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Case Report

Burn-induced neuroepithelial changes as a delayed cause of mortality in major burns: a case report and literature review

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Abstract: Background: Mortality in major burns is caused mainly by multisystem organ failure. Brain lesions in burn patients are rare and predominantly traumatic in nature. Here, we present an unusual case of burn-induced glioma causing rapid neurological deterioration and death. Case presentation: A 33-year-old male, with 85% total body surface area (TBSA) flame burns, presented initially with inhalation injury and acute compartment syndrome with no other associated injuries. Based on the initial assessment, the patient's cognitive status was not affected, with a Glasgow coma scale (GCS) on admission of 15/15 and normal brain computed tomography (CT) images. The patient was resuscitated and immediately admitted to the burns unit where he underwent multiple sessions of debridement and skin grafting. The patient's neurological status deteriorated dramatically, and brain magnetic resonance imaging (MRI) confirmed the presence of a heterogenous mass, highly suggestive of a high-grade glioma, that was not present during the initial assessment. Unfortunately, the patient died shortly afterwards as a result of cardiac asystole. Conclusions: Multiple studies have demonstrated a connection between chronic inflammatory processes and gliomagenesis. The case presented here supports the notion that high-grade gliomas can progress rapidly in immunocompromised patients, thus further reducing survival rates. Therefore, patients with inflammatory conditions combined with neurological symptoms/signs should be investigated thoroughly to evaluate the presence and extent of such pathology. Newly developed radiological modalities can help in early detection and timely management of the condition.

Keywords: Burn, brain tumors, glioma, mortality, neuropathology, immunosuppression

Background

Major burn injuries, involving more than 25% total body surface area (TBSA), can be devastating and disfiguring as they often result in serious physical and emotional morbidity. According to the World Health Organization, burn injuries result in 180,000 deaths annually worldwide [1]. Mortality in victims of major burns is attributed to several factors, including multi-organ failure, inhalation injury, respiratory failure, lung trauma, shock and sepsis [2]. Burn patients in general are highly susceptible to infections, and the likelihood of these infections progressing to fulminant sepsis is well-established in the medical literature [2]. The prevalence of sepsis is estimated to be approximately 61.8% in major burns, with *Pseudomonas* species being the most commonly isolated organism [2]. The incidence of sepsis-related deaths in burn patients ranges between 50% and 84% in adults and approximately 55% in children [3]. The pathophysiology is generally attributed to disruption of the integrity of the outer skin barrier, immunosuppression in patients with major burns, and opportunistic infections caused by contamination of the blood, wound, and respiratory tract [3].

Here, we present an unusual case of burn-related mortality in a patient with major burns complicated by cerebral lesion. To our knowledge, this is the first reported case of delayed mortality in a major burn caused by a cerebral lesion.

Case presentation

A 33-year-old male patient was brought to the emergency department with flame burns

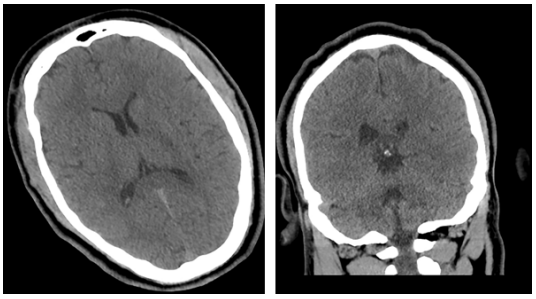

Figure 1. Brain CT at the time of the admission showing normal findings.

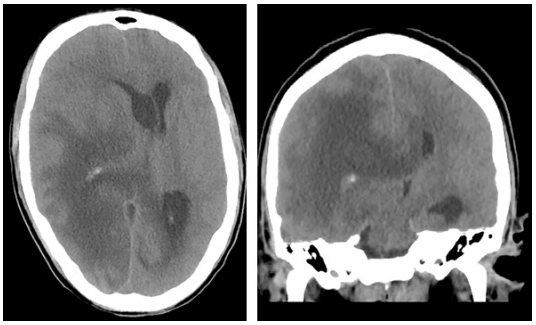

Figure 2. Brain CT at day 52 showing large white matter hypodensity. This finding was likely suggestive of vasogenic edema involving the right parietal, occipital and temporal lobes with significant mass effect and midline shift to the left side of approximately 8.7 cm associated with subfalcine herniation and left lateral ventricle entrapment and enlargement.

caused by an explosion at an electrical power station. He sustained 85% TBSA superficial and deep partial-thickness circumferential burns in addition to an inhalation injury and acute compartment syndrome of all limbs. Primary, secondary and tertiary surveys were carried out according to the Advanced Trauma Life Support (ATLS) protocol. No other major injuries were identified. The results of initial diagnostic imaging, consisting of routine trauma surveillance X-rays, FAST scan, and pan-CT (including brain CT), were negative for other injuries (**Figure 1**). Urgent operative escharotomies and fasciotomies were performed on all limbs and stabilization and resuscitation procedures were continued in the burn unit. After stabilization, the patient underwent multiple sessions of debridement and xenografts to all burned areas. Xenografts were eventually replaced with autografts once donor skin sites had healed for reharvesting. Tracheostomy was performed for prolonged intubation.

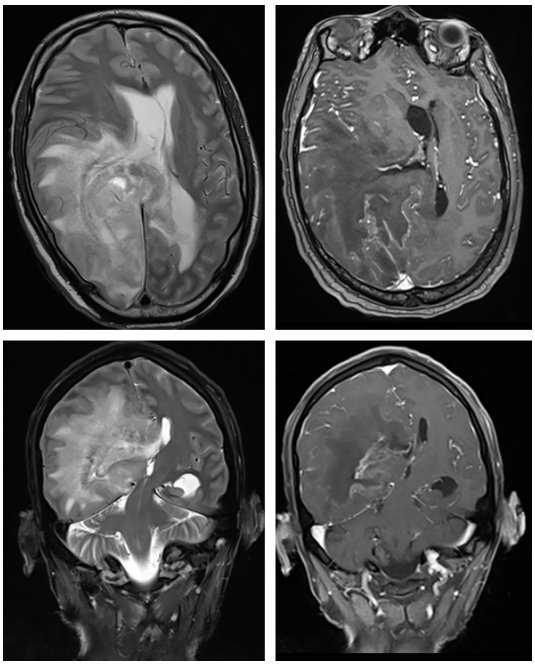

Figure 3. Brain MRI showing a high-density aggressive mass centered on the corpus callosum more to the right side, involving right frontal, parietal and temporal deep white matter crossing the midline at the level of the splenium. Associated with restricted diffusion, micro-hemorrhages and significant mass effect with a leftward midline shift suggestive of glioma.

During the period of his hospitalization, the patient developed several episodes of sepsis diagnosed on the basis of positive blood cultures for multiple organisms (*Acinetobacter baumannii*, *Candida albicans* and *Pseudomonas aeruginosa*). Each of these episodes was treated in collaboration with infectious disease specialists. However, at day 43 post-admission, his condition deteriorated into fulminant septic shock with positive blood cultures for *Pseudomonas aerugionosa*. He was resuscitated and managed medically with appropriate antimicrobial coverage in addition to exchange of all his intravenous lines and indwelling catheters. After modest improvement, the patient's condition further deteriorated on day 52, with a sharp decline in his cognitive statues and asymmetric non-reactive pupils with mydriasis on the right side. His Glasgow coma scale (GCS) score dropped from 11T/15 to 6T/15 and he became bradycardic. Immediate brain CT imaging showed a large region of white matter hypodensity that was not seen on the initial brain CT at admission (**Figure 2**). This finding

indicated vasogenic edema involving the right parietal, occipital and temporal lobes with significant mass effect and a midline shift to the left side of approximately 8.7 cm associated with subfalcine herniation and left lateral ventricle entrapment and enlargement. A high-grade tumor was suspected by the neurosurgery team and emergency brain MRI confirmed the presence of a heterogenous mass (9.7 × 5.3 × 8.6 cm) involving the right frontal, parietal and temporal deep white matter that was highly suggestive of an aggressive high-grade primary brain tumor (**Figure 3**). Due to the poor overall prognosis and after a thorough discussion with his family, surgical intervention was deferred and medical management of high ICP was continued. On day 53, his GCS score dropped further to 3T/15 and a repeat brain CT showed worsening vasogenic edema. The patient died on day 54 as a result of cardiac asystole.

Discussion

The leading cause of death in major burn injuries is multisystem organ failure in 64.9% of patients [4]. Other causes include neurological deterioration, cardiac arrest, aspiration, burn shock, cerebral stroke, toxic shock syndrome, pneumonia, hemorrhage, and carbon monoxide intoxication [4]. In a systematic review, the mortality rate in burns victims varied between 1.4% and 34% [5]. Risk factors of mortality include older age, larger TBSA, and inhalation injury. In addition, flame burns have the highest mortality rate [5]. Early mortality was attributed mainly to burn shock or inhalation injury. Late mortality was caused predominantly by multi-organ failure (25%-65%) followed by respiratory complications (34%), sepsis (2%-14%) and cardiac, renal or cerebral complications (< 5%) [5].

Burns patients are immunosuppressed and therefore, are at a higher risk of developing invasive infections and tumors [6]. With extensive burns, the human body undergoes various dynamic adjustments. Burn patients are in a chronic state of systematic inflammatory stimulation that results in massive production of anti-inflammatory cytokines (IL-4, IL-10, IL-13) that leads to the development of chronic anti-inflammatory response syndrome (CARS) [6]. Furthermore, a significant reduction in production of macrophage inflammatory protein 1α (MIP-1α) leads to disruption of monocyte and neutrophils recruitment [6].

Gliomas are the most common primary solid tumors of the central nervous system, with poor overall prognosis (median survival rate of 15 months for grade IV tumors) [7]. Survival rates vary considerably as high-grade gliomas tend to grow rapidly, rendering them untreatable [7]. Several epidemiological studies have suggested a causal link between inflammation and gliomagenesis [8], with a connection demonstrated between single nucleotide polymorphisms (SNPs) of immune-related genes (including IL-4, IL-10, and IL-13), and pro-inflammatory Cox2 and IL-6 [8]. In addition, chronic inflammation occurring within the microenvironment of the tumor lesion is thought to either initiate malignancy-conferring genetic mutations and/or release them as a result of oncogene expression [7].

Gliomagenesis involves three main phases: initiation, promotion, and progression. Chronic inflammation stimulates the glioma promotion phase and contributes to neovascularization [7]. Moreover, gliomagenesis is thought to be protected from the immune defense system due to the burn-driven immunosuppressive microenvironment [7]. Immunocompromised patients, such as patients with acquired immune deficiency syndrome (AIDS), are thought to be at a higher risk of developing gliomas [9].

Neuropathological changes in patients who sustained electrical burns occur via two mechanisms: direct injury due to the blast effect or mechanical trauma, and tissue exposure to current through thermal injury [10]. This type of injury can damage brain tissue and the surrounding vascular endothelium. Moreover, major burn injuries (> 35% TBSA) have been shown to result in increased release of a neurotoxic high-molecular weight lipoprotein, which causes encephalopathy and peripheral neuropathy [10]. Burn-induced sepsis may have contributed to the decline in brain function observed in our patient as deteriorating cerebral dysfunction in sepsis is not uncommon [11]. This may result from several inflammatory and non-inflammatory processes, including excessive microglial activation, cerebral perfusion impairment, blood brain barrier dysfunction and altered neurotransmission [11]. This is supported by evident changes in MRI, such as cytotoxic vasogenic edema, posterior reversible encephalopathy syndrome, white matter disruption and brain atrophy [11].

Conclusion

To the best of our knowledge, this is the first reported case of burn-related mortality secondary to new-onset high-grade gliomas. Unfortunately, the pathology was not confirmed as an autopsy was rejected by the patient's relatives. Such tumors should be considered in the differential diagnosis of patients with deteriorating neurological status.

Disclosure of conflict of interest

None.

Abbreviations

TBSA, Total body surface area; WHO, World Health Organization; ATLS, Advanced trauma life support; FAST, Focused assessment with sonography in trauma; CT, Computerized tomography; GCS, Glasgow coma scale; MRI, Magnetic resonance imaging; ICP, Intracranial pressure; CARS, Chronic anti-inflammatory response; MIP-1α, Macrophage inflammatory protein 1α; CNS, Central nervous system; SNPs, Single nucleotide polymorphisms; AIDS, Acquired immune deficiency syndrome.

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