

Unusual heat stroke caused by herbal therapy with traditional Chinese medicine

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ABSTRACT

يضم الطب الصيني التقليدي مجموعة من الممارسات الطبية التقليدية التي نشأت في الصين، بما في ذلك الأدوية العشبية كعلاج أساسي. وبطبيعتها الأربعة: وهي الباردة، والساخنة، والدافئة والمعتدلة، قد تنظم الأدوية العشبية الأعصاب الودية ومعدل الاستقلاب الأساسي وتأثيرها على الجهاز العصبي المركزي وعلى نظام الغدد الصماء. ضربة الشمس هي حالة مرتبطة بارتفاع درجات الحرارة التي تهدد حياتنا ويحدث غالباً خلال موجات حرارة الصيف ودرجات الحرارة العالية. يعتبر تناول الأدوية أو السموم واحدة من العوامل الخطرة التي تؤدي إلى ضربة الشمس، وقد تؤثر على حرارة الجسم. نستعرض في هذا التقرير حالة ضربة شمس المرتبطة بالتداوي بالأعشاب مع الطب الصيني التقليدي. تسلط هذه الحالة الضوء على المرضى الذين يستخدمون الطب الصيني التقليدي بانتباه.

Traditional Chinese medicine (TCM) comprises a range of traditional medical practices that originate in China, including herbal medicine as a major therapy. Through its 4 natures; namely, cold, hot, warm, and cool, herbal medicine may regulate sympathetic nerves and basal metabolic rate and affect the CNS and the endocrine system. Heat stroke is a severely life-threatening heat-related illness that is most commonly seen during summer heat waves and high environmental temperatures. The intake of medications or toxins is considered one of the risk factors leading to heat stroke, as they may affect body thermoregulation. We report a case of heat stroke that was associated with herbal therapy with TCM. This case highlights the importance of paying more attention to unidentified folk prescriptions in the use of TCM.

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Traditional Chinese medicine (TCM) represents a range of traditional medical practices originating in China, including herbal medicine as a major therapy. Through the 4 natures of TCM, which are cold, hot, warm, and cool, it exerts effects on the CNS and endocrine systems, and on the activity of regulating sympathetic nerves and basal metabolic rate, and so forth.¹ Ginger is commonly used due to its thermogenic properties (warm nature) in TCM. It has been reported that ginger plays a role on the endocrine system and the CNS through changes in the body's metabolism rate.² Heat stroke is a severely life-threatening heat-related illness that is most commonly seen during summer heat waves and high environmental temperatures. It may occur when the body's thermoregulatory mechanisms fail to maintain homeostasis. The clinical presentations of heat stroke are characterized as elevated body temperature with universal CNS dysfunction, as well as end-organ damage. Currently, heat stroke is a more preventable than treatable disease. Rapid cooling and supportive therapy would be helpful, but it leads to permanent neurological damage and very high mortality despite these efforts. Multi-organ system failure is the ultimate cause of mortality, and is directly related to peak temperature and duration of exposure.³ A complex interplay between direct heat cytotoxicity, coagulation

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dysfunction, the systemic inflammatory response, and multiple cytokine effects lead to encephalopathy, which could present as delirium, seizures, or coma and predominates early in the course of the disease.³ Other than commonly seen risk factors like chronic illness, exposure to hot environments or water depletion, and usage of drugs or toxins are also considered as a hazard to vulnerable patients.³ We report a case of heat stroke that was associated with herbal therapy with TCM. Our objective in presenting this case is to draw attention to the standardized usage and outcome evaluation of herbal medication, and to provide information on the prevention of heat stroke caused by medication and drug applications.

Case Report. A 49-year-old woman presented to our department with acute-onset unconsciousness. She had been diagnosed as right-sided idiopathic facial palsy and had received herbal therapy from a local TCM practitioner after a non-effective 20-day acupuncture treatment. She had an unremarkable history and was otherwise healthy before the therapy. Covered with a thick quilt, she lay down on a heated kang (brick bed) to induce diaphoresis. Meanwhile, she held ginger (*Zingiber officinale*, approximately 50 g) homogenates in each hand. She did not take any drugs, water, or food. After one-hour treatment, she complained of numbness in her face and bilateral upper limbs. Three hours later, she suddenly fell unconscious, with high fever, and urinary and fecal incontinence. Hypokalemia, hyponatremia, and hyperglycemia developed and brain CT in the local hospital was unremarkable. She was then transferred to the intensive care unit (ICU) in our hospital. She was otherwise healthy, without any remarkable history. On admission, she was deliriant and uncooperative; her body temperature was 41.2°C, and her blood pressure was 90/60 mm Hg. Right-sided facial palsy with bilateral horizontal nystagmus, nuchal rigidity, and right-sided hypermyotonia was noted, and Babinski sign was positive bilaterally. A brain MRI showed severe brain edema and extensive symmetric white matter lesions (Figure 1). The blood concentration of potassium was 2.76 mmol/L (normal range [NR]: 3.5-5.5 mmol/L) and that of glucose was 22.47 mmol/L (NR: <7.0 mmol/L). The white blood cell (WBC) count in the blood was $24.14 \times 10^9/L$ (NR: $4-10 \times 10^9/L$) (neutrophil percentage 88%; NR: 50-70%), and the platelet count was $24 \times 10^9/L$ (NR: $100-300 \times 10^9$). The blood coagulation routine was abnormal (prothrombin time 19.9s [NR: 12-14s] and fibrinogen 1.93 g/L [NR: 0.15-0.45 g/L]). Amylase in both serum and urine was elevated. The troponin T level was 5.4 ng/ml (NR: <1.5 ng/ml). Her blood urea

nitrogen was also increased (7.67 mmol/L; NR: 3.2-7.0 mmol/L). Heat stroke and multiple organ dysfunction syndrome (MODS) was diagnosed, and intensive symptomatic treatment was initiated immediately. Ice saline infusion and physical cooling were applied to cool her down. Mannitol was used to relieve intracranial edema, and supportive therapies were used to keep the vital signs stable. Two hours after admission, she suffered from generalized seizures twice (duration of 2 minutes each) presenting as extending of the limbs and bilateral mydriasis. The epilepsy was controlled with an injection of 200 mg luminal; however, she fell into a deep coma and disseminated intravascular coagulopathy and rhabdomyolysis were noted. Auscultation revealed extensive wet rales in bilateral lungs. The spontaneous respiration rate was 3 times per minute. Oxygen saturation (SaO₂) was 70% by oximetry. Artery blood gas analysis revealed metabolic acidosis (pH 7.21,

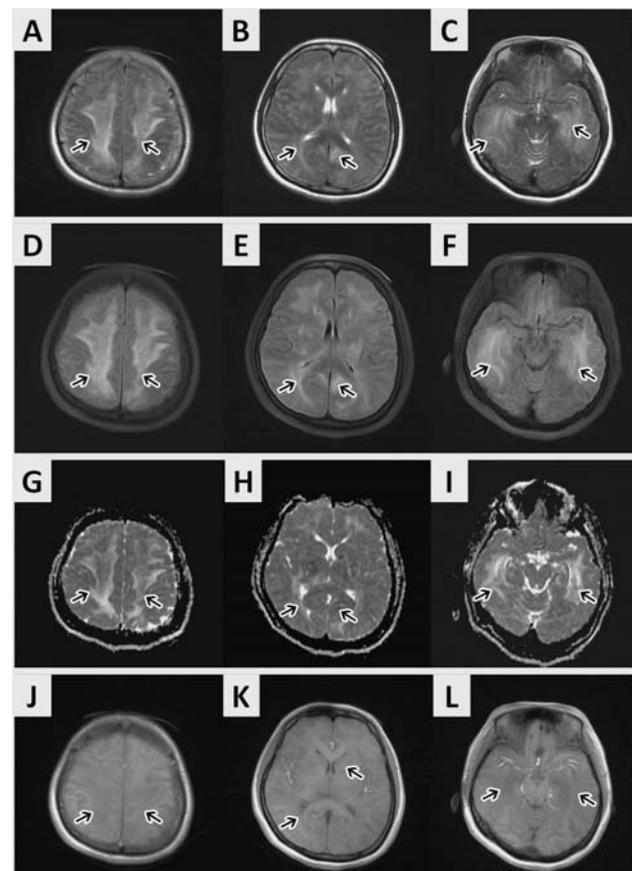


Figure 1 - Brain MRI revealed severe brain edema and extensive symmetric white matter lesions, without enhancement. A-C) T2 weighed images; D-F) Fluid-attenuated inversion recovery (FLAIR); G-I) Apparent diffusion coefficient maps; J-L) Enhanced MRI-T1 weighed images.

standard HCO_3^- 12.8 mmol/L, and lactic acid 8.1 mmol/L). Mechanical ventilation was initiated after intubation. Despite our intensive care, she remained comatose and the respiratory and circulatory system abnormality did not improve during the following days. Her family refused any further diagnostic and therapeutic procedures, and she was discharged. A follow-up phone-call revealed that she died one day after discharge.

Discussion. We described a case of heat stroke caused by atypical reasons; namely, herbal therapy with TCM. The patient developed MODS soon after admission. This report aims to draw attention to the standardized usage and outcome evaluation of herbal medication, and to provide information on prevention of heat stroke caused by medication and drug misuse.

Heat stroke characteristically presents with hyperthermia (core temperature of 40°C or more), anhidrosis, and altered mental status.⁴ Our patient had an ascertained history of exposure to heat and presented with typical clinical manifestations of heat stroke. Marked hyperthermia, usually above 40.5°C , and associated encephalopathy, may have occurred after thermoregulation was subordinated to circulatory and metabolic demands, and to the associated systemic inflammatory response. Exposure to high environmental temperatures and insufficient acclimatization can be the most important risk factors.^{4,5} Various medications such as beta-blockers, diuretics, psychiatric medications, and drug abuse with cocaine and amphetamines may predispose a patient to heat stroke. However, our patient denied taking any of these medications. The CNS can be involved in heat stroke, which is manifested by confusion, delirium, seizure, cerebellar dysfunction, and even coma.⁵ Ataxia may be an early sign and hallucinations or bizarre behavior can also be present. However, our patient complained merely of numbness in her face and bilateral upper limbs before she fell comatose.

Rhabdomyolysis is not uncommon in heat stroke, which usually leads to acute renal failure (ARF). However, other factors including hypovolemic shock secondary to heat shock can also contribute to the occurrence of ARF. Laboratory abnormalities might include evidence of hemoconcentration, elevated WBC count, elevated liver function tests, elevated creatinine phosphokinase (CPK) secondary to rhabdomyolysis, hypernatremia or hyponatremia, marked lactic acidosis, hypocalcemia, and hypoglycemia.⁶ Dysregulation between convection of heat from the core to periphery via blood circulation, and from the skins surface to ambient air, and evaporation of sweat into ambient

air are considered as the main problems that increase body temperature. The pathophysiology of heat stroke can be categorized as at least 3 aspects: (1) an increase in body temperature directly toxic to cells, resulting in protein denaturation and interrupting critical cellular processes, inducing apoptosis and cell death; (2) heat stress enhancing release of cytokines, which further causes the imbalance of the immune response; (3) elevated temperatures injuring vascular endothelium, increasing vascular permeability, activating the coagulation cascade, and disseminated intravascular coagulation.⁷ Therefore, a combination of direct cytotoxicity and overwhelming inflammatory response results in encephalopathy. Delayed treatment would lead to renal failure, coagulopathy, hepatic dysfunction, and ultimately MODS. Evaporative cooling and fluid replacement are of prime importance in preventing heat-related illnesses; however, overhydration should be avoided.⁵

As per the TCM theory, the external Cold & Hot natures of Chinese medicine may possibly reflect, in an ethological way, the changes of animals' temperature tropism, which might be internally regulated by the body's energy metabolism.⁸ Ginger is a rhizome, a thick underground stem that sprouts roots and shoots.⁹ Gingerols and related compounds in ginger have many pharmacological activities. Traditional Chinese Medicine holds that ginger "restores devastated yang" and "expels cold".¹⁰ The local TCM practitioner prescribed ginger to treat the patient's facial palsy that is believed to be caused by "cold" according to the TCM theory. Ueki et al² reported that systemic administration of ginger or its pungent constituents, induced a rapid, marked drop in body temperature accompanied by significant decrease in metabolic rate.²

In summary, the MRI findings add to our knowledge of brain imaging changes in heat stroke. Although TCM is widely accepted in China, some TCM therapies should be prescribed with caution. This case highlights the importance of paying more attention to unidentified folk prescriptions in TCM, as some of them may even kill the patients instead of curing them.

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References

1. Deng J, Qin H, Liu L, Liang Y. [Review and reflection on study of four properties of traditional Chinese medicine]. *Zhongguo Zhong Yao Za Zhi* 2009; 34: 3310-3312. Chinese.
2. Ueki S, Miyoshi M, Shido O, Hasegawa J, Watanabe T. Systemic administration of [6]-gingerol, a pungent constituent of ginger, induces hypothermia in rats via an inhibitory effect on metabolic rate. *Eur J Pharmacol* 2008; 584: 87-92.

3. Leon LR, Helwig BG. Heat stroke: role of the systemic inflammatory response. *J Appl Physiol (1985)* 2010; 109: 1980-1988.
4. Sucholeiki R. Heatstroke. *Semin Neurol* 2005; 25: 307-314.
5. Muldoon S, Bungler R, Deuster P, Sambuughin N. Identification of risk factors for exertional heat illness: a brief commentary on genetic testing. *J Sport Rehabil* 2007; 16: 222-226.
6. Hashim IA. Clinical biochemistry of hyperthermia. *Ann Clin Biochem* 2010; 47: 516-523.
7. Epstein Y, Roberts WO. The pathophysiology of heat stroke: an integrative view of the final common pathway. *Scand J Med Sci Sports* 2011; 21: 742-748.
8. Zhou C, Wang J, Zhang X, Zhao Y, Xia X, Zhao H, et al. Investigation of the differences between the "Cold" and "Hot" nature of *Coptis chinensis* Franch and its processed materials based on animal's temperature tropism. *Sci China C Life Sci* 2009; 52: 1073-1080.
9. Kubra IR, Rao LJ. An impression on current developments in the technology, chemistry, and biological activities of ginger (*Zingiber officinale* Roscoe). *Crit Rev Food Sci Nutr* 2012; 52: 651-688.
10. Wang WH, Wang ZM. [Studies of commonly used traditional medicine-ginger]. *Zhongguo Zhong Yao Za Zhi* 2005; 30: 1569-1573. Chinese.

CASE REPORTS

Case reports will only be considered for unusual topics that add something new to the literature. All Case Reports should include at least one figure. Written informed consent for publication must accompany any photograph in which the subject can be identified. Figures should be submitted with a 300 dpi resolution when submitting electronically or printed on high-contrast glossy paper when submitting print copies. The abstract should be unstructured, and the introductory section should always include the objective and reason why the author is presenting this particular case. References should be up to date, preferably not exceeding 15.