

## Case Report

# N-acetylcysteine therapy for ischaemic hepatic failure: a successful antidote

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### ABSTRACT

Acute liver failure (ALF) is characterised by severe liver injury with the onset of coagulopathy (INR  $\geq 1.5$ ) and encephalopathy in the absence of pre-existing liver disease. It is associated with a high mortality rate of 10-57%, which is largely driven by multi-organ failure, sepsis and cardiac arrhythmia. Current management focuses on identifying and treating the aetiology, providing supportive care and monitoring liver function. The use of N-acetylcysteine (NAC) therapy is well-studied in the treatment of paracetamol toxicity but is controversial in other causes of ALF. We reported the first case of ischaemic hepatic failure secondary to prolonged portal vein occlusion treated with 72 hours of NAC therapy. Although ischaemic hepatopathy is a relatively uncommon cause of ALF, it is associated with a high mortality rate. The case highlights how early use of NAC therapy may improve hepatic serology biomarkers and should warrant consideration in ALF secondary to ischaemic hepatopathy.

**Keywords:** NAC, Ischaemic hepatopathy, Acute liver failure

### INTRODUCTION

ALF is characterised by severe liver injury with the onset of coagulopathy (INR  $\geq 1.5$ ) and encephalopathy in the absence of pre-existing liver disease.<sup>1</sup> Although ischaemic hepatopathy is a relatively uncommon cause of ALF, it is associated with greater than 25% mortality.<sup>2</sup> Management involves supportive care, monitoring for evidence of end-organ hypoperfusion and treatment of complications. The use of NAC therapy is well-established in paracetamol-induced ALF, however its effects of improved regional blood flow, anti-apoptotic and antioxidant defences may be beneficial in other forms of ALF.<sup>3,4</sup>

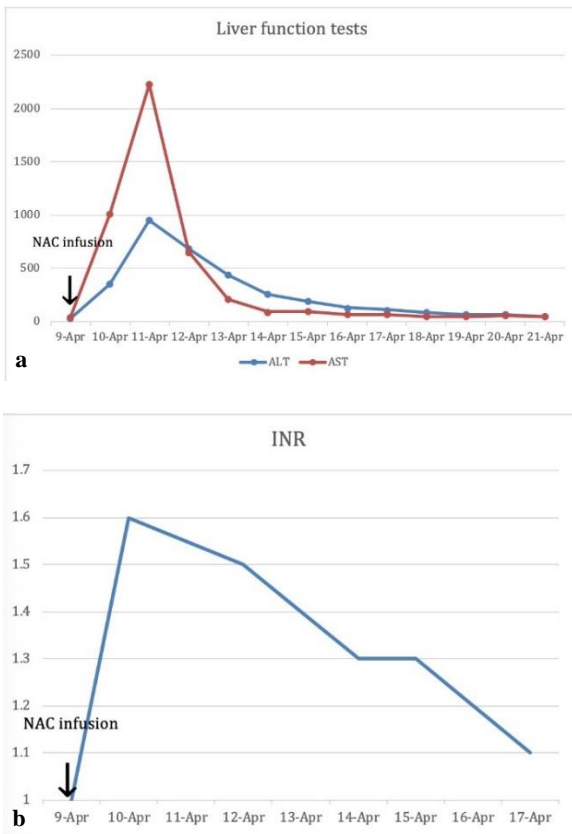
We reported a case of ischaemic hepatopathy secondary to prolonged vascular occlusion that resolved after NAC therapy.

### CASE REPORT

A 75 year old female presented to the emergency department with a one day history of severe epigastric pain and nausea. The pain was crushing in nature with no radiation and her bowel habits were unchanged. Her medical history included type 2 diabetes mellitus, hypertension and dyslipidaemia. On examination she was hypotensive with a systolic blood pressure of 77. Her abdomen was maximally tender in the epigastric region with signs of peritonism. Bedside ultrasound demonstrated free fluid in Morrison's pouch and the pouch of Douglas. An urgent computed tomography (CT) of the abdomen and pelvis demonstrated a ruptured hepatoma in the caudate lobe (Figure 1). She subsequently underwent embolisation of a small branch vessel from the right common hepatic artery and was haemodynamically stable post procedure.



**Figure 1: CT abdomen demonstrating patchy density adjacent to caudate lobe of the liver, likely ruptured hepatoma.**



**Figure 2: (a) Trend of liver function tests throughout admission; (b) Trend of INR throughout admission.**

The patient was discussed at the upper gastrointestinal multidisciplinary meeting and subsequently underwent an open resection of the caudate lobe. Intra-operatively, an inadvertent hole was made in the IVC due to the challenging nature of an oncological caudate lobe resection. We successfully achieved both inflow and outflow control by initiating a pringle manoeuvre to occlude the portal vein, hepatic artery as well as proximally and distally clamping the IVC. An occlusion time of 90 minutes was required to adequately repair the

IVC injury with interrupted prolene sutures. There was 4.5 l of intraoperative blood loss requiring activation of the massive transfusion protocol. The patient was subsequently admitted to the intensive care unit.

Post-operatively, the arterial blood gas demonstrated severe lactic acidosis, pH=6.92, lactate=10.3, pCO<sub>2</sub>=60, HCO<sub>3</sub>=12. Serum biochemistry showed deranged liver function tests (LFTs): AST=1012, ALT=348, GGT=143 and coagulation studies showed INR=1.6.

In the ICU, she remained intubated with ventilatory support and inotropes to maintain a mean arterial pressure >65. In view of her prolonged hepatic ischaemia, she was commenced on an NAC infusion, with 17 g in 500 ml of 0.9% normal saline running at 125 ml/hour followed by continuous bags of 8.5 g in 1000 ml of 0.9% normal saline running at 62.5 ml/hour for the remainder of the total 72 hours.

The patient's AST and ALT peaked at 72 hours and slowly improved over the course of her admission (Figure 2a). On post-operative day 9, her LFTs and INR were close to baseline (Figure 2b). She was discharged 12 days later.

## DISCUSSION

Ischaemic hepatitis is present in 1-2.5% of ICU admissions and is associated with a high in-hospital mortality between 25-50%.<sup>2,4,5</sup> Decreased perfusion of approximately 15-20 minutes is sufficient to cause hepatocyte necrosis.<sup>6,7</sup> In our case report, there was intermittent portal clamping for a total of 90 minutes due to difficulty gaining haemostasis from the iatrogenic IVC injury.

The main mechanism of NAC therapy in paracetamol-induced liver injury is the replenishment of glutathione.<sup>8,9</sup> It also scavenges free oxygen radicals that cause both direct and indirect injury which may explain its effectiveness in hepatocyte ischaemia.<sup>6</sup> Various trials have suggested that NAC has inotropic and vasodilating effects which improve hepatosplanchnic blood flow and therefore would theoretically assist reperfusion in ischaemic hepatopathy.<sup>8,10,11</sup> Singh et al conducted a prospective, double blinded trial which demonstrated improved transplant-free survival after 72 hours of NAC therapy for patients with non-paracetamol induced ALF.<sup>12</sup> Furthermore, in the patient population treated with NAC therapy, improvements in hepatic markers were seen within the first 4 days. This is reflected in our patient's LFTs which peaked on day 3 and progressively improved towards baseline function. In a review of six prospective studies, Amjad et al demonstrated reduced overall mortality and length of hospital stay in non-paracetamol induced ALF treated with NAC therapy.<sup>13</sup> There are a number of case reports describing the successful use of NAC therapy in ischaemic hepatopathy, but currently no secondary to prolonged vascular occlusion.

Currently, there is a protocol for a Cochrane review to determine the benefits of NAC versus placebo in non-paracetamol induced ALF.<sup>3</sup> Our case report suggests its successful use in ischaemic hepatopathy secondary to prolonged vascular occlusion. Furthermore, NAC is easily administered and is generally well-tolerated with minimal side effects.<sup>14</sup>

NAC therapy should thus be considered in ischaemic hepatopathy due to its possible benefits of improved hepatosplanchnic blood flow and free oxygen radical elimination as well as improved hepatic serology biomarkers.

## CONCLUSION

Ischaemic hepatopathy is a relatively uncommon cause of acute liver failure but is associated with a high mortality rate. Administration of NAC therapy has demonstrated reduced mortality and length of hospital stay. Hence, consideration of early administration of NAC therapy is warranted given its possible benefits, accessibility and minimal side-effects.

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