

Keep Cool and Carry On: Rapid Cooling in Heatstroke with Cerebral Edema
Bucky Ferozan DO, Karan Parmar DO, Edith Szabo DO

Introduction

Heat Stroke (HS) is defined as rectal temperature greater than or equal 106°F (41.1°C) along with change in mental status ranging from confusion, delirium, stupor to coma and/or convulsions.¹HS accounts for hundreds of deaths in United States annually, with 80% of the victims age 50 years and older.²A study showed 54% increase in heat related deaths where hyperthermia was included as a contributing factor to death, between 1993 and 2003.³Heat related deaths are preventable and mortality decreases with public health and healthcare workers preparedness.^{4,5} Here we discuss HS in a septic patient with an initial core temperature of 108.5°F who developed cerebral edema (CE) and was successfully resuscitated. To our knowledge, this is the first case report of a favorable outcome of a HS patient with concomitant CE.

Case Presentation

We present a case of a 55-year-old diabetic female who was brought in by EMS after being found unresponsive by her husband for an unknown amount of time on a late July afternoon in Bronx, NY. EMS reported that their apartment, located on the 7th floor, was scorching hot. Husband reported that there was no air conditioning in the apartment and that the last time he saw her was earlier that morning, when she complained only of a cough. Vitals on triage: rectal temperature of 108.5°F, pulse 139, blood pressure 88/61 mmHg, SpO₂ 86% on room air and finger stick glucose 182 mg/dL. Primary survey showed no gross signs of trauma, GCS 7 (E1V2M4), 2 mm pupils with corneal reflex, diffuse rhonchi in the lung fields with tachycardia and warm dry skin. Patient was intubated immediately; central venous access established for cold IV fluids along with ice water bath immersion. Rectal probe was inserted to monitor temperature continuously along with a Foley catheter to monitor urine output and cold-water lavage. Chest x-ray showed a right lower lobe infiltrate so the patient was started on empiric antibiotic coverage. Approximately 25 minutes from arrival, the rectal temperature was 101.5°F at which point ice water bath was discontinued.

Subsequent CT brain showed white matter effacement concerning for CE. Neurology was consulted with recommendations to maintain normothermia, cautious hydration to prevent osmotic neuronal damage, aggressive sepsis treatment (however, lumbar puncture was withheld, per neurology, due to concerns of elevated intracranial pressure secondary to CE) and to start mannitol if worsening signs of cerebral herniation, such as pupillary dilation, or worsening 24 hour repeat CT brain. Blood work showed WBC: 27,000 u/L, Lactic Acid: 4.8mmol/L, creatinine: 1.8mg/dL, CPK: 1683 IU/L, urine drug screen was negative along with serum toxicology screen including acetaminophen and salicylic acid. Further history from the husband revealed that she did not take any psychiatric medications, which decreased the likelihood of neuroleptic malignant syndrome or serotonin syndrome. Patient's temperature was 100.4°F approximately 45 minutes after arrival, and soon after was transferred to the ICU.

24-hour repeat CT brain showed stable white matter effacement without signs of increasing CE.

Patient's resuscitation was continued with IV antibiotics and IV fluids with white count, lactic acidosis, acute kidney injury and elevated CPK resolving within 48 hours. CE noted to be resolving on 48-hour repeat CT brain without the need to use mannitol. Sputum and blood cultures grew ESBL Klebsiella and CT chest showed right lobe lung abscess. Patient was extubated on day 10 of her hospital stay and post-intubation showed signs of dysmetria, though subsequent MRI only showed a small lacunar infarct. Patient was discharged to short-term rehab with complete recovery.

Discussion

Response to heat stress is a dynamic balance between the mediators of inflammation, including endothelial cells, leukocytes, inflammatory cytokines, and endotoxins. Proinflammatory cytokines identified in HS include tumor necrosis factor (TNF); interleukin (IL)-2, -6, -8, and -10; interferon- α and $-\beta$.⁶ In a study of 18 HS patients, circulating cytokine levels correlated with clinical HS severity index.⁷ Additional in vitro studies show that cooling delays the release of IL-1B, IL-6 and TNF.⁸

The brain is the most heat-sensitive organ in the human body¹⁰. It has been shown that irreversible changes of neural cells start at approximately 40°C (104°F)¹¹⁻¹⁴. The most important consequence of these changes are destruction of endothelial cells of the brain and leakage of serum proteins across the brain-blood barrier resulting in brain edema --- the most hazardous acute complication of pathologic brain hyperthermia^{9, 14}. Additional studies show, a strong relation between heat-induced neuronal damage and edematous areas of the brain¹⁶. Other experiments reveal that neurons can tolerate low temperatures of at least 30°C (86°F)^{16,17,18}. Although there is limited human data, animal models have illustrated that halting early gene expression of proinflammatory genes and excitatory neurotransmitters via rapid cooling and maintaining therapeutic hypothermia (TH) [defined as core body temperature less than 35°C within 6 hours of hospitalization] plays a central role in preventing neuronal cell death⁷. Further, TH also stabilizes the blood brain barrier and reduces CE by decreasing permeability to inflammatory cytokines and potential harmful substances such as free radicals and thrombin^{8, 9}.

Conclusion

To our knowledge, this is the first documented case of a successful outcome involving heat stroke complicated by cerebral edema that can be attributed by early aggressive rapid cooling measures. To date, evidence supports the use of hypothermia treatment in cardiac arrest patients and neonatal hypoxic-ischemic encephalopathy^{19,20}. However, hypothermia has not been proven to show benefit in patients with stroke and traumatic brain injury²¹. Our patient was induced into a hypothermic state within 1 hour of presentation to our emergency department. As a result, future investigational studies involving other neurological injuries (i.e. stroke, traumatic brain injury, heat stroke) should investigate a possible relationship between neurological outcome and duration of timing for inducing a hypothermic state.

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