

N-acetylcysteine in children with acute liver failure complicating dengue viral infection

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(Index words: dengue shock syndrome, encephalopathy)

Abstract

Objectives To describe the outcome after administration of N-acetylcysteine (NAC) to seven children with non-paracetamol induced acute liver failure (ALF) complicating dengue infection.

Methods Clinical records of children with non paracetamol induced acute liver failure complicating severe dengue viral infection, were retrospectively analysed for clinical and biochemical outcome following treatment with NAC.

Results Seven patients between ages six months to twelve years with plasma leakage and circulatory compromise complicating dengue infection developed ALF. Three were exposed to prolonged shock prior to hospitalisation. NAC infusion (100 mg/kg) was administered as soon as ALF was diagnosed, based on low GCS scores, raised transaminases and prolonged prothrombin/INR. Full clinical and biochemical recovery occurred in all patients.

Conclusions A successful outcome followed early administration of NAC to children with ALF complicating severe dengue infection.

Ceylon Medical Journal 2013; **58**: 80-82

Introduction

In recent years dengue viral infection has occurred in epidemic proportions in Sri Lanka. In keeping with experience elsewhere, acute liver failure (ALF) ranked high among the organ-specific complications that worsens prognosis [1]. Although case fatality rates in children with dengue infection and ALF is reported to be as high as 50%, its management lacks any specific therapy [2]. The aim of this paper is to describe the clinical course and outcome that followed administration of N-acetylcysteine to seven children with non-paracetamol induced ALF complicating dengue infection.

Methods

Clinical records of seven patients with a clinical diagnosis of dengue haemorrhagic fever or dengue shock syndrome (DHF/DSS) complicated by ALF were retrospectively analysed for outcome following treatment with N-acetylcysteine (NAC). All seven patients were managed in the University Paediatric Unit, Lady Ridgeway Children's Hospital, Colombo between 1 May 2011 and 30 April 2012. All had hepatomegaly, impaired level of consciousness, serum alanine transaminase levels (ALT) > 500 IU/l and prothrombin time / INR > 1.5.

In addition to standard supportive anti-liver failure regime NAC was administered at 100 mg/kg intravenously over 24 hours. In patients who continued to have clinical features of hepatic encephalopathy at the end of the first dose, NAC was continued up to 72 hours. Post treatment clinical and biochemical profiles were analysed for response.

Results

Ages ranged from six months to twelve years. Due to large numbers admitted during outbreaks, serological testing for dengue was not routine; but the four patients tested were all positive. All seven showed evidence of plasma leakage and circulatory compromise fulfilling the diagnostic criteria of DHF/DSS as well as haemorrhagic manifestations. Three required blood transfusions.

On admission to hospital, three patients were in shock and required immediate resuscitation (DHF grade 3 in two, DHF grade 4 in one). Four patients entered the 'critical phase' of plasma leakage whilst in hospital. Shock was averted in these patients with fluid boluses although 'impending shock' (narrowing of pulse pressure to 20 mmHg, cool extremities and low urine output) occurred. Glasgow Coma Scale (GCS) scores were low in all seven although none had received sedatives or paracetamol in excessive doses. Time of onset of drowsiness or confusion from onset of fever was 4 to 6 days. NAC was administered as soon as the diagnosis of ALF was made. Two patients underwent computerised tomography of brain due to focal seizures (1) and severe coma (1); to exclude intracranial haemorrhage.

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Platelet counts dropped to $< 100,000 / \text{mm}^3$ in all seven. Plasma leakage was confirmed with clinical, radiographic or ultra-sonographic evidence of pleural effusions (7), ascites (4), pericardial effusions (1), 20% rise of haematocrit (7), serum albumin $< 3.5 \text{ g/dl}$, (7) and

serum cholesterol $< 100 \text{ mg/dl}$ (2). Worst recorded pretreatment value ranges were: platelet count $54,000 - 5000 / \text{mm}^3$; prothrombin time/ internationalised normalised ratio 1.5 - 1.95, ALT 520 - 3384 IU/l, AST 494 - 13306 IU/l and serum albumin 31 - 26 g/dl .

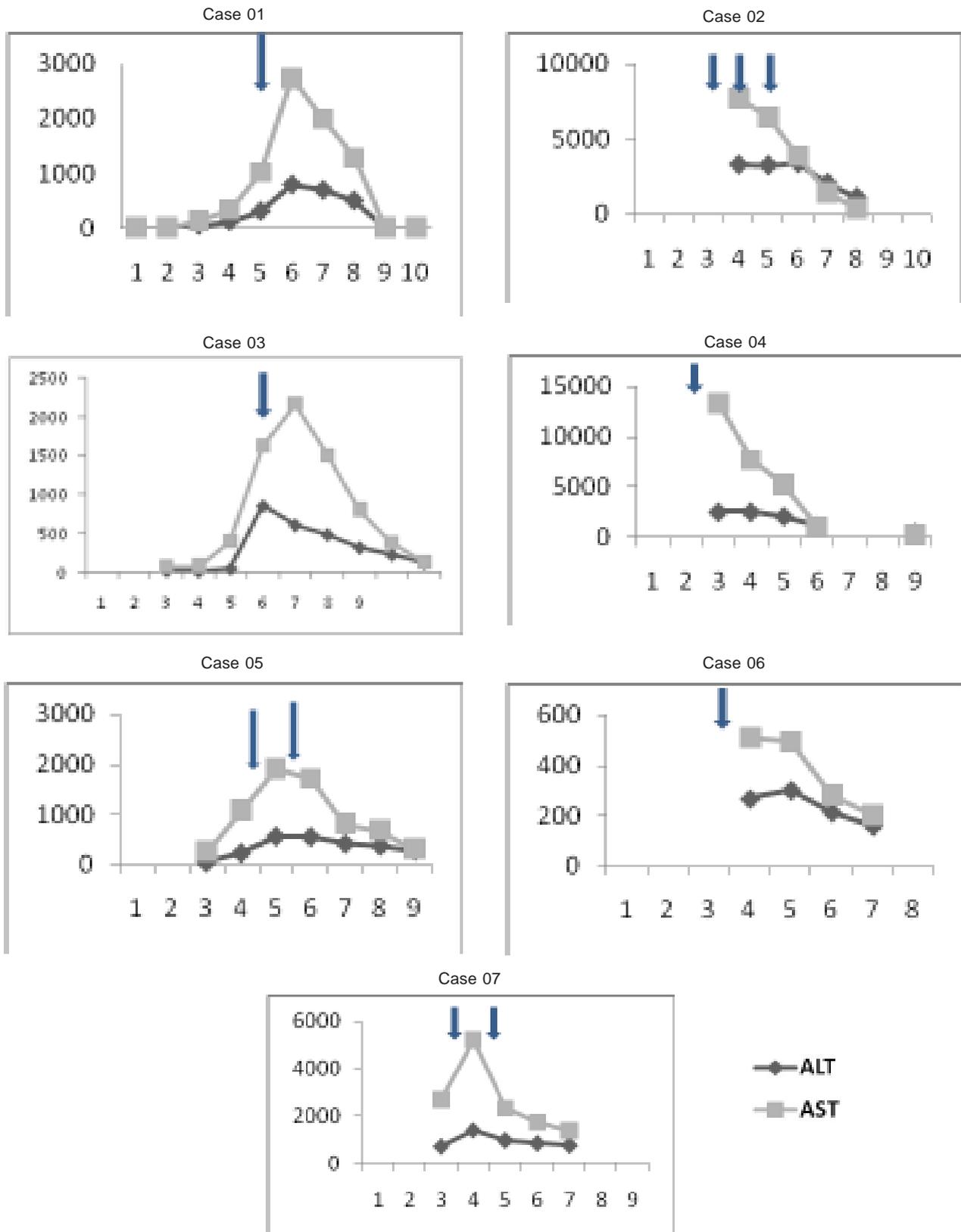


Figure. Profile of liver transaminase levels in relation to day of illness.

Following the first dose of NAC (100 mg/kg over 24 hours) four patients showed rapid clinical improvement of encephalopathy. Remaining three responded after second (2) and third (1) doses. In all seven patients, biochemical profiles showed improvement from first dose onwards (Figure). No side effects of NAC were noted. All seven made complete recovery without residual hepatic or neuro-developmental damage.

Discussion

Mild to moderate elevations in serum amino-transferase levels are common in dengue infections but ALF is a life-threatening complication for which there is no specific therapy and treatment is largely supportive. Cause of ALF in dengue infection is believed to be direct viral damage, dysregulated host-immune response or hypoxic damage [3]. Hypoxic damage is supported by the clinical observation of circulatory collapse which is a common association of ALF. In our series only three patients were exposed to prolonged shock.

NAC is of proven value in children with non-paracetamol induced liver failure. Its successful use in adults with ALF and severe dengue infection has been reported [4]. There is an isolated case report of its successful use in a child with fulminant liver failure

complicating dengue infection [2]. In our series all seven children with ALF and severe dengue infection showed marked biochemical and clinical improvement following treatment with NAC. All patients made a full recovery with no residual liver damage. No adverse effects of NAC were encountered. This case series in a paediatric population supports the clinical observation that early administration of NAC in ALF complicating dengue infection results in a good outcome. We found NAC to be safe in this clinical situation.

References

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Rate of stunting among a sample of postwar resettled families in the Vanni region: a study from the Mullaitivu District

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(Index words: nutritional deficiencies, stunting, chronic malnutrition)

Abstract

The Department of Family Medicine, University of Kelaniya conducted a health camp in Puthukudiyiruppu in March 2011. Height and weight measurements were carried out and data of 303 participants were analysed. The rate of stunting among children below six years in this population was 62% compared to 19.3% nationally. Thirty four percent of children and adolescents (6-18yrs) were underweight and 21.4% of adults had a BMI less than 18.5kg/m².

Ceylon Medical Journal 2013; **58**: 82-83

Introduction

The Department of Family Medicine, Faculty of Medicine, University of Kelaniya organised a health camp and goods donation campaign in Puthukudiyiruppu on 27th of March 2011 with the cooperation of the 14th Battalion of the Singha Regiment of the Sri Lanka Army.

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