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**Improved detection of heat stroke-induced brain injury
by high b-value diffusion-weighted imaging**

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Abstract

We report a case of heat stroke in which detection of brain injury was improved by high b-value diffusion-weighted imaging (DWI). High b-value DWI revealed moderate to marked hyperintensity at/ around bilateral dentate nuclei and part of thalami. Apparent diffusion coefficient (ADC) maps revealed ADC decrease of the dentate lesions. Routine DWI showed only mild hyperintensity of part of dentate lesions. High b-value DWI could be valuable for improved detection of heat stroke-induced brain injury.

Key Words

Heat stroke

Diffusion-weighted imaging

b-value

Restricted diffusion

Introduction

Heat stroke is characterized by elevated core body temperature $>40.6^{\circ}\text{C}$ (1, 2). The thermal insult could be environmental (classical heat stroke), endogenous (e.g. severe exertion), or a combination of both (2, 3). Heat stroke is potentially life-threatening and usually associated with multiple organ failure (1-3). Central nervous system (CNS) is extremely vulnerable to injury by heat stroke, and is virtually involved in all cases (3-6). Injury to CNS is considered to be caused by several mechanisms: direct toxicity by heat to certain cell types which contain abundant concentration of heat shock proteins (e.g., Purkinje cells of cerebellum), small vessel ischemia secondary to altered hemostasis (sepsis-like phenomenon), inflammation and apoptosis triggered by interleukin-1 release, and ischemia induced by prolonged vasogenic edema which results from cytokine-induced leakiness of blood-brain or blood-cerebrospinal fluid barrier (6-10). Cerebellum, basal ganglia, hypothalamus and limbic system are known to be highly vulnerable to heat stroke-induced brain injury (3, 6). Other vulnerable areas include thalamus, brain stem, cerebral cortex and anterior horn cells of spinal cord (3). White matter involvement is reported in a few cases (6, 11). CNS involvement results in long-term neurological sequelae such as pancerebellar syndrome, in 20% of survivors (1, 3, 12, 13).

Magnetic resonance imaging (MRI) is not a requisite for the diagnosis of heat stroke, but is sometimes performed to exclude edema, hemorrhage and other possible causes of hyperthermia and coma (3, 5). T2-weighted imaging (T2WI) and fluid-attenuated inversion recovery (FLAIR) imaging may show heat stroke-induced brain injury as hyperintense foci (4, 5, 11). Diffusion-weighted imaging (DWI) usually shows abnormalities more conspicuously

than T2WI or FLAIR imaging, or the abnormalities may be confined only to DWI (6, 11, 14). Contrast-enhanced examination may sometimes reveal enhancement of the lesions (6). MRI obtained in a late phase usually shows cerebellar atrophy (2, 5, 15).

We hereby report a case of heat stroke in which detection of heat stroke-induced brain injury was improved by high b-value DWI.

Case report

A 46-year-old man, reported by the family as healthy previously, was found collapsed in a sauna and brought to the hospital emergency and critical care center. The Glasgow Coma Scale (GCS) at the time of hospital admission was 3. His systolic arterial blood pressure was 70 mmHg. Respiratory rate was 40 per minute, and the oxygen saturation was 80% in room air. His core body temperature was 42°C. There were first degree burns all over the body. He was diagnosed as heat stroke. He was immediately intubated, and rapid cooling through external ice packs, rapid infusion of ample amount of intravenous fluid, mechanical ventilation and gastric ice lavage was performed. His core body temperature fell down to 38°C in one hour. Computed tomography (CT) of the brain was then performed, which revealed no obvious abnormality. Despite prompt treatment, he developed disseminated intravascular coagulation (DIC), acute hepatic and renal failure, and lactic acidosis, on the following day. He was treated with intravenous fluid, fresh frozen plasma and gabexate mesylate.

He remained unconscious (GCS = 3) so that MRI of the brain was performed on the eighth day, to exclude any intracranial pathology. MRI was done using a 1.5T scanner. Axial

fast spin-echo T2-weighted images {repetition time (TR)/ echo time (TE) = 4500/ 96 ms, echo train length (ETL) = 7, number of excitation (NEX) = 2, acquisition time (TA) = 3 min 58 s}, axial spin-echo T1-weighted images {TR/TE = 600/15 ms, NEX =1, TA = 1 min 59 s}, axial fast FLAIR images {TR/TE = 9000/114 ms, inversion time (TI) = 2500 ms, ETL = 11, NEX =1, TA = 3 min 20 s} and axial fast spin-echo echo-planar DWI {b-value (b) = 1000, 2000, 3000 s mm^{-2} } along with axial echo-planar T2-weighted images {b = 0 s mm^{-2} } were acquired {TR/TE = 5500/190 ms, NEX = 5, TA = 1 min 56 s}. High b-value {b = 2000, 3000 s mm^{-2} } DW images revealed moderate to marked hyperintensity at/ around bilateral dentate nuclei and small foci of hyperintensity at bilateral thalami (Fig 1A-1D). Apparent diffusion coefficient (ADC) maps revealed ADC decrease of bilateral dentate nuclei lesions. The ADC values of thalamic lesions were difficult to interpret due to too small lesion size. DW images at b-value of 1000 s mm^{-2} revealed only portion of dentate nuclei lesion and right thalamic lesion as very small foci of mild hyperintensity (Fig 1E, 1F). T2-weighted, T1-weighted and FLAIR images did not reveal any abnormality (Fig 1G, 1H). Contrast-to-noise (CNR) ratio measurement performed at bilateral dentate nuclei revealed improved CNR at high b-values (CNRs at b-value of 3000, 2000 and 1000 s mm^{-2} were 5.28, 4.67 and 3.33, respectively). The patient was considered to have heat stroke-induced brain injury.

Treatment with intravenous fluid, fresh frozen plasma and gabexate mesylate was continued. Continuous hemofiltration was performed to treat acute renal failure. Debridement and skin graft were done to burn lesions which had progressed to the third degree.

His level of consciousness improved gradually. MR examination was repeated on the

44th day of hospital admission. Axial T2-weighted images, FLAIR images, T1-weighted images, gradient-echo T2*-weighted images {TR/TE = 800/26 ms, NEX =1, flip angle (FA) = 20°, TA = 2 min 54 s} and post-contrast-enhanced T1-weighted images {TR/TE = 600/17 ms, NEX =1, TA = 1 min 59 s} using 0.1mmol/kg gadopentetate dimeglumine were obtained. Mild cerebellar atrophy was observed. No signal abnormality or abnormal enhancement was observed. There were no features suggestive of hemorrhage. He was transferred to a local hospital on the 61st day of admission. His GCS was 14, and he had truncal ataxia and tingling and numbness of extremities, at the time of transferral.

Discussion

In this case, high b-value DWI improved detection and delineation of heat stroke-induced brain injury. Improved CNR at high b-value is thought to improve detection and delineation of the lesions. At high b-values, the signal intensity of all tissues decline, but depending on the ADC values of the tissues (16, 17). Tissues with ADC decrease (i.e., restricted diffusion) suffer less signal decline than normal brain parenchyma, so as to improve CNR between these tissues and normal brain parenchyma (18). This is in consistent with the observation of improved CNR and consequent improvement in detection of abnormal tissues (tissues with restricted diffusion) of acute global cerebral anoxia, hyperacute cerebral infarction, and subacute sclerosing panencephalitis (SSPE), at high b-values (18-20).

The finding of restricted diffusion is consistent with the previous DWI reports of heat stroke-induced brain injury, except that by Mahajan et al (6, 11, 14). Among several

mechanisms proposed to give rise to heat stroke-induced brain injury, ischemia is thought to induce restricted diffusion. Ischemia of brain tissue results from attempts of the body's autoregulatory mechanisms to divert blood flow towards periphery to dissipate excessive heat (21, 22). Increased intracranial pressure secondary to venous congestion and brain edema as the result of increased permeability of blood-brain or blood-cerebrospinal fluid barrier may also give rise to ischemia (6-8). As in acute cerebral infarction or global cerebral anoxia, ischemia results in impaired functioning of $\text{Na}^+ - \text{K}^+$ ATPase pump (18, 19). This results in net flux of sodium and water into the cells, giving rise to cellular swelling. Extracellular space that surrounds the cells diminishes as the cells swell. This results in restricted diffusion of water molecules within the extracellular space, which is shown as hyperintensity on DWI. Evidence of cellular swelling including axonal dilatation has been documented in autopsy reports of acute heat stroke (15). Another autopsy finding that might be related to appearance of hyperintensity on DWI is vacuolation in myelin sheath or neurons. Bazille et al have reported of vacuolization within myelin sheath around dentate nucleus and presence of vacuole-containing ghost nerve cells in thalamus, in a patient with heat stroke who died in 28 hours (12). Restricted diffusion may result from limited extracellular space owing to vacuolization within myelin sheath or nerve cells (23). The exact underlying mechanism for vacuolization in acute heat stroke is not known, but it could also be a consequence of ischemia (24). Direct cytotoxicity may also give rise to restricted diffusion, but the mechanism is yet to be evolved (11). Apoptosis is another cause of cell death proposed to occur in heat stroke, but is considered less likely to produce hyperintensity on DWI, as it is reported to be associated with facilitated diffusion (6, 9, 10, 25).

It is considered that both dentate and thalamic lesions are the direct effects of heat stroke, rather than secondary degeneration. Although dentate nucleus and thalamus constitute part of cerebellothalamic tract, lack of abnormal signal at other areas that form the tract (i.e. cerebellar efferent pathway) does not favor consideration of secondary degeneration of either lesion (14). The appearance of cerebellar atrophy in the follow-up MRI is indicative of irreversibility of dentate nuclei lesions (3). Reversibility of thalamic lesions is difficult to determine due to too small lesion size.

In this case, b-value of 3000 s mm^{-2} provided higher CNR than b-value of 2000 s mm^{-2} . However, the lesion extent did not differ in between the two b-values. Considering compromise of signal-to-noise ratio or longer imaging time in acquiring DWI with higher b-values, b-value of 2000 s mm^{-2} may be appropriate for detection of heat stroke-induced brain injury (16).

In summary, we have reported a case of heat stroke in which high b-value DWI improved detection of heat-stroke-induced brain injury. The ability of high b-value DWI to improve contrast between lesions with restricted diffusion and normal brain parenchyma allowed improved detection of signal abnormalities. It may be thus advantageous to acquire high b-value DWI for detection of heat stroke-induced brain injury, as there is possibility of not observing abnormality on DWI with routine b-value or routine MRI sequences.

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Figure Legends

Fig 1.

MR images of the patient obtained on the eighth day. Diffusion-weighted imaging (DWI) at b-value of 3000 (Fig 1A, 1B) and 2000 s mm^{-2} (Fig 1C, 1D) reveals marked to moderate hyperintensity at/ around bilateral dentate nuclei and small foci of hyperintensity at bilateral thalami (white arrows). DWI at b-value of 1000 s mm^{-2} (Fig 1E, 1F) reveals only portion of dentate nuclei lesion and right thalamic lesion as very small foci of mild hyperintensity (white arrows). T2-weighted imaging (T2WI) does not reveal any abnormality (Fig 1G, 1H).















