

KEEP COOL AND CARRY ON: RAPID COOLING IN HEATSTROKE WITH CEREBRAL EDEMA

Ferozan, B. DO; Parmar, K. DO; Soler, J. DO; Fradlis, V. Szabo, E. DO
St. Barnabas Hospital, Bronx NY 10457

HISTORY/PHYSICAL

CHIEF COMPLAINT: Found Down
HISTORY OF PRESENT ILLNESS: 55-year-old obese female with past medical history of diabetes and hypertension 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: T (RECTAL) 108.5F P 139 BP 88/61 mmHg SPO2: 86% ON ROOM AIR, CBG 182mg/dL
PHYSICAL EXAM:
GEN: no gross trauma GCS 7 (E1M2V4)
HEENT: 2mm pupils, dry mucous membranes
CHEST: B/L coarse breath sounds, left rhonchi
HEART: Tachycardic, no murmurs
ABD: Soft Non distended.
EXT: +2 pulses in all extremities, no deformities
SKIN: Dry, warm flushed skin

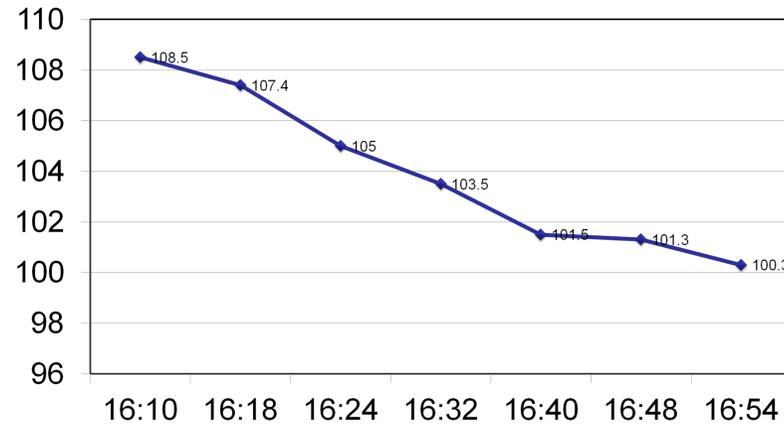
LABS

128	90	12	348	8.0	13.4	235
4.1	27	1.8	8.7	42.5		
AST:358	ASA None	INR 1.3				
ALT:98	APAP None	Troponin < 0.1				
ALP: 63	Ammonia	Lactic Acid 4.8				
TSH 0.68	77mg/dL	CPK 1663				

DIFFERENTIAL DIAGNOSIS

- Septic Shock
- Heat Stoke
- Encephalitis
- Meningitis
- Thyroid Storm
- Cocaine/Amphetamine
- Malignant Hyperthermia
- Serotonin Syndrome

Time and Temperature(°F)



BACKGROUND

Heat Stroke (HS) is defined as rectal temperature greater than or equal to 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}

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 - β .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.

REFERENCES

1. Knochel JP: Environmental heat illness. An eclectic review. *Arch Intern Med.* 1974;133:841-864. [PubMed: 4821779]
2. Delaney KA, Vassallo SU. Chapter 15. Thermoregulatory Principles. In: Nelson LS, Lewin NA, Howland M, Hoffman RS, Goldfrank LR, Flomenbaum NE, eds. *Goldfrank's Toxicologic Emergencies*, 9e. New York: McGraw-Hill; 2011
3. Anonymous: Heat-related deaths—United States, 1999-2003. *MMWR.* 2006;55:796-798.
4. Beard ME, Hickton CM: Haemostasis in heat stroke. *Br J Haematol.* 1982;52:269-274. [PubMed: 7129469]
5. Weiskopf MC, Anderson HA, Foldy S, et al: Heat wave morbidity and mortality. Milwaukee, Wis, 1999 vs 1995: An improved response? *Am J Public Health.* 2002;92:830-833. [PubMed: 1198845]
6. Bouchama A, De Vol EB: Acid-base alterations in heatstroke. *Intensive Care Med.* 2001;27:680-685. [PubMed: 11398693]
7. Huisse MG, Pease S, Hurtado-Nedelec M, et al: Leukocyte activation: The link between inflammation and coagulation during heatstroke. A study of patients during the 2003 heat wave in Paris. *Crit Care Med.* 2008;36: 2288-2295. [PubMed: 18664784]
8. Kimura A, Sakurada S, Ohkuni H, et al: Moderate hypothermia delays proinflammatory cytokine production of human peripheral blood mononuclear cells. *Crit Care Med.* 2002;30:1499-1502. [PubMed: 12130969]
9. Karibe H, Zarow GJ, Graham SH, Weinstein PR: Mild intracerebral hypothermia reduces postischemic hyperperfusion, delayed postischemic hyperperfusion, blood-brain barrier disruption, brain edema, and neuronal damage volume after temporary focal cerebral ischemia in rats. *Journal of Cerebral Blood Flow and Metabolism*, official journal of the International Society of Cerebral Blood Flow and Metabolism. 1994;14:620-7.
10. Maier CM, Sun GH, Cheng D, Yenari MA, Chan PH, Steinberg GK: Effects of mild hypothermia on superoxide anion production, superoxide dismutase expression, and activity following transient focal cerebral ischemia. *Neurobiol Dis.* 2002;11:28-42
11. Kawai N, Kawanishi M, Okauchi M, Nagao S: Effects of hypothermia on thrombin-induced brain edema formation. *Brain Res.* 2001;895:50-8.
12. Lepock JR: Cellular effects of hyperthermia: relevance to the minimum dose for thermal damage. *Int J Hyperthermia.* 2003; 19:252-266
13. Lepock JR, Cheng K-H, Al-Qaysi H, Kruuv J: Thermotropic lipid protein transitions in Chinese hamster lung cell membranes: relationship to hyperthermic cell killing. *Can J Biochem Cell Biol.* 1983; 61:421-427
14. Willis WT, Jackman MR, Bizeau ME, Pagliassotti MJ, Hazel JR: Hypothermia impairs liver mitochondrial functions. *Am J Physiol.* 2000; 278:R1240-R1246
15. Sharma HS: Hypothermia-induced brain edema: current status and future perspectives. *Indian J Med Res.* 2006; 123:629-652
16. Arai et al: Effect of low temperature on glutamate-induced intracellular calcium accumulation and cell death in cultured hippocampal neurons. *Neurosci Lett.* 1993; 163:132-134
17. Lucas et al: In vitro investigation of the effect of nonfreezing low temperatures on lesioned and uninjured mammalian spinal neurons. *J Neurotrauma.* 1994; 11:35-61
18. Dewhirst MW, Vigilanti BL, Lora-Michaels M, Hanson M, Hoopes PJ: Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia. *Int J Hyperthermia.* 2003; 19:267-294
19. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med.* 2002;346:549-556
20. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, et al: Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med.* 2005;353:1574-84
21. Song et al: Overview of therapeutic hypothermia. *Current Treatment Options in Neurology.* 2012; 14: 541-548