DOI: 10.34172/mejdd.2022.268

Acute Kidney Injury as a Rare Complication of Acute Hepatitis E in a Child; A Case Report

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Received: 10 Nov. 2020
Accepted: 07 May 2021
Publieshed: 30 Jan. 2022

ABSTRACT

Hepatitis E virus (HEV) infection is a significant public health problem, which infects 20 million individuals every year. The clinical presentation of acute HEV infection is similar to hepatitis A virus (HAV) infection, and few affected children may progress to develop acute liver failure. Extrahepatic manifestations involving other systems have been reported with acute and chronic HEV genotype 3 infections both in adults and children. Herein we report acute kidney injury as a rare complication of acute hepatitis E in a child who recovered with a medical line of management.

KEYWORDS:
Hepatitis E virus; Extrahepatic manifestations; Acute kidney injury

Please cite this paper as:
Kumar K. J, Velamala S, Kumar k, Manjunath VG. Acute Kidney Injury as a Rare Complication of Acute Hepatitis E in a Child; A Case Report. *Middle East J Dig Dis* 2022;**14**:141-144. doi: 10.34172/mejdd.2022.268.

INTRODUCTION

Throughout the world, hepatitis E virus (HEV) infection is a significant public health problem, which infects 20 million individuals every year, leading to symptomatic hepatitis E in 3.3 million cases.[1] Hepatitis E led to approximately 44000 deaths in 2015, which accounted for 3.3% of the mortality due to viral hepatitis.[1] Four genotypes of HEV have been reported to infect humans.[2] HEV genotypes 1 and 2 are responsible for endemic and sporadic cases with a high mortality rate among pregnant women (25%) and subjects with pre-existing liver cirrhosis.[2]

The clinical presentation of acute HEV infection resembles hepatitis A virus (HAV) infection, and few affected children may progress to develop acute liver failure.[2] Extrahepatic manifestations such as neurological disorders, acute pancreatitis, severe thrombocytopenia, hemolytic anemia, and the haemophagocytic syndrome are known to be associated with acute and chronic HEV genotype 3 infections both in adults and children.[2,3] However, the association of kidney injury with HEV infection is rare. Herein we report thrombocytopenia and acute kidney injury in a 3-year-old child caused by HEV infection.

CASE REPORT

A 3-year-old girl was brought to us for a fever of 8 days duration. She also had vomiting and loose stool during the previous 4 days. She had developed facial puffiness since 3 days earlier. Jaundice was noticed a day prior to her visit to us. On admission, her temperature was 98.6^{0}F, respiratory rate 24/minute, pulse rate 100/minute, and blood pressure (BP) 100/60 mmHg. Examination revealed icterus and bilateral pedal edema. Abdomen was distended. Further examination revealed a palpable liver measuring 3 cms, which was soft in consistency, and the border was smooth.

She was neurologically compromised with drowsiness and intermittent irritability. Her investigations done after admission are shown in table 1.

Clinical history, examination findings, and initial investigations prompted a provisional diagnosis of viral hepatitis with acute kidney injury (AKI).

Management was on the conservative line. Her urine output was 2 mL/kg/hour. Medical management included injection of cefotaxime, N acetylcysteine intravenous infusion, oral rifaximine, vitamin K, lactulose, and colonic wash. AKI was managed conservatively according to the protocol, which included 400 mL/m^2 of 5% dextrose per day plus replacing urine output with half normal saline per day.

24 hours after initiating treatment, her urine output improved to 2.8 mL/kg/hour. However, her blood pressure consistently remained above 95th percentile for age and sex, which was treated with oral nifedipine. There was

Table 1: Investigations At admission abdominal sonography revealed Hepatomegaly of 11cm with normal echotexture, normal size spleen with tiny hypoechoic nodules scattered throughout spleen and minimal ascitis. After 7 days abdominal sonography was normal. Her Echocardiography & chest x-ray was normal. Her urine for albumin and sugar was negative; microscopy normal (3 times). Her blood culture was sterile.Hepatitis E [anti HEV] serology tested positive and Hepatitis A, B, C were negative. Her dengue serology NS1 and IgM was negative.Her Widal, Weil-Felix, HIV and Leptospira serology was negative. Her complement C3 was normal

Investigations	1st day	2nd day	3rd day	4th day	5th day	6th day	8th day	9th day	15th day
Hemoglobin [g/dl]	11.7	11	11		10.8	10.3	10.2		
PCV (%)	34.1	32.9	33.7		31.1	31.3	30.7		
TLC [cells/mm^3]	5580	5520	4090		6650	6620	13050		
Platelet count [cells/mm^3]	1.39 Lakh	1.45 Lakh	1.43 Lakh		1.11 Lakh	84,000	90000		
CRP [U/L]	2					4.5			
Serum Bilirubin/ Direct[mg/dl]	3.68/3.34				2.84/2.12	1.93/1.8			1.14/0.94
SGOT(U/L)	1660		510		152	91			57
SGPT(U/L)	4752		3175		1608	998			104
PT[seconds]/INR	24.9/1.91		18/1.3		14.3/0.98				
APTT[seconds]	46.2		34.8		37.4				
Serum total protiens[gm/dl]	5.4				5.6	5.6			
Serum Albumin [gm/dl]	3.1				3.5	3.5			
Blood urea[mg/dl]	69	69	60	50	42	38		34	23
Serum creatinine [mg/dl]	2.1	2.2	2	1.4	1.1	0.9	0.7	0.7	0.7
Sodium [mEq/L]	128	135	134	136	132	140		139	134
Potassium[mEq/L]	4	4	3.1	3.0	3.4	3.3		5.5	4.8
Creatine Kinase (CK-Nac) [U/L]		58							

an apparent increase in abdominal girth for the next 48 hours, and the sensorium remained the same. Clinical improvement was noted after 72 hours of treatment. Her sensorium improved, and ictrus decreased. She regained her appetite. Her kidney function normalized, and BP was controlled with oral nifedipine. She was ambulatory and eating well by the 5th day after admission. By then, urine output had improved to 5 mL/kg/hour, and her edema decreased. She was discharged on the 10th day with oral nifedipine and was followed up by her family physician. She had her antihypertensive tapered and discontinued by 3 weeks post-admission to our unit. She was regularly followed up for blood pressure in our unit for 6 months. Her blood pressure and renal functions remained within normal limits (blood urea = 24 mg/dL, serum creatinine = 0.5 mg/dL) and hence completely discharged from further follow-up.

DISCUSSION

HEV infection in children is clinically similar to hepatitis A infection. However, few patients may develop acute liver failure.[2] Various extrahepatic manifestations due to HEV have been reported both in adults and children.[2,3] The exact mechanism responsible for extrahepatic manifestations is not clear. At times, these extrahepatic manifestations can overshadow the liver injury, and HEV may not be suspected.[2] Acute HEV infection can rarely cause AKI.[4] Acute hepatitis and renal function impairment related to HEV infection have been reported in a renal allograft recipient.[5] Severe hyperbilirubinemia and acute renal failure (ARF) have been reported in a patient with HEV that responded to hemodialysis.[6] However, renal biopsy was not done in both these cases. Verschuuren and colleagues reported non-oliguric ARF associated with HEV due to acute tubular necrosis in an immunocompetent patient.[7] A study from France showed that during HEV infection, there was a significant decrease in estimated glomerular filtration rate (eGFR) in both kidney and liver transplant patients. The authors noted a statistically significant but clinically non-significant decrease of eGFR (-5 mL/min) in 51 transplant patients during the acute phase of HEV infection genotype 3. Glomerular diseases were observed in kidney biopsies obtained during the acute and chronic phases. These included membranoproliferative glomerulonephritis and relapses in IgA nephropathy. Most of the patients had cryoglobulinemia that became negative after HEV clearance. Kidney function improved, and proteinuria decreased after HEV clearance. In HEV infection spectrum, renal injury included membranoproliferative glomerulonephritis, membranous nephropathy, relapsing IgA nephropathy, and nephroangiosclerosis, which most of them occurred in immunosuppressed patients.[8] The mechanism of HEV-induced kidney disease could be immune-mediated similar to that with HCV infection.[3] HEV RNA and HEV antigens were detected in the urine of patients, as well as in the urine of monkeys and rabbits that were chronically infected with HEV.[3] Causes of renal failure in liver disease are most often due to hepatorenal syndrome or acute tubular necrosis. Most often, in hepatorenal syndrome, oliguric renal failure is seen, and renal function restores simultaneously with hepatic function.[7] Another cause is acute glomerulonephritis, as seen in hepatitis B.

In our reported case, urine output was normal, and renal parameters took more time to normalize compared with the liver function. Verschuuren and others reported non-oliguric acute renal failure associated with hepatitis E due to acute tubular necrosis of unknown origin[7]. Similar to this case, our patient was also in the non-oliguric phase at presentation, and urine output increased (polyuric) by the 5th day. However, we did not perform a kidney biopsy to prove this. Another possibility of AKI may be due to acute glomerulonephritis as the patient developed hypertension, which persisted for a longer period. However, her urine microscopy was normal, and her complement levels (C3) were within normal range. HEV infection has been associated with thrombocytopenia. Woolson and co-workers found that out of 106 HEV-infected patients, 12 had thrombocytopenia.[3,9]

To conclude, even though HEV infection is often asymptomatic, the spectrum may range from mild hepatitis to fulminant liver failure and to extrahepatic manifestations like AKI and thrombocytopenia.

ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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