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Acute Liver Impairment in a Young, Healthy Athlete: Hypoxic Hepatitis and Rhabdomyolysis following Heat Stroke

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Key Words

Hypoxic hepatitis · Ischaemic hepatitis · N-acetyl cysteine · Rhabdomyolysis

Abstract

Any process that substantially diminishes arterial blood flow or arterial oxygen content to the liver can result in hypoxic (ischaemic) hepatitis. 90% of hypoxic hepatitis occurs in unstable patients in intensive care units with haemodynamic failure secondary to heart failure, respiratory failure and toxic shock. The rate of in-hospital mortality in hypoxic hepatitis is very high with studies recording mortalities of 61.5%. It tends to be very uncommon in healthy, young patients with no underlying medical problems. We report here the case of a young healthy athlete who developed heat stroke associated with rhabdomyolysis and hypoxic hepatitis while he was running the final stages of a marathon. The patient required intensive care admission and inotropic support for a few hours after he was admitted with heat stroke. He underwent a rapid recovery after he was resuscitated with fluids. N-acetyl cysteine was also given during the acute stage of the hepatitis. This case highlights an uncommon case of hypoxic hepatitis in a young, healthy patient secondary to hypotension and heat stroke. Inotropic support might have precipitated the hypoxic hepatitis in this young patient.

Introduction

The liver receives nearly 30% of the total cardiac output with 70% of the total hepatic blood flow passing through the portal venous system and 30% passing through the hepatic arterial system. More than half of the oxygen supply to the liver is delivered by hepatic arterial blood. Any process that substantially reduces arterial blood flow or

arterial oxygen content to the liver can result in hypoxic hepatitis. Hypoxic hepatitis tends to be commoner in patients with systemic hypotension and other concomitant conditions which decrease the systemic or the hepatic circulation [1], and it occurs mostly in intensive care unit patients who are haemodynamically unstable.

90% of cases occur secondary to heart failure, respiratory failure and toxic shock [2]. The most common cardiac disorders responsible for ischaemic hepatitis are acute myocardial infarction and arrhythmias. Valvular heart disease, cardiomyopathy and pericardial tamponade also can result in arterial hypotension complicated by ischaemic hepatitis. The rate of in-hospital mortality in hypoxic hepatitis is very high with studies reporting mortalities of 61.5%. Mortality tends to be higher in patients with septic shock (83.3%) and cardiac arrest (77.7%) [3]. Cases of hypoxic hepatitis were also reported in relation to specific conditions such as obstructive sleep apnoea [4], profound anaemia [5], complicated aortic aneurysms, acute lower limb ischaemia [6], hereditary haemorrhagic telangiectasia [7] and grand mal seizures [8]. However, hypoxic hepatitis rarely occurs in young healthy patients. Diminished portal venous blood flow increases the susceptibility to hypoxic hepatitis during episodes of arterial hypotension or hypoxia. Furthermore, diminished hepatic venous outflow (i.e. secondary to congestive heart failure, Budd-Chiari syndrome) and biliary obstruction also increase an individual's risk for ischaemic hepatitis with hypotension or hypoxia [1].

Hypoxic hepatitis was previously known as 'ischaemic hepatitis' or 'shock liver'. Liver ischaemia was until recently considered to be the only haemodynamic mechanism responsible for hypoxic hepatitis, and it was believed that a shock state was required. However, other haemodynamic mechanisms of hypoxia, such as passive congestion of the liver, arterial hypoxaemia and dysoxia, have been shown to be important mechanisms in inducing hepatocyte damage with a shock state being observed in only 50% of cases of hypoxic hepatitis. Accordingly, 'ischaemic hepatitis' and 'shock liver' are misnomers and the term 'hypoxic hepatitis' better describes this condition [2].

The diagnosis should be suspected in patients who have evidence of past or present cardiac disease, in the presence of electrocardiographic abnormalities or radiographic pulmonary abnormalities (found in about half of all patients with acute hypoxic hepatitis) and in patients with marked increases in transaminase activity together with a degree of initial renal impairment [9]. The outcome of hypoxic hepatitis is influenced by the severity of liver impairment and the aetiology and severity of the underlying conditions. Peak aspartate transaminase, lactate dehydrogenase, INR and lactate levels are higher in intensive care unit patients with fatal hypoxic hepatitis. The duration of hypoxia also appears to increase mortality [10].

Management involves treatment of the underlying conditions, with plenty of fluids in patients with hypotension and septic shock, maintaining adequate oxygenation in patients with underlying respiratory conditions and prompt management of cardiac disorders in order to restore haemodynamic stability.

Case Report

We report here the case of a young healthy athlete who developed heat stroke associated with rhabdomyolysis and ischaemic hepatitis while he was running the final stages of a marathon. The athlete was a 25-year-old Hungarian gentleman who had been training for the Malta Marathon (held over 42.2 km) for several months. He was fit, having had regular medical check-ups during his training and before the marathon. The patient was feeling very well during the race, so much that he was improving on his usual time and towards the end of the race (41st km) decided to sprint the last few metres towards the finish line. He was noticed to collapse a few hundred metres from the finish and his next recollection was waking up in the intensive care unit at our centre. Upon his collapse, the paramedics found him to be severely hypotensive with unrecordable blood pressure. A peripheral line was inserted and he was started on intravenous fluids. He was rushed to accident and emergency where he was found to be confused, with a Glasgow Coma Score of 10. He had a temperature of 105.4°F on admission and he was sweaty, tachycardic (heart rate of 160 bpm) and had a systolic blood pressure of 90 mm Hg. Preliminary investigations are shown in [table 1](#).

He was taken to the intensive care unit where he was resuscitated with plenty of fluids. His blood pressure remained very low, requiring inotropic support with ephedrine for 6 h. A CT scan of his brain was normal. He was also started on intravenous co-amoxiclav. Repeat blood investigations the day after admission revealed an elevated creatinine phosphokinase (CPK) level (178,850 U/l), suggesting underlying rhabdomyolysis. It was also noticed that the serum alanine aminotransferase (ALT) had started rising with a level of 143 U/l on day one post admission.

The patient improved clinically, was responsive within a few hours and was transferred from intensive care to a general medical ward the following day. However, his ALT peaked on the second day of admission ([table 2](#)). On examination, there were no signs of chronic liver disease, no flap, and he was not jaundiced. Liver screen was normal with negative viral screen, autoimmune screen and mildly raised ferritin levels ([table 2](#)). An ultrasound of his liver was also normal. All non-essential treatment (including the antibiotic) was stopped and intravenous N-acetyl cysteine (NAC) was started at a dose of 100 mg/kg 16-hourly. He was discharged home with an early outpatients follow-up once both CPK and ALT were improving progressively ([fig. 1](#), [fig. 2](#)).

Discussion

Graveling and Frier [11] reported a similar case report of a young insulin-dependent diabetic patient who suffered an episode of nocturnal hypoglycaemia which provoked a tonic-clonic seizure the day before a marathon. Despite this he ran in the marathon the following day during which he collapsed with severe hypoglycaemia and a further associated seizure. He subsequently developed severe myalgia accompanied by a pronounced and persistent elevation of plasma CPK, indicating rhabdomyolysis, and deranged liver function, suggestive of hypoxic hepatitis. The authors concluded that the rhabdomyolysis and hypoxic hepatitis occurred as a result of prolonged physical exercise following severe hypoglycaemia.

Studies have shown that up to 11% of intensive care unit patients develop hypoxic hepatitis. Regression analysis has demonstrated a strong mortality risk for admissions with hypoxic hepatitis requiring vasopressor therapy, unlike hypoxic hepatitis in the absence of vasopressor therapy which does not appear to be significantly associated with mortality [12]. While it is relatively unexpected that a healthy, young athlete should develop hypoxic hepatitis, the vasopressors used for a short period in intensive care might have precipitated the hypoxic damage to the liver in our patient. The relatively short period of vasopressor use might also explain this patient's rapid recovery with rapid improvement in his ALT levels.

NAC has been shown to limit liver injury and improve prognosis in patients with acute liver failure secondary to paracetamol overdose. NAC limits liver injury by replenishing hepatic glutathione and increasing oxygen delivery to peripheral tissues [13]. While little evidence exists on the benefits of NAC in hypoxic hepatitis, it has been tested as a treatment for acute liver failure not related to paracetamol overdose. A placebo-controlled trial on 173 patients with acute liver failure that was not due to paracetamol overdose showed that patients treated with NAC had more transplant-free survival and less orthotopic liver transplantation at 1 year when compared with those receiving placebo [14]. Patients with grade 1 or 2 encephalopathy receiving NAC also had better 1-year survival than those receiving placebo. For this reason, NAC may have an important therapeutic role in the management of acute hepatitis secondary to hypoxia.

Table 1. Initial blood investigations on admission

	Values on admission	Normal range
White blood cells	12.3	$3.5\text{--}11 \times 10^9/\text{l}$
Neutrophils	8.0	$2.5\text{--}7.5 \times 10^9/\text{l}$
Haemoglobin	17.8	13–18 g/dl
Platelets	254	$140\text{--}400 \times 10^9/\text{l}$
Creatinine	228	62–106 $\mu\text{mol/l}$
Urea	5.90	1.7–8.3 mmol/l
Potassium	4.66	3.5–5.1 mmol/l
Random glucose	4.08	3.9–9.0 mmol/l
INR	1.12	0.88–1.1
CPK	515	39–308 U/l
ALP	110	40–129 U/l
ALT	34	5–41 U/l
GGT	29	8–61 U/l
Bilirubin	7.4	1.72–17.1 $\mu\text{mol/l}$
Lactate	1.8	
Drugs of abuse screen	negative	
Urine myoglobin test	negative	

Table 2. Patient's liver function tests and hepatitis screen on day 2 following admission

	Values on day 2
ALP	110
ALT	2,912
GGT	128
Bilirubin	36
Hepatitis B surface antigen	negative
Hepatitis B core IgM antibody	negative
Hepatitis A IgM antibody	negative
Hepatitis C antibody	negative
Ferritin	621 (28–365 ng/ml)
Anti-smooth muscle antibody	negative
Anti-mitochondrial antibody	negative
Anti-nuclear antibody	negative

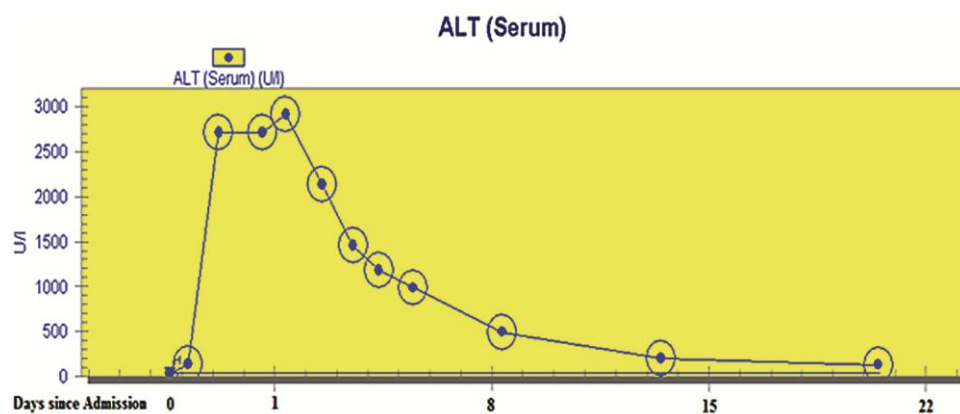


Fig. 1. Chart describing the trend in ALT from admission until week 3 after discharge. The ALT level peaked at 2,912 U/l on day 2 post admission and then improved progressively. NAC was started on day 2.

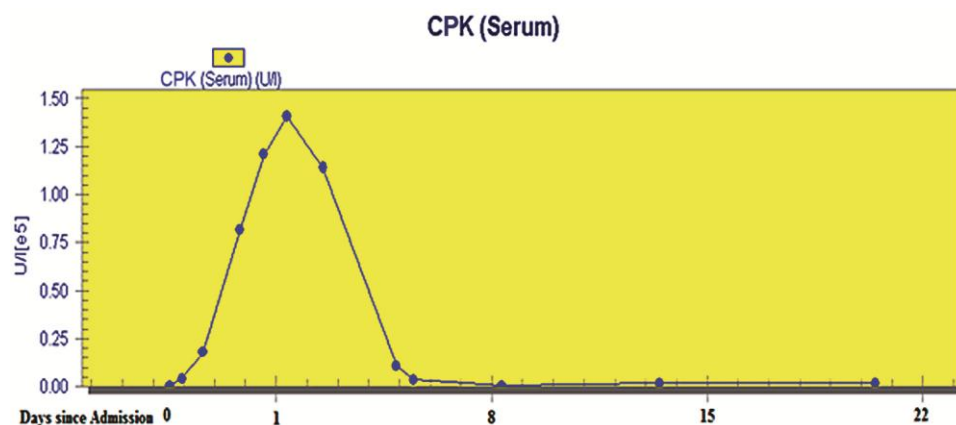


Fig. 2. Chart describing the trend in CPK from admission until week 3 after discharge. The CPK level peaked at 178,850 U/l on day 1 post admission and improved rapidly with rehydration.

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