Extreme Heatstroke Causing Fulminant Hepatic Failure Requiring Liver Transplantation: A Case Report

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ABSTRACT

Introduction. Exertional heatstroke with liver involvement is a rare and potentially fatal condition. In this setting, fulminant hepatic failure (FHF) occurs as a result of severe hypoxic hepatitis.

Case Report. We report the case of a young male athlete who developed exertional heatstroke associated with rhabdomyolysis and hypoxic hepatitis while running the final stages of an ultra-marathon (62 km). The patient rapidly developed multiorgan failure, including fulminant hepatic failure, requiring intensive care admission for mechanical ventilation, hemodialysis, and inotropic support. He failed to improve with supportive measures and underwent an emergency hepatectomy followed by orthotopic liver transplant, after which he recovered completely.

Conclusions. We discuss the rationale for liver transplantation in this setting, possible alternative treatments, and the pathophysiology of fulminant liver failure in this rare case.

THE OCCURRENCE OF HYPOXIC HEPATITIS leading to fulminant hepatic failure (FHF) is extremely rare. The majority of cases (~90%) occur in extremely unwell patients with severe hemodynamic instability as a result of heart failure, respiratory failure, and severe sepsis. It is most uncommon in young healthy patients with no underlying medical problems. We have reported herein the case of a young male athlete who developed exertional heatstroke associated with rhabdomyolysis and hypoxic hepatitis while running the final stages of an ultra-marathon (62 km). The patient developed multiorgan failure, including liver failure, requiring intensive care admission for mechanical ventilation, hemodialysis, and inotropic support. He failed to improve with supportive measures and underwent an emergency hepatectomy followed by orthotopic liver transplantation (OLT), after which he recovered completely.

CASE REPORT

A 40-year-old athlete collapsed toward the end of an ultra-marathon run held on a day with an outdoor temperature of 29°C (84.2°F). He was an elite runner, having competed in many similar long distance runs, and felt well before this event. He denied using any performance-enhancing substances, protein supplements, or other medication. He was found collapsed toward the latter stages of the 62-km run. Paramedics at the scene began resuscitation and transported him to the nearest hospital, where he had a Glasgow Coma Scale score of 3 upon arrival. He was intubated, ventilated, and resuscitated with intravenous fluid. Despite this, he was anuric.

Biochemical investigations revealed acute kidney injury, likely secondary to rhabdomyolysis (urea, 22 mmol/L; creatinine, 594 mmol/L; creatinine kinase, 25640 U/L). Further laboratory investigations demonstrated severely deranged liver function tests, including a significantly elevated International Normalized Ratio (14). Computed tomography of the brain and abdomen were performed, demonstrating diffuse brain injury but no focal intracranial pathology. Abdominal findings were significant for uniform low attenuation within the liver, suggestive of diffuse inflammation or steatosis. No thrombus was identified in the portal vein, inferior vena cava, or hepatic veins.

In the 24-hour period after his admission, he developed severe liver failure in addition to renal failure, respiratory failure, and circulatory shock. He was transferred to the National Liver Unit where he was managed according to a FHF protocol and commenced on continuous renal replacement therapy. Despite this he continued to deteriorate, with increasing inotropic requirements, and worsening metabolic acidosis and liver function (Fig 1). Other causes of acute liver failure were excluded with negative viral serologies. He was reviewed by the liver transplant team, who listed

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the patient for a super-urgent OLT. On day 3 after the onset of heatstroke, he continued to deteriorate clinically, having become profoundly toxic and coagulopathic (International Normalized Ratio, 24), so the decision was made to take him to the operating room for total hepatectomy and portocaval shunting. He was then transferred back to the intensive care unit in an anhepatic state and was kept on hemodialysis. Twelve hours after explantation, a suitable liver donor became available and he underwent an orthotopic OLT. The procedure was performed without venovenous bypass, using the modified piggyback technique developed by Belghiti et al [1], to minimize hemodynamic instability and vascular reconstruction time. For arterial revascularization, an infrarenal conduit using one of the donor’s ileal arteries was used, because the recipient hepatic artery was thrombosed at the time of arterial reconstruction.

Postoperatively, his liver and renal function recovered over a 21-day period and he was transferred from intensive care unit to the liver in-patient ward on the posttransplant day 21. He had a relatively uncomplicated postoperative course, although he did develop biochemical signs of acute cellular rejection of the liver graft on day 7. This was confirmed with a percutaneous, ultrasonography-guided liver biopsy and was successfully treated with pulsed doses of corticosteroids. He was discharged home on postoperative day 42, with an immunosuppressant regimen of tacrolimus and oral corticosteroids. He is now 6 months postoperative and continues to do well.

DISCUSSION

Heatstroke is a life-threatening condition characterized by varying degrees of organ impairment, including central nervous system dysfunction, rhabdomyolysis, renal failure, arrhythmias, cardiac failure, liver failure, and disseminated intravascular coagulation [2]. Prolonged physical activity in the presence of high environmental temperatures and humidity greatly predisposes athletes to the risk of heatstroke [3]. Although hepatic involvement is common in exertional heatstroke, FHF is exceedingly rare in this setting [4]. The management of FHF secondary to exertional heatstroke in young adults is controversial [5]. Thus far, there have been 4 reported cases of heatstroke-induced FHF requiring OLT [6–10]. Of these, 1 patient (a 16-year-old boy) died on posttransplant day 10 from a cardiorespiratory arrest secondary to persistent multiorgan failure [11]. A second patient (a 25-year-old man) died 41 days posttransplant from a complicating infection. A third patient (a 30-year-old man) died 11 months posttransplant from complications of chronic graft rejection [7]. Several other cases of exertional, heatstroke-induced liver failure have been successfully managed with nonoperative treatment [5]. Therein lies a dilemma regarding the decision to undertake OLT in such circumstances. The prognosis of patients presenting with liver failure from exertional heatstroke is largely unpredictable; therefore, indications for OLT in this specific setting are unclear. In our case, the decision to proceed with urgent hepatectomy was based on the patient’s dramatic and rapid clinical demise, which was not responding to escalating medical therapy and seemed to be driven by worsening hepatic failure. Indeed, pathologic examination of our patient’s liver confirms that the ischemic hepatic injury was irreversible given that all of the main vessels contained occlusive thrombus (Fig 2). Ultimately, he made a complete recovery soon after OLT, with resolution of liver, respiratory, renal, and central nervous system dysfunction.

The mechanism underlying liver failure in heatstroke is not well understood, but seems to be initiated by ischemia causing a state of hypoxic hepatitis. The causes of intrahepatic circulatory failure may be systemic hypoperfusion, or thrombosis of inflow vessels (portal vein and/or hepatic arteries) or outflow congestion secondary to cardiac failure. In this case, it is most likely that the ischemic hepatitis was secondary to a combination of profound hypoperfusion and poor inflow owing to thrombosed inflow vessels, leading to massive hepatocyte necrosis. In such cases where irreversible hepatic damage has occurred, the only possible treatment is OLT. Nonoperative strategies that have been effective in less severe cases of acute hepatic failure include fluid...
resuscitation, restoring acid-base and electrolyte balance, and use of the molecular adsorbent recirculating system [12]. Once committed to performing OLT for FHF, surgical options include the traditional orthotopic transplantation using a nonliving donor or, more recently, the living donor OLT approach has been successfully employed [9].

Another interesting finding in this case was the unexpected degree of hepatic steatosis in this athletic lean patient’s native liver. Fatty liver is most commonly identified in obese and morbidly obese individuals [13]. However, there are reports proposing high-intensity sport as a risk factor for nonalcoholic fatty liver disease and nonalcoholic steatohepatitis [14]. Postulated mechanisms for this include an increase in the production of reactive oxygen species, which is believed to play a central role in the development of nonalcoholic fatty liver disease [15]. The increased free radical production during very high volumes of exercise leads to oxidative modification of low-density lipoprotein, which is a precursor to the development of fatty liver disease [11]. This may have predisposed our patient to developing FHF in the setting of heatstroke.

In conclusion, exertional heatstroke with liver involvement is a potentially fatal condition. Although there are cases that may respond well to supportive therapies, resulting in resolution of liver failure, the option of OLT should be borne in mind for those with biochemical and clinic evidence of massive hepatocellular damage. It would be useful to establish a prognostic scoring system for patients with FHF, to appropriately stratify the severity of organ failure, and to help predict mortality. This may help to select out those patients who would benefit from OLT early in their presentation, leading to better outcomes. Further clinical experience is necessary to better compare conservative therapy with organ transplantation in the treatment of FHF associated with heatstroke.

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REFERENCES