A REVIEW ANALYSIS OF THE TREATMENT OF SERIOUS INFECTIONS OF THE SKIN AND SOFT TISSUES

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Abstract
Intensive care, source control, and broad-spectrum antibiotics are necessary during the first stage of disease for severe SSTIs. Rapid diagnostic tests are being used more often to aid in the selection and de-escalation of antibiotics for SSTIs. Additionally, clinical prediction scores have shown potential in identifying individuals who don't need antibiotics that fight methicillin-resistant Staphylococcus aureus. Immune state has been shown to have a significant impact on certain forms of SSTIs, but not all. In the most current literature, the argument over the advantages of intravenous immunoglobulin is still being fought. Due to geographical differences in the most prevalent infections, patterns of antibiotic resistance, and host immune responses, severe SSTIs are frequent and their treatment is complicated. The role of surgical consultation and source control, among other particular features of treatment for severe SSTIs, are covered. Also reported are the distinctive characteristics of SSTIs in immune compromised hosts.

Keywords-*Gas gangrene; necrotizing fasciitis; severe skin and soft tissue infections*

Introduction
With over 14 million outpatient visits annually [1] and almost 900000 hospital admissions in the United States [2], skin and soft tissue infections (SSTIs) are a prominent cause for patients to seek inpatient and outpatient medical treatment. The choice of an empiric antibiotic treatment is challenging since pathogen isolation in SSTIs is limited by presently available diagnostics and affected by host and regional variables [3,4,5]. Patients with severe SSTIs need surgical debridement for source control, despite challenges in choosing an empiric treatment. We highlight the key aspects of treating severe SSTIs in this study.

DEFINING SEVERITY IN SOFT TISSUE INFECTIONS
Although there isn't a commonly accepted severity ranking system, the degree of skin structure involvement somewhat corresponds with the severity of the sickness caused by SSTI. We will define patients with toxic shock syndrome (TSS), necrotizing fasciitis, or gas gangrene/myonecrosis as having a severe SSTI for the purposes of this study. Patients will also be deemed to have a severe SSTI if they have any SSTI and fulfill the criteria for severe sepsis or septic shock or have a fast Sequential Organ Failure Assessment score of at least 2.

SEVERE SOFT TISSUE INFECTION TYPES
Immune state, exposure history (to animals, water, trauma), and travel history (especially to areas with high frequencies of multidrug-resistant organisms) are significant factors that should be taken into consideration when making empiric antimicrobial choices for all SSTIs [4,6]. Patients with severe cases of purulent

SSTIs, cellulitis, or surgical site infections should have source control when necessary in addition to broad-spectrum antibiotic treatment.

Toxic shock syndrome

TSS is a fulminant infection generally caused by Streptococcus pyogenes or Staphylococcus aureus, however related symptoms may also be caused by group B, group C, group G, and Clostridium species. Although local rates may vary, the yearly incidence of staphylococcal TSS (SaTSS) and streptococcal TSS (SeTSS) are 0.5/100 000 and 0.4/100 000, respectively [7]. Mortality rates for monthly SaTSS are less than 5%, for nonmenstrual SaTSS they are 5-22%, and for SeTSS they are 30-70% [7]. Clostridial toxic shock is uncommon, and it's unclear how often it occurs [8,9].

Empiric treatment must address drug-resistant infections when TSS is suspected. Expert opinion highlights vancomycin and clindamycin or linezolid alone as potential treatment regimens based on retrospective investigations and in-vitro evidence [10–13]. For methicillin-sensitive SaTSS, nafcillin or oxacillin are effective options, but they must be used with clindamycin since nafcillin alone may enhance toxin production [12]. Since they decrease the development of super antigens in both SaTSS and SeTSS, clindamycin or linezolid are crucial components of the therapy [11–13]. As soon as susceptibilities are known, antibiotics should be tapered off while still containing a substance that prevents the formation of toxins until clinical stability is reached. Clindamycin and penicillin should be given for clostridial TSS, while there isn't much information on this condition to help with therapy.

Although the therapeutic effects of intravenous immunoglobulin (IVIG) are debatable, it nonspecifically binds and inactivates superantigens, reducing cytokine storm in TSS. The rarity of TSS has made recruitment for randomized controlled trials (RCTs) with IVIG challenging [14]. According to one trial, patients who got IVIG or clindamycin for SeTSS had considerably lower fatality rates [15]. Less research has been done on IVIG in SaTSS, however in one study, none of the five verified individuals who received IVIG died [16].

Even while only around one-third of patients with mixed bacterial etiology of necrotizing SSTI received IVIG, neither death nor functional outcomes were improved [17]. In a recent propensity score-matched examination of patients with necrotizing fasciitis and shock, IVIG usage was uncommon but not linked to better outcomes, independent of the pathogen type, which furthers the discussion [18]. IVIG may be investigated in patients with TSS due to the continued conflicting data, but the effectiveness is uncertain and precise dose regimens are not thoroughly established.

Gas gangrene/myonecrosis and necrotizing fasciitis are examples of necrotizing soft tissue illnesses.

Treatment for necrotizing SSTIs is challenging and requires for intensive care, rigorous surgical debridement, and broad-spectrum antibiotics. Infection source management is crucial, and repeated surgical debridements are often needed. Debridement is normally recommended every 24 to 48 hours until there is no longer any sign of necrosis,

while the number and frequency of debridements needed vary. To check for persistent infection (such as bullae, devitalized tissue, or spreading erythema) that would need repeated debridement, wound dressing changes should be performed every day. Repeat debridement should be discussed if there is an increase in the need for critical care support or if there are laboratory findings that point to a worsening infection (e.g., advancing renal failure, rising leukocytosis, rising lactate). Due to considerable tissue edema, necrosis, inflammation, and penetrating vessel thromboses, diffusion of antimicrobials into afflicted tissues is constrained, making surgical management of infection especially crucial [20].

Gas gangrene/myonecrosis

Clostridium species are the source of gas gangrene or myonecrosis, which should be treated surgically with additional broad-spectrum antibiotics while awaiting culture results . Even though they are uncommon, Clostridium sordellii infections are noteworthy because they may be linked to a state resembling toxic shock, especially in patients who have recently given birth or had an abortion [8,9,21]. Since TSS from clostridial infections differs pathophysiologically from SeTSS or SaTSS, IVIG may not be helpful [8,9,21].

Fasciitis with necrosis

A uncommon SSTI that affects the deep fascia is necrotizing fasciitis [19]. Based on location, rates of necrotizing fasciitis range from 0.18 to 15.5 per 100,000 people and are rising over time [22,23]. Despite having a more severe disease than those with cellulitis, patients with necrotizing fasciitis had a comparable in-hospital and 90-day death rate, according to a recent research [24]. This is likely because cellulitis patients had a larger load of comorbidities. The research may not have had enough power to detect a difference in mortality between the groups due to the study's tiny patient population.

Polymicrobial organisms, comprising both aerobic and anaerobic species, cause type I necrotizing fasciitis. S. pyogenes is the typical causative agent of type II necrotizing fasciitis, however S. aureus may also cause this condition. Because there are many uncommon agents that may cause necrotizing fasciitis, doctors must understand the value of surgical debridement with accompanying bacterial cultures in conjunction with broad-spectrum antibiotics as the initial lines of treatment [25,26].

Although the traditional diagnosis of necrotizing fasciitis is pain that is excessive compared to the results of a physical examination, it's vital to keep in mind that superficial nerves might succumb to necrosis, causing numbness in the afflicted regions. Due to the heterogeneity of physical examination results and the limited sensitivity of imaging modalities, a high level of suspicion for necrotizing SSTI is necessary. Imaging results may postpone surgical intervention, which is linked to poor outcomes, and cannot completely rule out necrotizing fasciitis [27]. However, MRI may be useful in clinically stable individuals in separating necrotizing from nonnecrotizing illness [28].

The lower extremities is where necrotizing fasciitis predominates, and risk factors including diabetes and peripheral vascular disease reflect this localisation. There are

no clinical studies available to help determine the length of treatment because of the relative rarity and variability of microbiologic causes. Recent recommendations recommend antibiotic treatment focused against cultured organisms for at least 48 to 72 hours after patients are clinically stable and don't need any more surgical operations [4].

Surgical considerations

General resuscitative procedures should be followed in line with institutional protocols for all patients with severe SSTIs. Source control is crucial, and in the case of menstruation TSS, this may include surgical debridement, the removal of intrusive equipment, or a vaginal inspection. Extended intervals between presentation and the first surgical operation are linked to higher mortality [27,29]. Source control was linked to lower mortality in a mixed group of patients with severe sepsis/septic shock, including those with SSTIs, despite patients needing source control having more severe disease [30].

Vacuum-assisted closure of wounds in combination with successive debridements may promote healing [31]. A temporary colostomy may be necessary to aid in wound healing in situations of necrotizing infection affecting the perineum or other areas that might be contaminated by feces. Based on comorbidities, lower limb necrotizing fasciitis amputation rates range from 15 to 72% [32], with diabetes being a significant risk factor.

Amputations, among other things, may be linked to considerable functional impairments following discharge, despite the fact that they may be life-saving [33].

Hyperbaric oxygen therapy

Due to conflicting benefits, a dearth of RCTs, and uneven access to hyperbaric oxygen chambers, the utility of hyperbaric oxygen treatment (HBOT) for necrotizing SSTI is still debatable [34–38]. We are unable to advocate for or against the use of supplemental HBOT for the treatment of necrotizing SSTI in the absence of RCTs or well-done propensity score studies. HBOT may be used in facilities where it is easily accessible, however it shouldn't be used in place of or cause a delay in surgical or antibiotic treatment.

Antimicrobial considerations

All severe SSTI should, in general, be empirically treated with broad-spectrum antibiotics that are targeted at common bacteria, including MRSA, resistant Gram-negatives, and anaerobes. Notably, if empiric antimicrobials are suitable for isolated infections, patients with difficult SSTI attain clinical stability more quickly [39]. Local antibiograms should be taken into account by all practitioners when selecting empiric antimicrobials since they might vary greatly. It may be wise to remove MRSA coverage from empiric treatment in individuals with low risk of MRSA infections in areas like Northern Europe with low prevalence of MRSA [40]. MRSA risk prediction methods in SSTIs have shown some early promise, but more information is required before deploying these technologies and eschewing empiric MRSA coverage [41].

De-escalation of antibiotic treatment should be based on clinical improvement, microorganisms that have been cultivated, and, where available, the findings of quick diagnostic testing. Rapid diagnostic testing for SSTIs is a relatively new field, but encouraging findings suggest that its usage increases the appropriateness of

medication and boosts de-escalation rates [42].

Considerations with certain antimicrobials

Long-acting semi-synthetic lipoglycopeptides dalbavancin and oritavancin are approved for use against a variety of Gram-positive pathogens. Before their use for severe SSTI, however, can be advised, further research is required. Patients with necrotizing fasciitis and high creatine kinase levels may not benefit from using daptomycin. Linezolid treatment in MRSA bacteremia may be related with poorer outcomes in patients with acute physiology and chronic health assessment II scores of at least 14 since MRSA is one of the most prevalent causes of SSTIs and severe illness is associated with greater rates of bacteremia [43]. Tedizolid has been demonstrated to be comparable to linezolid over a spectrum of SSTI severity [44], but there is still worry regarding its empiric usage since there is no evidence that it would be more effective in treating MRSA bacteremia. Telavancin is more harmful than other SSTI treatments currently on the market, hence we do not advise using it while alternative treatments are available. Although tigecycline has been licensed for SSTIs, it has been associated with inferior results in individuals with serious disease. In individuals with infections that are resistant to therapy, tigecycline may potentially increase the likelihood of treatment failure. As a result, we advise staying away from tigecycline medication when alternatives are available.

Future treatments

Delafloxacin and omadacycline are two intriguing new medications that are being developed for the treatment of SSTI; however, other papers in this issue will examine these medications' applications. Antibodies against the staphylococcal alpha toxin, for example, have lately showed some promise in animal models but are not yet accessible for use in humans [45].

Immuno compromised hosts

The physical examination findings of SSTI, the potential pathogens, and the therapeutic and diagnostic strategies are all altered by immunodeficiency. A wider spectrum of infections, such as invasive fungal, mycobacterial, and parasitic infections, as well as non-infectious reasons are included in the differential diagnosis for dermatologic symptoms in the immuno-compromised host [4,19]. Early dermatologic examination for immunocompromised individuals may be advantageous because of the larger differential diagnosis and increased risk for decompensation [4,46]. Dermatology consultation may help critically sick patients get the best diagnosis possible for their dermato-logic findings and use fewer antibiotics [46,47]. Dermatologists' knowledge may be useful in differentiating between various dermatologic diseases that resemble infection [19,48].

A comprehensive cutaneous examination should be performed on all immuno compromised patients who are severely sick, since immuno suppression tends to lessen the physical exam findings of SSTIs.

Pathogens are more prone to spread cutaneously in immuno compromised people.

According to a recent research, immuno compromised individuals with S. pyogenes

were more likely than immuno competent patients to have necrotizing fasciitis, septic shock, and death [49]. Contrarily, immuno compromise was not a risk factor for death in a group of patients with S. aureus infections, some of whom had SSTIs [50].

For serious infections, immuno suppression reduction should be taken into consideration whenever feasible. The Multinational Association of Supportive Care of Cancer score is crucial for predicting complication rates in patients with febrile neutropenia [51]. Considerations for surgery in neutropenic patients include the likelihood of length of neutropenia and the severity of infection. Patients who have had neutropenia for a shorter amount of time are more likely to recover from surgical procedures and are thus probably better candidates for surgery.

Poor research has been done on the management of necrotizing SSTIs in neutropenic individuals, hence personalized treatment plans should be used.

CONCLUSION

SSTIs may manifest in a number of ways and become serious enough to need acute care. Practitioners should be knowledgeable of the variety of clinical SSTI presentations that need for prompt surgical debridement in order to prevent delays in surgery, which may worsen results. All severe SSTI need aggressive source management and wide spectrum antibiotics, with empiric treatment determined by patient risk factors, the local antibiogram, and, where available, quick diagnostic tests.

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