Case Report

Hepatitis A Virus Infection Induced Prolonged Cholestasis: A Case Report

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ABSTRACT

Introduction: Hepatitis A is one of the most common causes of Viral Hepatitis among children. Children have asymptomatic or mild form of disease. Serious manifestation like cholestatic jaundice is very rare in Hepatitis A infection in young children. There have been some reports of manifestations of childhood Hepatitis A occurring in isolation. In this article a young child with Hepatitis A infection who had cholestatic jaundice is reported. The child had flu like symptoms with nausea, vomiting and loss of appetite. **Methods:** Routine investigations along with LFT (Liver function test) and Hepatitis viral markers were carried out which revealed hyperbilirubinemia suggestive of cholestatic jaundice with Hepatitis A positive. **Conclusion:** This case illustrates the importance of clinicians having a high clinical suspicion for cholestatic jaundice in patients of Hepatitis A infection.

Keywords: Cholestatic jaundice, Hepatitis A, Children, Viral infection, LFT.

Article Information

Received: 28-08-2021

Revised : 07-11-2021

Accepted: 15-02-2022

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INTRODUCTION

Hepatitis A is the most common acute viral hepatitis worldwide.[1]

Acute viral hepatitis due to hepatitis A (HAV) is almost always a mild illness with benign outcome in infants and children.[2] Although the disease is often symptomatic in adults, fulminant form occurs infrequently[2-3] and also is infrequent along with other atypical clinical forms of infection such as relapsing hepatitis, prolonged hepatitis and cholestasis hepatitis.[4-5]

The cholestasis variant is characterized by pruritus and jaundice as well as elevation of serum bilirubin and alkaline phosphatase, whereas aminotransferase activities remain normal.[1]

Physiological bile secretion necessary for bile flow through the biliary tract is maintained by a set of hepatocanalicular proteins transporting major biliary lipids from hepatocytes into the bile canaliculi.[6]

Access this article online

Website: www.jcramonline.com

Quick Response code

DOI: 10.5530/jcram.2.1.5

The composition of phospholipid within the hepatocanalicular membrane is maintained by ATP-binding cassette proteins whereas the nuclear receptor FXR (Farnesoid X receptor) regulates the expression of enzymes and transporters involved in bile salts metabolism. Previous genetic studies demonstrated that dysfunction of their transport protein result in cholestasis disorder[7,8] and several common and rare variants within the transports have been identified as genetic risk factors for cholestasis.[9-10] Carriers of the risk variants develops cholestasis in the presence of additional triggers affecting the expression or function of the transporters destabilizing the liver function i.e drug, hormones, B_{12} or infections.[11-12]

CASE REPORT

A 13 year old boy was presented with Flu like symptoms fever, cough and cold for about a week for which symptomatic treatment was given but there was no improvement seen and about after a week he complained of nausea, vomiting, loss of appetite and loss of weight, than he consulted to the physician. His sclera and skin were jaundiced. A tender hepatomegaly was palpated below the costal margin. He had generalised itching all over the body. For that lab investigation was done. Total Bilirubin (direct and indirect), SGOT (Serum glutamic oxaloacetic transaminase), SGPT (Serum glutamic pyruvic

Table 1: Investigations of patient.

Date	SGOT (U/L)	SGPT (U/L)	GGTP (U/L)	ALP (U/L)	Total Bilirubin (mg/dl)	Bilirubin Direct (mg/dl)	Bilirubin Indirect (mg/dl)	Protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	A:G Ratio
26/11/20	277	777	97	379	11.41	7.57	3.48	6.70	3.48	3.21	1.09
03/12/20	162	207	86	437	16.6	13.7	2.9	8.2	3.8	4.4	0.86
10/12/20	148	122	67	441	20.13	12.6	7.49	7.57	4.11	3.46	1.19
17/12/20	108	91	47	398	17.27	9.37	7.90	7.28	4.22	3.06	1.38
24/12/20	94	62	31	262	14.35	7.69	6.65	7.34	3.99	3.35	1.19
31/12/20	117	71	29	337	13.29	6.92	6.37	7.66	4.18	3.48	1.20
07/01/21	144	111	22	217	7.07	3.52	3.55	7.51	4.34	3.17	1.37
14/01/21	64	65	23	232	3.54	1.55	1.99	7.76	4.30	3.46	1.24
21/01/21	46	55	25	273	1.03	0.65	0.38	7.30	4.80	3.0	1.60

Table 2: Patients Prothrombin time (PT) and INR ratio.

Date	PTINR		
	PT	Prothrombin ratio	INR
07/12/20	13.60sec	1.15	1.15sec
14/12/20	12.60sec	1.07	1.07sec
21/12/20	11.90sec	1.01	1.01sec
28/12/20	12.70sec	1.08	1.14sec
04/01/21	12.30sec	1.04	1.04sec
11/01/21	12.80 sec	1.08	1.08sec
18/01/21	12.90sec	1.09	1.09sec

transaminase), GGTP (gamma-glutamyl transpeptidase), ALP (Alkaline phosphatase), Protein total, Albumin, Globulin, A:G ratio, PT (prothrombin time) INR (international normalized ratio) values are shown in Table 1,2. In the follow up gradually the levels declined. An ultrasonography of abdomen showed no evidence of extrahepatic obstruction. The patient was thought to have the cholestatic form of Hepatitis A. So investigated for Hepatitis A and found to be positive (anti-HAV IgM titre was 9.01) and was non-reactive for HBV and HCV (Hepatitis B and Hepatitis C virus). Because of intense pruritus and high bilirubin levels, ursodeoxycholic acid (UDCA) was started 300 mg once a day for about six WKS along with supportive therapy like adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhea. After about one month the bilirubin levels began to decrease towards normal value and all other hepatic parameters reached towards normal value after about 6-7 wks.

The UDCA (ursodeoxycholic acid) treatment was stopped after all the symptoms disappear and patient started to gain weight and felt better.

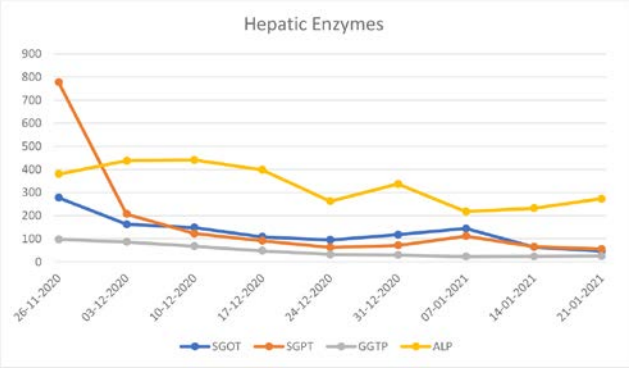

Figure 1: Changes in various hepatic enzymes (IU/L).

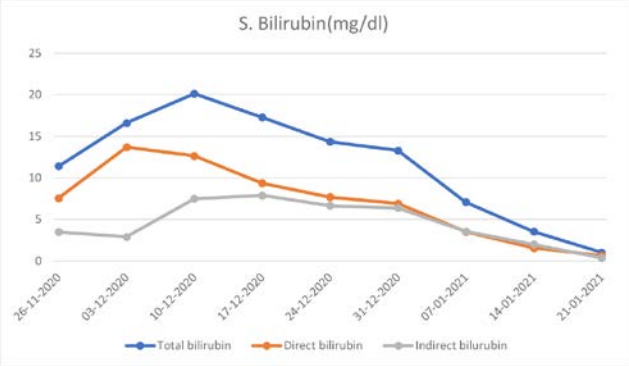

Figure 2: Change in pattern of bilirubin (mg/dl) of the patient.

DISCUSSION

Though Hepatitis A is usually a self-limiting disease, atypical manifestations including prolonged and relapsing course are well known.[13-14] Prolonged cholestasis for a period of up to five to seven months with Hepatitis A has been reported. In a series of 108 children with acute viral hepatitis A, 8.3% showed an

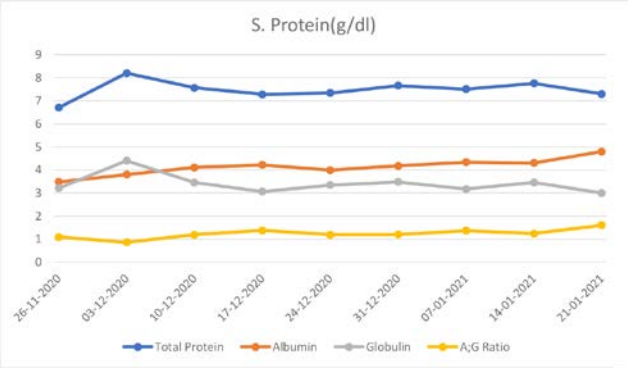

Figure 3: Change in levels of S. Protein (g/dl) of the patient.

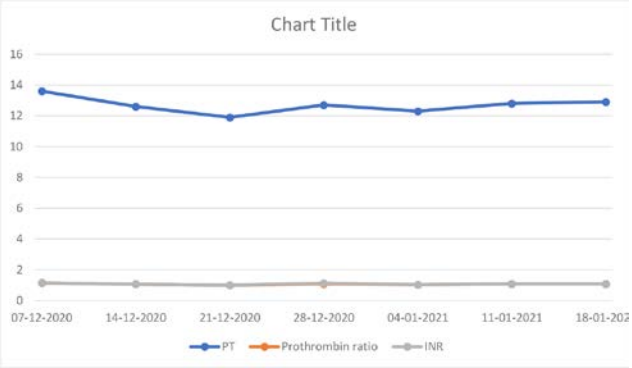

Figure 4: Change in Prothrombin Time (in seconds) and Prothrombin ratio of patient.

atypical course, after a short period of progressive enzyme level normalization relapse occurred.[15] Relapse usually occurs after a short period (usually less than 3 weeks) but clinically milder than the first phase.[16] Chronic HAV infection usually does not occur, and the liver enzymes are almost always normal within 5-6 months of infection.[1]

In one study comparing the clinical courses of disease, incidence of relapses in adults and children were reported to be equally frequent (12% vs 10%).[17] In another study investigating 910 patients with Hepatitis A 93.3% of patients has atypical features.[18]

In our case maximum level of Bilirubin total was 20.13mg/dl, at one month of disease course, after that values of Bilirubin started to decrease gradually and after about 2 months values were reached towards normal levels. Same trend was seen with PT INR value. Values of all the hepatic enzymes reached highest at about one month after that their values started to decrease.

He was treated with UDCA (ursodeoxycholic acid) and other symptomatic treatment was given. No corticosteroids were used in our patient. It is known that corticosteroids hasten the resolution but may dispose the patient to develop relapse of the Hepatitis. We could not find any data showing UDCA (ursodeoxycholic acid) causing a relapse of Hepatitis. Although the cholestatic form of hepatitis A is rare but we should always keep in mind while treating a case of Hepatitis A. We emphasize that children with the Hepatitis A should be examined frequently at regular interval to avoid cholestatic form and relapse.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Koff RS. Hepatitis A. Lancet. 1998;351(9116):1643-9. doi: 10.1016/S0140-6736(98)01304-X, PMID 9620732.
2. Tong MJ, El-Farra NS, Grew MI. Clinical manifestations of hepatitis A: Recent experience in a community teaching hospital. J Infect Dis. 1995;171;Suppl 1: S15-8. doi: 10.1093/infdis/171.supplement_1.s15. PMID 7876641.
3. Lednar WM, Lemon SM, Kirkpatrick JW, Redfield RR, Fields ML, Kelley PW. Frequency of illness associated with epidemic hepatitis A virus infections in adults. Am J Epidemiol. 1985;122(2):226-33. doi: 10.1093/oxfordjournals.aje.a114093, PMID 3860002.
4. Yao G. Clinical spectrum and natural history of viral hepatitis A in a 1988 Shanghai epidemic. In: Hollinger FB, Lemon SM, Margolis H, editors Viral hepatitis and liver disease. Baltimore: Williams and Wilkins1991. p. 14-20.
5. Sagnelli E, Coppola N, Marrocco C, Onofrio M, Scarano F, Marotta A, *et al*. HAV replication in acute hepatitis with typical and atypical clinical course. J Med Virol. 2003;71(1):1-6. doi: 10.1002/jmv.10455, PMID 12858402.
6. Kullak-Ublick GA, Beuers U, Paumgartner G. Hepatobiliary transport. J Hepatol. 2000;32(1);Suppl:3-18. doi: 10.1016/s0168-8278(00)80411-0, PMID 10728790.
7. Stieger B, Geier A. Genetic variations of bile salt transporters as predisposing factors for drug-induced cholestasis, intrahepatic cholestasis of pregnancy and therapeutic response of viral hepatitis. Expert Opin Drug Metab Toxicol. 2011;7(4):411-25. doi: 10.1517/17425255.2011.557067, PMID 21320040.
8. Müllenbach R, Lammert F. An update on genetic analysis of cholestatic liver diseases: Digging deeper. Dig Dis. 2011;29(1):72-7. doi: 10.1159/000324137, PMID 21691109.
9. Müllenbach R, Linton KJ, Wiltshire S, Weerasekera N, Chambers J, Elias E, *et al*. ABCB4 gene sequence variation in women with intrahepatic cholestasis of pregnancy. J Med Genet. 2003;40(5):e70. doi: 10.1136/jmg.40.5.e70, PMID 12746424.
10. Stapelbroek JM, Van Erpecum KJ, Klomp LW, Houwen RH. Liver disease associated with canalicular transport defects: Current and future therapies. J Hepatol. 2010;52(2):258-71. doi: 10.1016/j.jhep.2009.11.012, PMID 20034695.
11. Bijleveld CM, Vonk RJ, Kuipers F, Havinga R, Fernandes J. Benign recurrent intrahepatic cholestasis: A long-term follow-up study of two patients. Hepatology. 1989;9(4):532-7. doi: 10.1002/hep.1840090404, PMID 2925156.
12. Summerfield JA, Scott J, Berman M, Ghent C, Bloomer JR, Berk PD, *et al*. Benign recurrent intrahepatic cholestasis: Studies of bilirubin kinetics, bile acids, and cholangiography. Gut. 1980;21(2):154-60. doi: 10.1136/gut.21.2.154, PMID 7380339.
13. Purcell RH, Emerson SU. Natural history and experimental models. In: Thomas HC, Lemon SM, Zuckerman AJ, editors. Viral hepatitis.3rd ed. Malden,mass: Blackwell Pub; 2005. p. 109-25.
14. Coppola N, Genovese D, Pisaturo M, Taffon S, Argentini C, Pasquale G, *et al*. Acute hepatitis with severe cholestasis and prolonged clinical course due

to hepatitis A virus Ia and Ib coinfection. Clin Infect Dis. 2007;44(9):e73-7. doi: 10.1086/513430. PMID 17407028.

15. Mondello P, Patti S, Pecoraro G, Portelli V, Cascio G, Spano C. Diphasic or prolonged course of viral hepatitis A in children. Boll Sieroter Milan1985;64. 1985;64(6):443-6. PMID 3006727.
16. Glikson M, Galun E, Oren R, Tur-Kaspa R, Shouval D. Relapsing hepatitis A. Review of 14 cases and literature survey. Med (Baltim). 1992;71(1):14-23. doi: 10.1097/00005792-199201000-00002, PMID 1312659.
17. Stránský J, Honzáková E, Vandasová J, Kyncl J. A relapsing and protracted form of viral hepatitis A: Comparison of adults and children. Vnitr Lek. 1995;41(8):525-30. PMID 7483334.
18. Jelic 0, Fornet-Sapcevski J, Kovacevic L, Pandak N, Jelic D. Recurrences of viral hepatitis A. Acta Med Iugosl1990;44:565-76.

Cite this Article : Kushwaha V, Agrawal P, Shukla V. Hepatitis A Virus Infection Induced Prolonged Cholestasis: A Case Report. J. Clin. Res. Applied Med. 2022;2(1):15-8.