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Abnormal lymphocyte response after pediatric thermal injury is associated with adverse outcomes

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ABSTRACT

Background: Burns are a leading cause of morbidity in children, with infections representing the most common group of complications. Severe thermal injuries are associated with a profound inflammatory response, but the utility of laboratory values to predict infections in pediatric burn patients is poorly understood.

Materials and methods: Our institutional burn database was queried for patients aged 18 y and younger with at least 10% total body surface area burns. Demographics, mechanism, laboratory results, and outcomes were extracted from the medical record. Patients were classified as having an abnormal or normal total white blood cell count, neutrophil percentage, and lymphocyte percentage using the first complete blood count drawn 72 or more hours postinjury. Outcomes were compared between groups.

Results: White blood cell data were available for 90 patients, 84 of whom had neutrophil and lymphocyte percentages. Abnormal lymphocyte percentage 72 h or more after burn injury was associated with a significant increase in infections (67.9% *versus* 32.3%, $P = 0.003$), length of stay (33.1 *versus* 18.8 d, $P = 0.02$), intensive care unit length of stay (13.1 *versus* 3.7 days, $P = 0.01$), and ventilator days (5.8 *versus* 2.3, $P = 0.02$). It was also an independent predictor of infection (odds ratio 7.2, 95% confidence interval 2.1-24.5).

Conclusions: Abnormal lymphocyte percentage at or after 72 h after burn injury is associated with adverse outcomes, including increased infectious risk.

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Introduction

Each year, approximately 127,000 children are seen in U.S. emergency departments for burn injuries and over 12,000 are hospitalized.[1] Burn patients are at high risk for adverse outcomes, including infectious complications,[2] which are the greatest cause of morbidity after thermal injury.[3-5]

Critical illness from thermal injury causes profound changes in the immune system and in particular cellular immune responsiveness.[6] This is characterized by an initial proinflammatory phase termed the systemic inflammatory response syndrome (SIRS), which involves a large systemic release of cytokines and is defined by at least two of the following four criteria: fever, tachycardia, tachypnea, and leukocytosis or leukopenia.[7] This process is concurrent with an anti-inflammatory response as the body attempts to return to homeostasis, termed the compensatory anti-inflammatory response syndrome (CARS).[8] CARS results in a large numerical and functional reduction of many immune cell populations, including neutrophils, monocytes, macrophages, lymphocytes, and natural killer cells.[6] The typical post-traumatic cellular response is an elevation of the white blood cell (WBC) and neutrophils and depression of the lymphocyte count. Persistent immunosuppression resulting from prolonged CARS is believed to contribute to morbidity and mortality in critically ill patients, and this has been associated with an increased rate of nosocomial infection in critically injured children.[9,10] Failure of the immune cellular counts to normalize after 72 h has been associated with adverse outcomes in both sepsis and trauma.[11,12]

Making the clinical diagnosis of infection after moderate-to-large thermal injury is particularly challenging, given the massive inflammatory response that follows and the need for repeated debridement and/or grafting procedures. The lack of skin barrier function in burn patients makes it all the more important to evaluate the cellular elements of the immune system. Our primary objective in this study was to determine the predictive value of normalization of the immune response. Normalization was defined as restoration of the WBC count, neutrophil, and/or lymphocyte percentage 72 h or more after burn injury. We hypothesized that failure to normalize the immune response 72 h or more after burn injury would lead to adverse outcomes.

Material and methods

Study design

This was a single-center retrospective study from a free-standing children's hospital that is an American Burn Association–verified pediatric burn center. The study was approved by our Institutional Review Board.

Study population/data source

We used our institution's burn registry to identify patients less than or equal to 18 y old who sustained at least moderate thermal injury (defined as greater than or equal to 10% of total body surface area [TBSA]) and survived at least 3 d following admission. Patients also must have had at least one complete blood count (CBC) with differential (WBC count, neutrophil count, and lymphocyte count) between postinjury days 3 and 7. Patients were excluded if they had an underlying immunologic disorder or were taking any immunomodulatory therapy on presentation.

We retrieved the following information from the burn registry: age, sex, mechanism of burn, TBSA burn, length of stay (LOS), intensive care unit (ICU) LOS, ventilator days, infectious complications, and mortality.

The data for the CBC and differential were drawn as part of routine clinically indicated laboratories and were acquired from the electronic medical record retrospectively. All CBCs with differential obtained within the first week (7 d) of admission were extracted for the analysis with recording of the absolute WBC count (k/mm^3), percentage of neutrophils, and percentage of lymphocytes.

Infection data

Reviews of the electronic medical record were conducted to determine the development of infectious complications. Infectious complications were categorized into pneumonias, urinary tract infections, bloodstream infections, and burn wound infections. Infection was defined using Centers for Disease Control criteria for blood and urine.[13-15] Burn site infections were determined by the burn surgeons along with documentation in the medical record and decision to treat with antibiotics and/or excision. Pneumonias were diagnosed by positive lower respiratory culture and decision to treat by the clinicians. Analysis was limited to short-term infections diagnosed within the initial hospitalization while excluding those diagnosed more than 30 d post injury.

Statistical analysis

The normal ranges for WBC, neutrophils, and lymphocytes are established by the clinical laboratory at the hospital and vary with age (Table 1). Any value outside of the normal range for

Table 1 – Institution-specific normal ranges for WBC, neutrophil, and lymphocyte percentage by age.

Age range	WBC (k/mm^3)	Neutrophil (%)	Lymphocyte (%)
0 d	9.0-38.0	43-87	19-36
1-6 d	9.4-34.0	42-80	26-36
7-13 d	5.0-21.0	27-65	36-46
14-27 d	5.0-20.0	20-58	43-53
28-179 d	5.0-19.5	21-47	41-71
6 mo-1.9 y	6.0-17.5	18-44	46-76
2-3.9 y	6.0-17.0	20-46	44-74
4-5.9 y	5.5-15.5	28-56	35-65
6-9.9 y	5.0-14.5	37-65	27-57
10-15.9 y	4.5-13.5	36-72	28-48
16-20.9 y	4.5-13.5	39-75	25-45