Successful use of intravenous N-acetylcysteine in dengue haemorrhagic fever with acute liver failure

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Introduction

Mild hepatic dysfunction in dengue haemorrhagic fever is not unusual. However, acute liver failure (ALF) is rare. When present, its management according to most current guidelines is supportive and carries a poor prognosis. We present a patient with dengue haemorrhagic fever complicated acute liver failure and hepatic encephalopathy who was successfully treated with N-Acetylcysteine (NAC) leading to complete recovery.

Case report

A 52-year old hypertensive patient was transferred to intensive care unit from a private health care facility for management of suspected dengue haemorrhagic fever. She had a history of fever for five days associated with severe postural giddiness, mild shortness of breath, headache, abdominal pain, nausea and vomiting. She did not have mucosal bleeding. On examination she was drowsy, febrile, dyspnoeic and moderately icteric. There were generalised flushing and flapping tremors. She had a blood pressure of 170/90 mmHg, pulse rate of 118 mn with warm peripheries and a capillary refilling time of < 2 seconds. Her respiratory rate was 24 breaths per minute and breath sounds were diminished bilaterally in the lower zones with stony dull percussion note. Her oxygen saturation (SaO_2) was 93 % on room air. She had clinical evidence of ascites with right hypochondrial tenderness. A clinical diagnosis of severe dengue haemorrhagic fever with hepatic encephalopathy was made.

Summary of investigations are given in Table 1.

Chest X-ray showed right sided pleural effusion. Ultrasound scan (USS) of the abdomen revealed bilateral pleural effusions, a small amount of peritoneal fluid and evidence of hepatitis. ECG showed generalised T inversions suggestive of myocarditis but troponin I was negative. Subsequently dengue IgG and IgM antibodies became positive.

Table 1. Summary of investigations

Day after onset of fever	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*
Day of NAC		*D1*	*D2*	*D3*	*D4*	*D5*	*D6*	*D7*	*D8*
Hb (g/dl)	13.8	13.2	10.6	10.5	10.2	10.3	11	10.8	10.2
PCV %	39%	36	33.2	31	32	36	39	37.5	35.9
Platelet (10^3/µl)	5	23	50	31	56	73	83	96	145
WBC (10^3/µl)	22	23	21.7	16.2	9.2	8.3	6.46	5.26	5
SGPT (IU/l)		1857	2086	1457	1059	757	455	380	273
SGOT (IU/l)		90.4	179	3249	1593	672	319	250	153
S.Bilirubin (µmol/l)			92	78	22	4.8			
PT/INR		1.71	1.24	1.06	1.13	0.97	0.98	0.96	0.98
S.Creatinine (µmol/l)		105	94	82	68	60	55	48	50

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Treatment was initiated according to national dengue management guidelines [1]. Intravenous thiamine, oral metronidazole, intravenous vitamin K and broad spectrum antibiotics were given. N-acetyl cysteine (NAC) was initiated on day 6 of fever (just after admission) with the onset of features of hepatic encephalopathy at a dose of 150mg/kg in 100 ml normal saline over 1 hour, 50 mg/kg in 200 ml normal saline over 4 hours and 150 mg/kg in 500 ml normal saline over 24 hours for 3 days. For each 500 ml of normal saline 50ml of 50% dextrose was added to supplement the failing liver. Patient's general condition improved dramatically over the next few days and had a complete recovery. She was sent home 10 days following admission with all parameters returning to normal levels.

Discussion

There are only a few reported cases of acute liver failure complicating dengue fever and of that only few patients had shown complete recovery [2,3]. The mechanism of hepatic involvement and hepatocyte damage in dengue fever is poorly understood. The histopathological findings of fulminant hepatitis associated with dengue haemorrhagic fever is often characterised by hepatocellular necrosis, typically localising to zone 2 of the hepatic plate, a pauci-cellular inflammatory infiltrate and fatty changes. Councilman bodies are frequently present and may represent necrosis around virparticles [4]. It is well established that most viral infections cause damage by an interplay of direct infection and concomitant host response, evidenced by up-regulation of cytokine production, notably TNFα, IL-2, IL-6, IL-8 and other chemicals [5].

Despite the severity of the problem, no specific treatment is recommended in liver failure associated with dengue haemorrhagic fever. There are isolated reports of rapid improvement in the biochemical profile and encephalopathy with molecular adsorbent recirculating system [6]. Liver transplantation is difficult because of haemodynamic instability, bleeding manifestations and organ dysfunction caused by the infection itself, and may not be a treatment option in most countries where dengue is prevalent.

There are a few studies with successful use of N-acetylcysteine in non-acetaminophen induced acute liver failure including dengue fever [7, 8, 9]. NAC may benefit patients with nonacetaminophen induced acute liver failure by improving systemic haemodynamics, by tissue oxygen delivery or via other favourable effects on the acutely injured liver. The benefit is seen when NAC is used in the early stages of liver failure but not when it is advanced [8, 9].

This patient presented with dengue haemorrhagic fever with acute liver failure and grade 2 hepatic encephalopathy. Early initiation of NAC was undertaken and improvement of general well being, liver enzymes and PT/INR were evident by day 4 after starting NAC. This indicates that NAC has had an effect on improvement of liver failure in this patient. The use of NAC in liver failure associtated with dengue fever needs further studying. Until this evidence is available it seems a safe and effective option.

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