be with a sign of liver failure [17] or other diagnosis being considered for the patients.

Gao and colleagues [12] in their study were evaluated the clinical picture and diagnosis conditions such as mis-diagnosis in 128 Wilson's cases. Based on their results, 55 patients (42.9%) of patients initially diagnosed with other diseases and the most common cause for mis-diagnosis in Wilson's cases, including hepatitis A and chronic hepatitis.

In general, it seems hepatitis A super infection in Wilson's disease cases that have not been diagnosed nor have not severe symptoms may worsen the symptoms of this disease. Hepatitis A can be considered as a factor for acute decompensation in undiagnosed patients with Wilson's disease. Therefore, considering the diagnosis of Wilson's disease in patients with similar signs like our patient and screening biochemical tests in them to evaluate Wilson disease are recommended.

References

1. Członkowska A, Gromadzka G, Büttner J, Chabik G (2010) Clinical features of hemolysis, elevated liver enzymes, and low platelet count syndrome in undiagnosed Wilson disease: report of two cases. Arch Gynecol Obstet 281:129-134.
2. Ferenci P (2005) Wilson's Disease. Clin Gastroenterol Hepatol 3:726-733.
3. Thomas GR, Forbes JR, Roberts EA, Walshe JM, Cox DW (1995) The Wilson disease gene: spectrum of mutations and their consequences. Nat Genet 9:210-217.
4. Rudolp JF, Blistreri WB (2006) Metabolic disease of the liver, Nelson Textbook of pediatrics. 17th ed. Philadelphia: WB Saunders; p: 1321-1322.
5. Rosencrantz R, Schilsky M (2011) Wilson disease: pathogenesis and clinical considerations in diagnosis and treatment. Semin Liver Dis 31:245-259.
6. Kitzberger R, Madl C, Ferenci P (2005) Wilson disease. Metab Brain Dis 20:295-302.
7. Mak CM, Tam S, Fan ST, Lisu CL, Lam CW (2006) Wilson's disease: a patient undiagnosed for 18 years. Hong Kong Med J 12:154-158.
8. Sofian M, Aghakhani A, Farazi AA, Banifazl M, Etemadi G, et al. (2010) Seroepidemiology of hepatitis A virus in children of different age groups in Tehran, Iran: implications for health policy. Travel Med Infect Dis 8:176-179.
9. Merat S, Rezvan H, Nouraie M, Abolghasemi H, Jamali R, et al. (2010) Seroprevalence and risk factors of hepatitis A virus infection in Iran: a population based study. Arch Iran Med 13:99-104.
10. Ozcay F, Canan O, Akcan B, Bilezikei B (2007) Hepatitis A super infection as a cause of liver failure in a child with Wilson's disease. Turk J Pediatr 49:199-202.
11. Brůha R, Marecek Z, Martásek P, Nevsímalová S, Petrtýl J, et al. (2009) Wilson's disease. Cas Lek Cesk 148:544-548.
12. Gao WS, Liu YW, Chen J (2001) Analysis of 128 Wilson's disease. Zhongguo Yi Xue Ke Xue Yuan Xue Bao 23:506-508.
13. Wang XP, Wang XH, Bao YC, Zhou JN (2003) Apolipoprotein E genotypes in Chinese patients with Wilson's disease. QJM 96:541-542.
14. Stuehler B, Reichert J, Stremmel W, Schaefer M. (2004) Analysis of the human homologue of the canine copper toxicosis gene MURR1 in Wilson disease patients. J Mol Med (Berl) 82: 629-634.
15. Vento S, Garofano T, Renzini C, Cainelli F, Casali F, et al. (1998) Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. N Engl J Med 338:286-290.
16. Sallie R, Chiyende J, Tan KC, Bradley D, Portmann B (1994) Fulminant hepatic failure resulting from coexistent Wilson's disease and hepatitis E. Gut. 35:849-853
17. Hamid SS, Atiq M, Shehzad F, Yasmeen A, Nissa T, et al. (2002) Hepatitis E virus superinfection in patients with chronic liver disease. Hepatology 36:474-478.