Fatal hyperthermia following acute cervical spinal cord and head injury

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Abstract

A 22-year-old man with schizophrenia presented with cervical spine damage caused by a crush injury. Upon admission, we performed anterior cervical decompression and fusion of vertebrae C5, C6, and C7. The patient experienced treatment-resistant hyperthermia with a body temperature >40°C. He did not show any evidence of drug use that might induce malignant hyperthermia. He also did not exhibit symptoms of common forms of malignant hyperthermia, including rigidity of the arms and legs, myoglobin in the urine, or anesthesia toxicity. The patient's condition did not improve, and he died of hypotension 15 hours after admission. We speculate that the cause of death was malignant hyperthermia due to acute cervical spinal cord injury. The physiological origin of hyperthermia in this patient is unknown. Recognition of hyperthermia symptoms and risk factors in patients with cervical spinal cord injury may enable early intervention to prevent progression to fatal fever.

Key words: Spinal cord injury, head injury, hyperthermia, malignant hyperthermia, thermoregulation.

Introduction

Control of hyperthermia due to infectious and non-infectious disease is an important factor affecting the outcome of patients in the intensive care unit (ICU). Traumatic quadriplegia after acute cervical spinal cord injury has been associated with potentially fatal non-infectious hyperthermia characterized by an extreme, idiopathic elevation in core body temperature beyond 40°C. (1) This condition, termed hyperthermic thermoregulatory dysfunction, is often referred to as "quad fever". A literature review revealed very few reports of quad fever and its pathophysiologic mechanisms are poorly understood. Here, we present a case of fatal hyperthermic thermoregulatory dysfunction in a patient treated for quadriplegia at our hospital.

Case presentation

A 22-year-old man was admitted to the emergency room because of quadriplegia with neck pain. He had fallen head first from the fourth floor of a building. His history included schizophrenia that was being treated at a rehabilitation center for the last 14 years and was presently well controlled. General clinical examination performed upon his admission yielded the following results: blood pressure, 124/82 mmHg; heart rate, 100 beats/min; respiratory rate, 12 beats/min; body temperature, 36.2°C; and peripheral oxygen saturation when breathing room air, 98%. The patient appeared fully conscious and aware, but he did not remember jumping from the building.

The patient presented with extensive physical injuries. He had an epidermal contusion to the parietal area (7x5x5 cm). An initial manual muscle test result of 0/5 indicated that his limbs were paralyzed and he presented broad sensory dysfunction below the Th1 level. Magnetic resonance imaging (MRI) was performed within 1 hour of injury. MRI revealed vertebral fractures in C5, C6, and C7, excluding the vertebral endocranium sac in C5 and C6 (**Figure 1a**). T2-weighted imaging revealed increased signal around the C5-C7 vertebral bodies and arch, consistent with edema (**Figure 1b**). Function MRI showed no evidence of intracranial lesions. The chest and abdomen appeared normal on physical examination and computed tomography. Laboratory findings showed elevated AST level (174 U/L), ALT level (214 U/L), and leukocytosis (15,400/mm3, with 87% neutrophils), but not elevated serum C-reactive protein level (0.61 mg/dL). An arterial blood gas test performed in room air showed normal pH (pH 7.393), partial

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pressures of 38.2 mmHg and 94 mmHg for CO2 and O2, respectively, and a normal base excess of -1.4. The rapid antigen test for influenza A and B was negative.

After admission, his temperature increased gradually to 40°C, and his level of consciousness deteriorated. Five hours after admission, we performed anterior decompression and fusion of the vertebral fractures in C5, C6, and C7. The patient's temperature was 40°C during and after surgery. He was immediately, admitted to the ICU and treated with antibiotics (ampicillin 6 g/day), steroid pulse therapy (Solu-Medrol 10 g/day), and whole-body cooling. Medication did not relieve his fever. He presented tachypnea and hypotension 10 hours post-admission, but we did not observe rigidity of his arms and legs or myoglobin in his urine. We were unable to control his hypotension with vasopressor drugs, and he died 5 hours after the onset of hypotension. Two hours after his death, the patient's temperature remained at 40°C.

Discussion

We report a case of quadriplegia and fatal fever after acute cervical spinal cord and head injury. Fever is associated with poor outcome in up to 67% of ICU patients with or without infection. Non-infectious severe hyperthermia, such as malignant hyperthermia, neuroleptic malignant syndrome, and hyperthermic thermoregulatory dysfunction are particularly problematic. (1) As discussed below the case presented here did not show typical signs and symptoms of common forms of hyperthermia.

Malignant hyperthermia, a potentially fatal genetic disorder, typically manifests in susceptible patients upon administration of anesthesia. The patients exhibit elevated body temperature, unexpected tachycardia, arrhythmia, unstable circulation, muscle rigidity, and/or cola-colored urine; malignant hyperthermia can lead to multiple organ failure and death. (2,3) Some clinical findings of our case were similar to those of malignant hyperthermia; thus, we initially suspected malignant hyperthermia due to volatile inhalation of anesthetic agents (induction with vecuronium and propofol and maintenance with sevoflurane). However, the onset of malignant hyperthermia typically occurs within 1 hour of beginning general anesthesia, whereas our patient showed fever before administration of anesthetic drugs. In addition, our patient did not show some clinical signs, such as masseter rigidity, tachycardia, tachypnea, acidosis, and increased muscle metabolism (>20,000 U/L) throughout treatment. Larach et al. (3) reported a clinical grading scale to predict malignant hyperthermia susceptibility. Our case was scored 15, which ranks low on this prediction scale.

Neuroleptic malignant syndrome is triggered by an adverse, idiosyncratic reaction to neuroleptic or antipsychotic drugs. Symptoms that distinguish it from malignant hyperthermia include muscle rigidity, tremors, sweating, unstable blood pressure, and dysrhythmias. Our patient showed none of these symptoms. In addition, the only medication he was taking was a sleep agent (brotizolam), and his care was managed well by the psychiatric facilities treating him. Therefore, we do not suspect neuroleptic malignant syndrome or drug-induced hyperthermia.

Therefore, we think that our patient had hyperthermic thermoregulatory dysfunction, a condition first described in a 1982 case report of acute cervical spinal cord injury and commonly called quad fever. (1) A literature review using PubMed search revealed very few cases of quad fever. The pathologic mechanisms of this condition are thus poorly understood.

Sugarman et al. (1) found that thermoregulation is impaired by crush injuries following high falls. Feuerman et al. (4) demonstrated a similar condition in pigs with spinal cord injury and presented a case report of stress-induced malignant hyperthermia in a 21-year-old man with head injury. It is unclear, however, if this represented a genuine case of stress-induced malignant hyperthermia. Nevertheless, these authors proposed that a hyperadrenergic, hypermetabolic state induced by a major head injury might cause hyperthermia. However, this hypothesis has not been further explored.

Kras et al. (5) demonstrated that that spinal prostaglandin E2 (PGE2) levels increase significantly after painful facet joint injury. We thus speculate that PGE2 elevation in the cerebrospinal fluid following injury may ectopically stimulate the hypothalamic axis to cause malignant hyperthermia. However, further research is needed to determine the pathologic basis of malignant hyperthermia after brain and spinal cord injury.

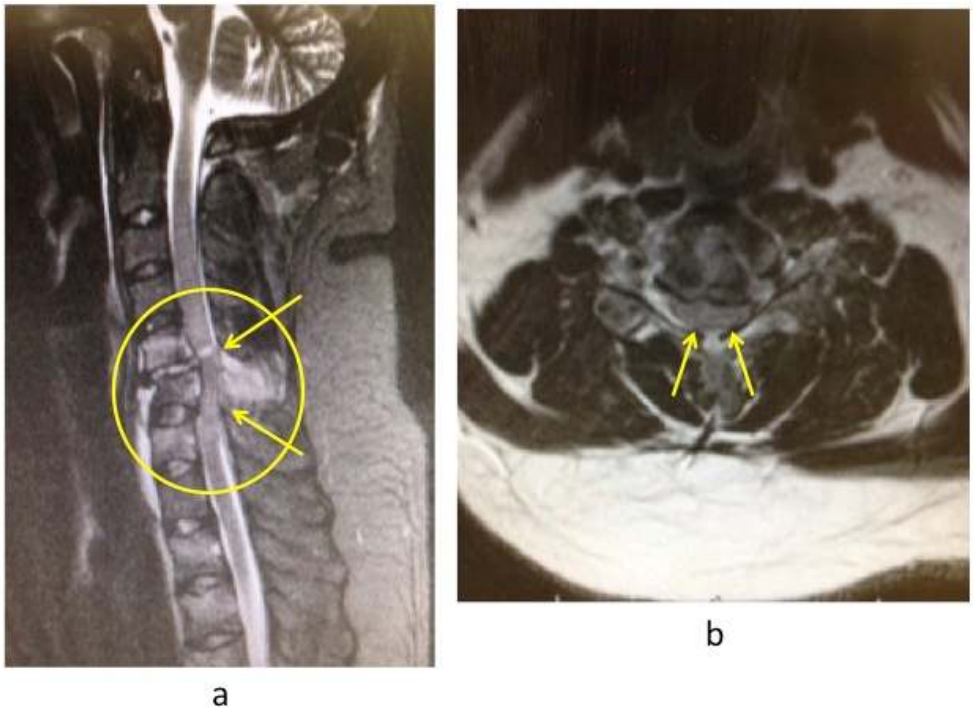
Conclusion

The cause of quadriplegia and fatal fever after acute cervical spinal cord injury is uncertain. We speculate that changes in the hypothalamic axis result in thermoregulatory dysfunction following head and spinal cord injury. Early recognition of risk factors for fatal fever after this type of injury may enable prompt treatment, thereby preventing progression of malignant hyperthermia.

Conflict of interest

None.

Figure 1. Axial (a) and sagittal (b) magnetic resonance images of the cervical spine



Legend: This MRI showing multiple fractures in C5, C6, and C7 (arrows), excluding the endocranium sac in C5 and C6 (arrows indicates narrowing of the spinal canal resulting in exclusion of the endocranium sac)The circle (a) shows the region around the C5-C7 vertebral bodies and arch that had increased signal intensity on T2-weighted imaging, which is suggestive of edema.

References

1. Sugarman B, Brown D, Musher D. Fever and infection in spinal cord injury patients. JAMA 1982;248:66-70.
2. Hadad E, Weinbroum AA, Ben-Abraham R. Drug-induced hyperthermia and muscle rigidity: a practical approach. Eur J Emerg Med 2003;10:149-54.
3. Larach MG, Localio AR, Allen GC, Denborough MA, Ellis FR, Gronert GA, et al. A clinical grading scale to predict malignant hyperthermia susceptibility. Anesthesiology 1994; 80:771-9.
4. Feuerman T, Gade GF, Reynolds R. Stress-induced malignant hyperthermia in a head-injured patient. Case report. J Neurosurg 1988;68:297-9.
5. Kras JV, Dong L, Winkelstein BA. Increased interleukin-1 alpha and prostaglandin E2 expression in the spinal cord at 1 day after painful facet joint injury: evidence of early spinal inflammation. Spine (Phila PA 1976) 2014;39:207-12.