EDITORIAL

Necrotizing Soft Tissue Infections: More than What Meets the Eye

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Necrotizing soft tissue infections (NSTIs) are characterized by fulminant tissue destruction, systemic toxicity driven by an inflammatory cytokine cascade, and carry substantial risk of morbidity and mortality with delayed diagnosis and intervention. The NSTIs are variously labeled as cellulitis, fasciitis, and myositis depending on the involvement of skin and subcutaneous tissue, fascia, and muscle, respectively. Early diagnosis, aggressive surgical debridement, and appropriate broad-spectrum antibiotic therapy are cornerstones of its management.[1]

We must thank Kurian et al.[2] for their study published in the current issue of the Indian Journal of Critical Care Medicine (IJCCM) looking into the patient characteristics and outcomes of NSTIs in a moderately large prospective cohort of patients admitted in a tertiary care surgical intensive care unit. We consider this an important piece of literature given the relative scarcity of published data regarding NSTIs from the Indian subcontinent.[3]

The reported mortality rate in this study was 34% which is considerably higher when compared to the improved outcomes seen in recent patient cohorts.[4,5] The authors suggest one of the possible reasons for high mortality in their cohort is a delayed presentation to the health care facility. Indeed the median days from symptom onset to surgical intervention was 7 days in their study. The patients in this cohort were also comparatively sicker with a median APACHE score of 17 (interquartile range [IQR] 12–24), and 76% were hypotensive and 59% had some degree of acute renal impairment at baseline. A retrospective review of 89 patients with necrotizing fasciitis (NF) found a delay in operative intervention of more than 24 hours from the time to admission was the only factor associated with an increased risk of an adverse outcome (relative risk 9.4, $p < 0.05$).[6] While this is understandable given the beneficial role of early, aggressive, and extensive surgical debridement in such patients, the real challenge lies in making an early diagnosis of NF that would guide the decision toward the early surgery.

Initial clinical manifestations of skin edema, swelling, erythema accompanied by fever may often lead the clinician to incorrectly treat it as cellulitis. Hence, one must look for the "red flag" signs, viz. severe pain out of proportion to clinical findings, erythema extending beyond skin margins, hemorrhagic bullae, skin necrosis, and systemic involvement in the form of hypotension and altered mental status.[7] Concurrent use of antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs) may mask the inflammatory signs making the clinical picture even more confusing. The diagnosis is clinical, and it is essential to get an early surgical referral based on clinical suspicion.

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score uses a combination of laboratory parameters such as hemoglobin, C-reactive protein, creatinine, white cell count, serum sodium, and glucose to differentiate NF from milder soft tissue infections. Patients with a numeric score of more than six in a relevant clinical scenario have a high likelihood of having NF (positive predictive value [PPV] 96%, area under the receiver operating characteristic [AUROC] 0.92).[8] However, one should not use a low LNIREC score to rule out NF.

Imaging modalities such as computed tomography (CT) may be used in the cases of diagnostic uncertainty. CT findings of NF include heterogeneous contrast enhancement of involved tissues, fat stranding, and fluid collection with or without the presence of gas.[9]

Broad-spectrum antibiotic therapy is warranted in such cases given the fact that such infections are frequently polymicrobial. The current study used an empiric combination antibiotic therapy with beta-lactams, beta-lactamase inhibitors, or carbapenems along with clindamycin. Methicillin resistant staphhylococcus aureus (MRSA) coverage was not used empirically given their hospital had a <10% incidence of MRSA. The recently published WSES guidelines recommend empiric coverage with an anti-MRSA agent (vancomycin or linezolid) in combination with broad-spectrum gram-negative cover (piperacillin–tazobactam or carbapenem) along with clindamycin due to its antitoxin effect.[10] The optimal duration of antibiotic therapy is less clear, but it seems justified to continue antimicrobials till no further debridement is necessary and at least 72 since clinical improvement. Narrowing of antimicrobials guided by culture sensitivity results seems reasonable.

The cornerstone of management of NF is aggressive surgical debridement, necrosectomy, and fasciotomy. A limited primary debridement was associated with a 7.5-fold higher risk of mortality.[11] The patient may need repeat reexplorations in the next 12–24 hours after the initial surgery in the case of persistent areas of nonviable tissue. Hence, close attention to the wound is required to look at local signs of infection. Negative pressure wound

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therapy using vacuum-assisted closure (VAC) dressings are being increasingly used by surgeons in open wounds and seem to help by removing exudates, promoting the formation of granulation tissue, and helping in earlier wound closure.[12] VAC dressings need to be changed every 24–72 hours.

Kurian et al. found significant renal impairment (AKIN stage 3), mechanical ventilation, for more than 3 days, shock, and low serum albumin values to be associated with mortality. Few other studies have reported advanced age, high white blood cell (WBC) count >30,000/mm^3, renal impairment, delay in operative intervention, presence of toxic shock syndrome, clostridial NF, and infections at specific sites (head, neck, thorax, and abdomen) to be associated with poor outcomes.[6,13–15]

While some of these risk factors might be nonmodifiable or simply a reflection of systemic inflammatory response syndrome (SIRS) (e.g., WBC count); more attention needs to be focused on modifiable determinants of mortality in NF patients. While renal impairment might be a reflection of disease severity, these patients have an ongoing capillary leak and might benefit from volume expansion and optimization of renal perfusion. It is pertinent to limit the use of NSAIDs and other nephrotoxic agents.

Predictably, the authors found an association between hypoalbuminemia and mortality (odds ratio (OR) 0.43, 95% confidence interval [CI] 0.22–0.85). Notably, their patient cohort had hypoalbuminemia on presentation (mean albumin 2.4 g/dL, SD 0.7). This group of patients tends to lose fluids, electrolytes, and protein across wound surfaces making them prone to hypoalbuminemia and fluid depletion. Albumin has proven to be a good marker of disease severity in septic patients, yet targeting predetermined levels of albumin have repeatedly failed to confer any outcome benefit in critical care.[16,17] It remains to be explored if aggressive replacement of albumin or its use as resuscitation fluid can improve outcomes in this group of patients. Nevertheless, it is a good clinical practice to pay close attention to their nutrition and ensure adequate protein supplementation during the recovery phase of their illness.

The clinical role of intravenous immunoglobulin (IVIG) in NF stems from its ability to neutralize bacterial exotoxins. However, most of the studies that show a benefit with IVIG are limited by small sample sizes, methodological flaws, and differences in rates of surgical intervention between groups.[18,19]

The evidence in favor of the adjunctive role of hyperbaric oxygen therapy (HBO) in NSTI comes from a large retrospective database over a 20-year period in the United States. Four hundred and five patients who received HBO had a lower risk of dying (OR 0.49, 95% CI 0.29–0.83), though they had a longer hospital length of stay and understandably higher costs.[20]

In summary, NF is a life-threatening disease that requires multidisciplinary care. Early surgical intervention is crucial, and the intensivists should pay close attention to resuscitation, appropriate use of antimicrobials, and prevention of secondary organ injury.

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