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RESISTANT AND PROLONGED HYPOGLYCEMIA COMPLICATING THE COURSE OF SEVERE ACUTE HEPATITIS A : A CASE REPORT

Paediatrics

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ABSTRACT

Acute liver failure (ALF) is a severe and acute liver injury which presents infrequently. Hepatitis A virus (HAV) occurs commonly in resource poor regions like India. It is one of the commonest cause of acute hepatitis in India, but rarely progressed to ALF. Hypoglycemia in association with liver disease has generally been considered as uncommon entity occurring primarily in circumstances of rapid massive hepatic necrosis. Previous retrospective studies had emphasized rarity of hypoglycemia in viral hepatitis. We present a case of 2 year boy who developed resistant and prolonged hypoglycemia secondary to Hepatitis A induced acute liver failure. Along with difficult to manage hypoglycemia his disease was also complicated with Hepatic encephalopathy and prolonged cholestatic Jaundice. He had a stormy hospital course but survived without Sequelae. We report this case with the aim to raise awareness about this rare but fatal metabolic complication of Hepatitis A infection as viral hepatitis has become a global health-care problem.

KEYWORDS

Hypoglycemia, Hepatitis A, Hepatic encephalopathy, Gluconeogenesis, Glycogenolysis

OBJECTIVE

Hepatitis A is the most common form of acute viral hepatitis in the world[1] especially in endemic areas with poor sanitation infrastructure.[2] It is estimated that hepatitis A virus (HAV) infects approximately 1.4 million persons per year globally[3] and remains one of the most common and rampant causes of acute viral hepatitis in children.[4] The disease spectrum of HAV infection is wide ranging from an asymptomatic self-limited infection to a life-threatening and fulminant hepatitis.[5] Fulminant Hepatic Failure (FHF) or acute liver failure (ALF) is defined as "the rapid development of hepatocellular dysfunction, specifically coagulopathy and mental status changes (encephalopathy) in a patient without known prior liver disease.[1]

The importance of the liver in blood glucose homeostasis has long been recognized but hypoglycemia in viral hepatitis is not reported commonly. Furthermore, in the cases in which hypoglycemia has been reported, the mechanisms responsible for disordered blood glucose regulation have not been established. Failure of glycogen synthesis" and hyperinsulinism resulting from inadequate hepatic insulin degradations have been postulated, but have not been systematically evaluated. Little information is available regarding possible alterations in gluconeogenesis. This is probably the first report from our region regarding prolong and resistant hypoglycemia in a child suffering from Hepatitis A. This report highlights the critical role of hepatitis A vaccination and argues for consideration of its inclusion in the national vaccination program in order to avert similar devastating consequences of yet another vaccine preventable disease.

CASE PRESENTATION

A 2 year-old boy presented to pediatric emergency department, NIMS Medical college, Jaipur with history of high grade fever for 15 days, yellowish discoloration of skin and urine for 12 days, recurrent non bilious vomiting for 2 days and irritability for 1 day. There was no abnormal body movement, bleeding, breathing difficulty. Past history was not significant. Her mother had similar illness 1 month back for which symptomatic treatment was taken and recovered. On examination, there was deep icterus with pitting edema over feet. He was drowsy but arousable on admission.

His deep tendon reflexes were brisk . There was hepatomegaly as liver was palpable 3 cm below subcostal margin. Initial impression of acute viral hepatitis was made. His laboratory workup showed hemoglobin 8.1 g/dl , total leukocytes count 19400/mm^3 with 62% lymphocytes, and normal thrombocyte count. His clotting parameters were severely deranged with INR of 4.99.

His transaminases were elevated ALT 2159 IU/L, AST 1302 IU/L . His serum bilirubin levels were markedly elevated TSB 25.7 mg/dl, DSB 22.7 mg/dl . His creatinine and electrolytes were normal. CRP and Procalcitonin level were also in normal range. USG abdomen was done which showed Hepatomegaly (Liver span 10.5 cm) with increased periportal echogenicity, mild spleenomegaly, bilateral mild pleural effusion and mild ascites. Hepatitis A IgM antibody test was done which came positive. Serology for Dengue fever, Malaria and Scrub typhus were negative. Blood test for other viral hepatitis came negative. ANA IFA and Anti LKM antibody test were also done to rule out autoimmune cause of hepatitis which also came negative. Clinical and laboratory findings were suggestive of acute viral hepatitis A with hepatic encephalopathy stage II.

On admission he had severe hypoglycemia (RBS 27 mg/dl) for which dextrose bolus was given and dextrose containing isotonic fluid was started. Initially blood sugar was measured hourly and planned to maintain blood sugar levels > 60 mg/dl. He had recurrent episodes of hypoglycemia for which he required multiple boluses of dextrose with simultaneous increase in glucose infusion rate (GIR) . Central line was placed in right internal jugular vein as he required 14 % dextrose solution and GIR of 12.5 mg/kg/min to achieve euglycemia. After 24 hrs of stabilization of blood glucose level we planned to decrease the GIR but patient had episode of hypoglycemia which was managed with dextrose bolus. He required GIR > 12 mg/kg/min for 9 days to maintain blood sugar levels of >60 mg/dl. On every attempt to decrease the GIR; he start to had episodes of hypoglycemia. During this period blood sugar level was measured hourly. After this period he start to hold the blood sugar levels for which dextrose concentration was lowered gradually with introduction of sugar fortified feed. By day 12 of admission he was able to maintain blood sugar level on hepatic diet.

During hospital stay he was managed with IV fluid therapy along with intravenous antibiotic and other supportive treatment. Supportive treatment included N acetyl cysteine infusion, tab ursodeoxycholic acid, tab rifaximin, multivitamin. Vitamin K injection was given for management of coagulopathy.Fresh frozen plasma was not given as he

don't have clinically significant bleeding.

With time laboratory parameters were improved. He was discharged after 14 days of hospitalization in clinically stable condition. At the time of discharge he had total serum bilirubin of 9.5 mg/dl,direct serum bilirubin of 8.4 mg/dl, ALT 198 U/L, AST 332 U/L, INR 1.45. He was discharged on tab ursodeoxycholic acid and multivitamin supplement. He showed full recovery in next 2 wks.

This child presented with acute onset fever, icterus, recurrent vomiting and irritability.

On the basis of clinical features was initially suspected of having a hepatitis. He had signs of hepatic encephalopathy as well. As viral hepatitis is most common cause of hepatic injury in our country so serology for all common viral hepatitis was sent. Among these serology for Hepatitis A came positive in our patient. We observed the typical fulminant course of acute hepatitis A including fever, deep jaundice, severe coagulopathy and hepatic encephalopathy in our patient. However, the development of resistant and prolonged hypoglycemia has not been described in acute viral hepatitis A patients earlier. Usually euglycemia in hepatitis A patients can be easily achieved at GIR of 5 - 7 mg/kg/min but this patient required GIR up to 12.5 mg/kg/min to maintain euglycemia.

Table 1 : Investigations at the time of admission

HB	8.1 g/dl
TLC	19.4 x 103
Platelets	280 x 109
total bilirubin	25.7 mg/dl
direct bilirubin	22.7 mg/dl
alanine aminotransferase (ALT)	2159 u/l
aspartate transaminase (AST)	1302 u/l
PT	48 sec
INR	4.99
blood glucose	27 mg/dl
blood urea nitrogen (BUN)	21mg/dl
Serum creatinine	0.2 mg/dl
Serum.sodium	138 mg/dl
Serum.potassium	4.3 mg/dl
Serum.Calcium	10.6 mg/dl
Serum.Chloride	96 mg/dl
Ammonia	108
Dengue NS1Ag & Serology	Negative
Scrub typhus IgM	Negative
ICT for malaria	Negative
Anti-HAV IgM	Positive
Anti-HCV IgM	negative
Anti-HEV IgM	negative
HBsAg	negative
Serum albumin g/dl	3.0
Serum globulin g/dl	3.7
Lactate dehydrogenase u/L	408
ANA - IFA	Negative
Anti LKM	Negative
IgG	1739

DISCUSSION

HAV usually causes subclinical and mild infection during the childhood. Nonetheless, it can also cause acute liver failure and death both in childhood and adults. Fulminant hepatitis is a rare complication of HAV. HAV contaminates via fecal-oral route and spreads in crowded and unhealthy conditions. The mechanisms responsible for the development of acute liver failure and subsequent fulminant hepatitis in some patients infected with HAV are not clear. However, host factors, virulence and amount of transmitted virus load are claimed to be effective in the pathogenesis.

Genetic predisposition has also been claimed to play a role in the severe course of the HAV; however, it is not well established.[6] It may also be supposed that pathogenicity of some strains of HAV is stronger. However, Fujiwara et al.,[7] recently reported that genotype of HAV is not the main factor that determine the severity of disease during HAV infection. In view of these circumstances, it appears that host factors are main factors affecting the course of the infection. As well, a genetic predisposition might also be considered responsible for the severity.

Common complications of hepatitis A include cholestatic hepatitis, relapsing hepatitis, and autoimmune hepatitis. Extrahepatic complications may include acute kidney injury, autoimmune hemolytic anemia, aplastic anemia, acute pancreatitis, mononeuritis, reactive arthritis, Guillain–Barre syndrome and pleural or pericardial effusion, glomerulonephritis, polyarteritis nodosa, cryoglobulinemia, and thrombocytopenia.[8,9]

Hypoglycemia of such extent that require high concentration of dextrose for prolong duration is not a common complication of hepatitis A. Patients of hepatitis A usually require dextrose containing fluid with usual concentration of 5% dextrose to maintain euglycemia. We could not find any case report in available literature regarding such resistant and prolong hypoglycemia in pediatric population. Lindner W.[10] published a case of 64-year old woman with a histologically confirmed Au-SH antigen negative acute virus hepatitis with an otherwise normal course, an extreme hypoglycemia lasting four days developed and was treated with intravenous glucose drips. In spite of the supply of 130 g/24 hrs glucose on the 2nd day of hypoglycemia, the fasting blood sugar level next morning was 0 mg% ("aglycemia"). The hypoglycemia ran a course without autonomic or psychoneurological symptoms. As the hepatitis regressed, the carbohydrate metabolic disorder regained its equilibrium. Multiple mechanisms has been proposed for hypoglycemia in liver injury patients. Failure of glycogen synthesis, possible alterations in gluconeogenesis and hyperinsulinism resulting from inadequate hepatic insulin degradation have been postulated Felig et al,[11] done study on glucose homeostasis in viral hepatitis. In this study, Fifteen consecutive patients admitted to the University Medical Service of the Yale-New Haven Hospitalwith well documented classic viral hepatitis were studied. In that study hypoglycemia was observed in over 50 per cent of patients with acute viral hepatitis uncomplicated by massive or subacute hepatic necrosis. It was noteworthy that none of the patients that study were severely ill. Furthermore, the occurrence of hypoglycemia in several patients with a normal prothrombin time and serum albumin level indicated that the glucoregulatory role of the hepatocyte may be compromised while other, protein synthetic functions remain unimpaired. Regarding the mechanism of hypoglycemia, there was no evidence of hyperinsulinism as a consequence of inadequate hepatic insulin degradation.

On the contrary, insulin secretion was appropriately reduced in the patients in whom hypoglycemia developed. Liver glycogen content, determined histologically, was markedly reduced in the patients with hepatitis. According to that study, acute viral hepatitis results in serious impairment in hepatic glycogen synthesis and gluconeogenesis and frequently gives rise to fasting hypoglycemia.

Management of hypoglycemia requires dextrose containing IV fluids and frequent monitoring of blood sugar levels. Blood glucose level start to improve once glycogen synthesis and gluconeogenesis restarts. Glucagon had no therapeutic role in management of viral hepatitis induced hypoglycemia.

CONCLUSION

This is likely first report of resistant and prolong hypoglycemia secondary to Hepatitis A infection with a fulminant course in pediatric population. With the passage of time and more awareness, the outcome of fulminant hepatitis A is improving but it still remains a deadly disease. The availability of Hepatitis A vaccination could be the only way to prevent deadly complications of Hepatitis A infection. High index of suspicion and intense monitoring is required to diagnose rare complications in pediatric patients. Supportive care and symptomatic management is the key to manage these type of patients.

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REFERENCES

1. Franco E, Meleleo C, Serino L, Sorbara D, Zaratti L. Hepatitis A: epidemiology and prevention in developing countries. World J Hepatol 2012;4(3):68–73.
2. Patterson J, Abdullahi L, Hussey GD, Muloiwa R, Kagina BM. A systematic review of the epidemiology of hepatitis A in Africa. BMC Infect Dis 2019;19 (1):651.
3. Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of viral hepatitis and preventive strategies. World J Clin Cases 2018;6(13):589– 99.
4. Sood V, Lal BB, Gupta E, Khanna R, Siloliya MK, Alam S. Hepatitis A virus-related paediatric liver disease burden and its significance in the Indian subcontinent. Indian Pediatr 2019;56(9):741–4.
5. Lemon SM, Ott JJ, Van Damme P, Shouval D. Type A viral hepatitis: a summary and

update on the molecular virology, epidemiology, pathogenesis and prevention. J Hepatol 2017;68(1):167–84.
6. Brown GR, Persley K. Hepatitis A epidemic in the elderly. South Med J 2002;95:826–33.
7. Fujiwara K, Yokosuka O, Fukai K, Imazeki F, Saisho H, Omata M. Analysis of full-length hepatitis A virus genome in sera from patients with fulminant and selflimited acute type A hepatitis. J Hepatol 2001;35:112–9.
8. Jeong S., Lee H. Hepatitis A: clinical manifestations and management. Intervirology. 2010;53(1):15–19. doi: 10.1159/000252779.
9. Amarapurkar D. N., Amarapurkar A. D. Extrahepatic manifestations of viral hepatitis. Annals of Hepatology. 2010;1(4):192–195.
10. Lindner W. Hypoglykämie-Aglykämie bei Virushepatitis [Hypoglycemia - aglycemia in virus hepatitis (author's transl)]. MMW Munch Med Wochenschr. 1975 May 16;117(20):855-60. German. PMID: 806000.
11. Felig P, Brown WV, Levine RA, Klatskin G. Glucose homeostasis in viral hepatitis. N Engl J Med. 1970 Dec 24;283(26):1436-40. doi: 10.1056/NEJM197012242832604. PMID: 5481777.