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Impact of early positive cultures in the elderly with traumatic brain injury

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ABSTRACT

Background: Traumatic brain injury (TBI) is a leading cause of morbidity and mortality in the United States, especially in the elderly, who have the highest rates of TBI-related hospitalizations and deaths among all age groups. Sepsis is one of many risk factors that is associated with higher mortality and longer length of hospital stay in this population partially due to the immunosuppressive effects of TBI. The significance of early indicators of infection, such as a positive blood, sputum, or urine culture, is not well described. The purpose of this study was to determine if early positive cultures predict higher mortality in elderly patients with TBI.

Methods: All trauma patients aged ≥65 years with TBI, admitted between January 1, 2009 and December 31, 2013 to the surgical intensive care unit, were retrospectively reviewed. Clinical data including results from sputum, blood, and urine cultures were reviewed.

Results: Overall, 288 elderly patients with TBI were identified, and 92 (32%) had a positive culture. Patients with positive cultures had longer intensive care unit (median 6.0 *versus* 2.0 days, $P < 0.001$) and ventilation days (median 7.0 *versus* 2.0 days, $P < 0.001$). Patients who had positive cultures within 2-3 days of admission had a higher adjusted hazard ratio for mortality than those patients who had positive cultures after 6 or more days.

Conclusions: In elderly patients with TBI, early positive cultures are associated with a higher risk of mortality. Further research is required to determine the role of obtaining cultures on admission in this subpopulation of trauma patients.

Introduction

Traumatic brain injury (TBI) is one of the leading causes of morbidity and mortality in the United States. Statistics from the Center for Disease Control show that TBI alone resulted in more than 2.5 million emergency department visits and accounted for 275,000 hospitalizations and 52,000 deaths in 2010.[1] The direct medical and indirect overall costs of TBI-related disabilities were estimated at $60 billion in 2000.[2] These injuries occur at a higher incidence at the extremes of age, 900 and 659 per 100,000 for those younger than 10 and older than 74 years, respectively.[3] The elderly are at the

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greatest risk of a TBI-related hospital admission primarily due to motor vehicle collisions and falls and have the highest TBI-related mortality among all age groups.[1,4,5]

Among patients with TBI, 16.9% die before hospital admission, whereas 5.6% die as an inpatient.[6] Multiple risk factors for mortality have been identified for inpatient TBI-related deaths including age, injury severity, pupillary abnormalities on presentation, abnormal imaging findings, hypotension, and the presence of existing comorbidities. Laboratory markers, such as S100B and neuron-specific enolase, are potential predictors of mortality.[7] Patients admitted with TBI carry a higher incidence of sepsis, respiratory failure, intensive care unit (ICU) stay, hospital stay, and mortality rate.[8] Sepsis is more common in severe TBI and is an independent risk factor for inhospital death and prolonged length of stay,[9] and this is, in part, due to the proposed immunosuppressive effects of TBI,[10] resulting in alterations of the innate and adaptive immune systems.[11,12] The significance of early signs of infection, such as a positive blood, sputum, or urine culture, is not well described. If mortality is increased, obtaining empiric cultures at admission, may better diagnose and treat these patients. The purpose of this study was to investigate the effect of the timing of the development of a positive culture with outcomes in elderly trauma patients with TBI. We hypothesized that the earlier a culture is positive, the higher the associated mortality.

Methods

The trauma registry at an urban level I trauma center, was queried for all trauma patients aged ≥65 years, who were admitted to the surgical ICU with TBI, defined as head Abbreviated Injury Scale (AIS) score ≥ 3, from January 1, 2009 to December 31, 2013. Demographic and injury data were collected. To examine the effect of timing of a positive culture on outcomes, blood, urine, and respiratory culture results from the entire hospital stay were reviewed and recorded along with the date they were obtained. All patients had empiric surveillance cultures drawn at the time of ICU admission, with the expectation that these cultures might better guide later treatment. Patients were classified into two groups: those with one or more positive cultures and those with negative cultures throughout their hospital course. Positive cultures were considered as those with any growth for blood samples, those with more than 100,000 CFU/mL for urine samples, and more than 10,000 CFU/mL for sputum samples.[13,14] For the sputum samples in particular, the threshold of 10,000 CFU/mL was used, given the fact that the majority of samples were obtained via bronchoalveolar lavage.[15] The timing of the cultures was determined by the hospital day on which the culture was obtained and categorized in the following manner: a positive culture within the first 2 days (day 1 or 2), on day 3, on day 4, on day 5, or on day 6 or after. The day of admission was defined as hospital day 1. Details regarding the type of TBI were also collected, including subarachnoid (SAHs), subdural (SDHs), epidural (EDHs), intraparenchymal (IPHs), intraventricular hematoma (IVHs), contusions, and herniation.

Parametric (t-test) and nonparametric (Mann–Whitney) tests were used for the comparison of normally and abnormally distributed continuous variables, and categorical variables were analyzed using the Pearson chi-squared test or Fisher's exact test. Clinically relevant categories were applied for Injury Severity Score (ISS: ≥16 *versus* < 16), head/neck, chest, abdomen/pelvis, and extremity AIS (>3 *versus* ≤ 3), admission Glasgow Coma Scale (GCS: ≤8 *versus* > 8), and admission systolic blood pressure <90 mmHg *versus* ≥ 90 mmHg.

The primary outcome was inhospital mortality. Secondary outcomes included hospital length of stay, ICU-free days, and ventilator-free days. Adjusted odds ratios with 95% confidence intervals (95% CI) for all outcomes were obtained from a multivariable logistic regression model, accounting for all statistically significant differences between the two groups. A P-value < 0.05 was considered statistically significant. A forward logistic Cox regression model was also used to identify independent predictors of mortality. The presence of multicollinearity between predictor variables was excluded using a linear regression model with the variance inflation factor, assuming a value of <5 being exclusive of significant collinearity.

Patients with positive cultures were further analyzed based on the timing of their positive culture after admission. Using "6 or more days" as the reference group, the adjusted hazard ratio (AHR) for mortality was calculated using Cox regression model incorporating a time-dependent variable to account for the timing of the positive culture and to adjust for all differences between the compared groups.

All statistical analyses were performed using the IBM SPSS Statistics for Windows, Version 20.0 (IBM, Armonk, NY). The study was approved by the Cedars-Sinai Medical Center's Institutional Review Board; the requirement for informed consent was formally waived.

Results

Over the 5-year study period, 288 patients aged ≥65 years with TBI were admitted to the surgical ICU. The median age was 81 years, and 50.7% were male. Overall, 14.6% were admitted with a GCS ≤8, and 65.3% had an AIS head >3 (Table 1). SDH were most common (64.6%), followed by SAH (50.3%) and cerebral contusion(s) (20.1%).

A total of 92 patients (31.9%) had at least one positive culture during their hospital stay. When compared to patients with negative cultures, those with a positive culture were more severely injured (median ISS 19.5 *versus* 17.0, $P = 0.030$), more likely to receive a blood transfusion(s) (14.1% *versus* 3.6%, $P = 0.001$), and more likely to have a SAH (62.0% *versus* 44.9%, $P = 0.007$), an IPH (26.1% *versus* 12.2%, $P = 0.003$), or an IVH (15.2% *versus* 6.6%, $P = 0.020$) (Table 1).

Among patients who had at least one positive culture, 54.3% had a positive sputum, 9.8% a positive blood, and 62.0% a positive urine culture (Table 1). The most common pathogens isolated from sputum cultures were *Klebsiella pneumonia* (20.0%), followed by *Enterobacter cloacae* (12.0%), *Staphylococcus aureus* (8.0%), and *Serratia marcescens* (8.0%) (Table 2). Coagulase-negative *Staphylococcus* was almost the dominant