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An Unusual Combination of Relapsing and Cholestatic Hepatitis A in Childhood

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Clinical variants of hepatitis A include the prolonged, relapsing and cholestatic forms. Here, the first childhood case of hepatitis A, with a combination of the relapsing and cholestatic forms is presented, a 14-year old boy. In the first phase of the illness, while the AST and ALT levels were declined, th total and direct bilirubin and GGT were increased. The patient was thought to have the cholestatic form of hepatitis A. Du to intense pruritus and high bilirunbin levels, ursodeoxycholic acid (UDCA) therapy was started. On the 17th day, the decreased AST and ALT levels began to increase, reaching levels as high as 484 U/L and 862 U/L, respectively. The UDCA treatment was stopped on the 64th day. On the 164th day, all his laboratory parameters were within normal limits, but the anti-HAV IgM was still positive.

Key Words: Relapsing and cholestatic hepatitis A, childhood

INTRODUCTION

The hepatitis A virus (HAV), a picornavirus, is a common cause of hepatitis worldwide.[1] The single most important predictor of the clinical course of an acute HAV infection is age; symptomatic infections are uncommon in young children. Serological studies showed that 90% of children with anti-HAV IgG never present with jaundice.[2] In adults, 75 to 95% of infections are symptomatic, with jaundice in the majority of these cases. In symptomatic cases, the illness usually persists for a few weeks. Clinical variants include the prolonged, relapsing and cholestatic forms1. In a few cases, prolonged cholestatic jaundice has been mentioned, but recovery is the rule.[2] In some individuals, HAV causes a biphasic illness, with a second bout of jaundice and cholestasis six to 12 weeks after the primary infection.[3,4] There has only been one adult patient presenting with both the two atypical forms of hepatitis A: the relapsing and cholestatic forms.[5] Here, the first paediatric patient presenting with a combination of these two atypical forms is presented.

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CASE REPORT

A 14-year old boy was admitted to the Paediatrics department, with the complaints of abdominal pain, jaundice, vomiting and pruritus. The first symptom was abdominal pain, which beginning 13 days prior to admission, followed by vomiting and jaundice. The pruritus became manifest after an increase in the jaundice. His anthropometric measurements were within the normal range (weight and height between 25th and 50th percentiles). His sclera and skin were jaundiced. A tender hepatomegaly was palpated 3-cm below the costal edge at the midclavicular line. There was generalized stratching and excoriation on the skin due to pruritus. From the laboratory investigations, the hemoglobin, white blood cell and platelet counts were 12.3 g/dl, 11800/dl, and 99000/dl, respectively. There was no reticulocytosis. is fasting triglyceride and cholesterol levels were 425 and 176-mg/dl, respectively. The total bilirubin (T bil), direct bilirubin (D bil), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma glutamyl transpeptidase (GGT) values are

shown in Table 1. The total protein (T protein), albumin, prothrombin time (PT) and activated partial thromboplastin time were 7.8 and 4.5-g/dl, 12.3 and 35.4 seconds, respectively. The serum ammonia and factor II, V and VII levels were normal. The anti-HAV IgM and IgG were positive. The patient was hospitalized due to vomiting; with the exception of short-term intravenous hydration, no other medication was started. In the follow-up, while the AST and ALT levels declined, the T bil, D bil and GGT increased. An ultrasonography of the abdomen showed no evidence of an extrahepatic obstruction. The patient was thought to have the cholestatic form of hepatitis A. Because of the intense pruritus and high bilirubin levels, ursodeoxycholic acid (UDCA) therapy was started at a dose of 15-mg/kg on the 5th day of admission. The serial PT and PTT and ammonia levels were determined. After 5 days of UDCA therapy, the bilirubin levels began to decrease. On the 17th day the decreased AST and ALT levels began to increase, and reached levels as high as 484 and 862 U/L, respectively. In that phase, the other agents that cause elevations of the transaminases, such as hepatitis B, hepatitis C, cytomegalovirus infection, rubella, toxoplasmosis, herpes virus infections, syphilis and brucellosis, were investigated, but were all negative. The courses and the graphical patterns of the T bil, D bil, AST, ALT, GGT and ALP levels are shown in Table 1 and Fig. 1 and 2. The UDCA treatment was stopped on the 64th day. On the 164th day, all the laboratory parameters were within normal limits, but the anti-HAV IgM was still positive.

DISCUSSION

The unusual clinical manifestations of acute hepatitis A include cholestatic, relapsing and fulminant hepatitis. In recent years, relapses, and the protracted course, of the disease have been described.[6,7] In a series of 108 children with acute viral hepatitis A, 8.3% showed an atypical course; after a short period of progressive enzyme level normalization, a relapse occurred.[9]

In relapsing hepatitis a biphasic or polyphasic clinical course may be observed. Weeks, to months, after an apparent recovery, symptom and liver function test abnormalities may recur. Relapse usually occurs after a short period (usually less than 3 weeks), but is clinically milder than the

Table 1. Serum AST, ALT, Bilirubin, ALP and GGT Levels of the Patient in Respect to Days Followed

Days	AST (U/L)	ALT (U/L)	T.BIL (mg/dl)	D.BIL (mg/dl)	ALP (U/L)	GGT (U/L)
1st	98	256	16.9	12.1	1240	142
3rd	68	122	18.5	13.7	1046	122
5th	62	85	20.8	14.8	1104	386
9th	76	87	23.7	16.7	964	366
10th	82	83	21	16.3	900	136
13th	87	96	19	13.5	868	128
17th	145	166	15	11.2	807	109
23rd	346	382	10.7	6.4	741	95
28th	559	779	6	3.5	692	70
39th	484	862	3.3	1.5	849	63
46th	457	765	2.7	1.3	873	55
64th	227	352	1.3	1.1	873	50
82nd	49	74	0.8	0.5	968	40
164th	21	12	1.3	0.7	476	24

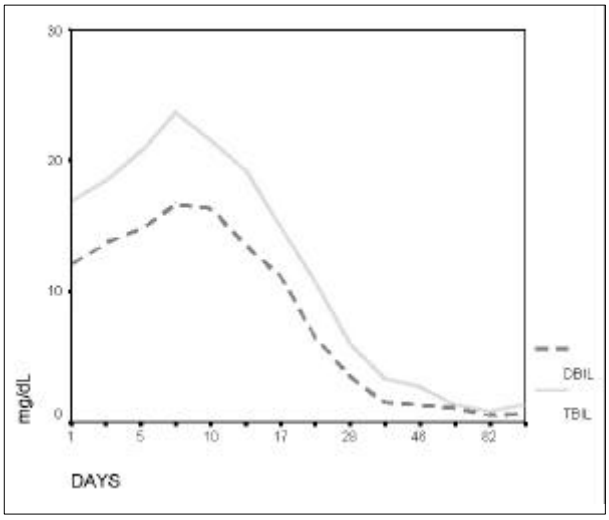

Fig. 1. The course of serum total and direct bilirubin levels of the patient.

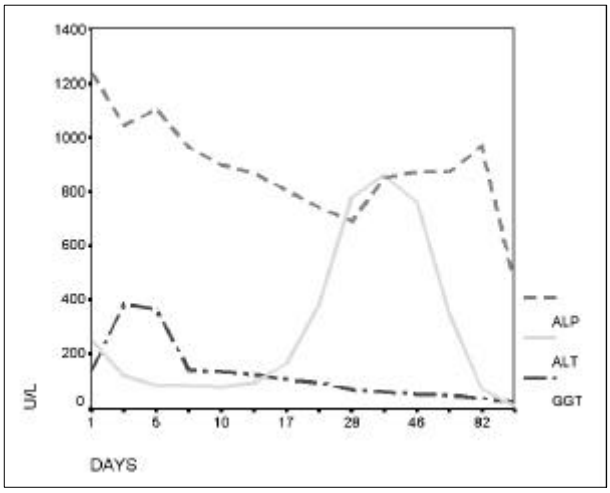

Fig. 2. The course of serum ALP, ALT and GGT levels of the patient.

first phase.[6] The virus is shed during the illness, and patients recover completely within months. A chronic HAV infection does not occur, and the liver enzymes are almost always normal within six months of infection.[3]

In a study comparing the clinical courses of the disease, and the incidence of relapses and protracted forms of the disease, in adults and children, relapses of the disease were reported to be equally frequent (12% vs. 10%), but protracted courses of hepatitis were more frequent in adults (23.5% vs. 10%).[10] In another study, investigating 910 patients with hepatitis A, 93.3% of patients had typical clinical features, with a monophasic course in 3.7%, after an asymptomatic interval of 4-8 weeks, relapsing hepatitis occurred.[4]

In our case, the second phase was also observed approximately 3 weeks after the first. The second phase was clinically milder, but the AST and ALT levels were higher than in the first phase. This may be due to the late admission of patient in the first phase of the illness. Cholestatic hepatitis is an uncommon variant of hepatitis A. In this form, while the transaminases decline toward normal levels, the bilirubin level increase to above 15-mg/dl, and may persist for more than eight weeks. Pruritus may be prominent, and in some patients, persistent anorexia, diarrhoea and weight loss may accompany.[3,11] In the first phase with our patient, while the transaminases were declined, the serum bilirubin level increased to levels as high as 23.7-mg/dl. This cholestatic phase continued for approximately 8 weeks, despite the administration of UDCA. The AST and ALT levels in our patient were re-elevated 3 weeks after the first phase, while the bilirubin levels were normal. Only one adult patient has been reported in the literature to have had a biphasic form of viral hepatitis A, with a combination of two variants, those being the relapsing and cholestatic forms.[5] Describing the patient one month after resolution of the first phase, he was readmitted with jaundice and intense pruritus. During hospitalization, his serum bilirubin level increased to 50.2-mg/dl, with a slight increase in the transaminases. He was treated with UDCA, and later with corticosteroid therapy, resulting in the resolution of symptoms and an improvement of his liver function test after 2 weeks.[5] No corticosteroids were used in our patient. It is known that corticosteroids hasten the resolution, but may predispose the patient to develop a relapse of the hepatitis.[12] We could not find any data showing UDCA administration causing a relapse of hepatitis A, but because our case developed a relapse, while on UDCA, this issue is now in doubt. To our knowledge, this is the first childhood case of such a combination of relapsing and cholestatic hepatitis A. Although the cholestatic form of hepatitis A is rare, it should be kept in mind, that when presenting with the cholestatic form, the

possibility of a relapse can not be excluded. Consequently, we emphasize that the children with the cholestatic form of hepatitis A should be followed with more frequent check-up examinations to avoid missing of a relapse.

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