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Complicated and suppurative skin soft tissue infections: our four-year cases

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Abstract

Skin and soft tissue infections (SSTIs) are common community and hospital-acquired infections and rarely result in severe morbidity and mortality. It is not always possible to obtain cultures and isolate the causative agent in these patients, primarily treated with empirical antibiotics. In this retrospective cross-sectional study, 57 patients with complicated SSTI followed between 2018 and 2022 with purulent and necrotizing characteristics or growth in blood cultures were included. Thirty-eight patients (66.7%) were male, and 39 (68.4) had diabetes. In 43 (75.5%) patients, the infection was in the lower extremity and gluteal region. Gram-positive agents were detected in 35 patients (61.4%), Gram-negative agents were found in 13 patients (22.8%), and Gram-positive and Gram-negative mixed growth was detected in 1 patient (1.8%), and no causative agent could be produced in 8 (14%) patients. Of the 21 *Staphylococcus aureus* produced, 4 (19%) were methicillin-resistant (MRSA). Growth was detected in blood cultures in three patients (5.3%), and all were streptococcal bacteria. It was observed that 31 patients (54.4%) required hospitalization for treatment, and 29 (50.8%) required surgical intervention such as drainage, aspiration, debridement, or amputation. Three patients (5.3%) died, and four (7%) underwent amputation. There was no significant difference between diabetic and non-diabetic patients regarding factors and mortality-morbidity. In the logistic regression analysis, none of the variables of gender, type of causative agent, presence of diabetes, and site of infection significantly affected severe morbidity and mortality. Since it was detected at a low rate in our cases, it can be said that MRSA and *Paeruginosa* do not need to be considered in every patient for the initial empirical treatment, Gram-negative rods can be taken into account, especially in diabetics, and broad-spectrum and combined antibiotics are not needed in the vast majority of patients. Microbiological follow-up and sensitivity studies at regional and global scales will need to continue to guide empirical treatments in SSTIs.

Keywords: Infectious skin disease, soft tissue, bacteria, abscess

Introduction

Skin and soft tissue infections (SSTIs) are among the most common diseases among community-acquired infections. It can occur in a broad clinical spectrum, from simple forms that do not require systemic treatment and recover only with topical antibiotic therapy to necrotizing forms that threaten life and extremities and cause sepsis. It usually occurs when the skin's protective mechanisms are impaired following trauma, inflammation, maceration due to excessive moisture, decreased

tissue perfusion, or other factors that disrupt the stratum corneum.

It is not necessary to take a culture in uncomplicated SSTI where outpatient treatment is sufficient and does not require parenteral therapy. Cultures are necessary in complicated cases involving deep structures, treatment failure, and drainage-requiring situations. The sensitivity of blood culture is low. If the patient has a purulent discharge, it is appropriate to use this pus for culture. Deep tissue samples in necrotizing infections and purulent fluids aspirated or drained in subcutaneous abscesses

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should be used for culture and stained microscopic examinations. If there is a non-purulent clinical picture such as cellulitis and erysipelas, tissue biopsy or skin aspiration and blood culture should be used for culture [1]. Using unsuitable superficial swab samples for culture may result in the evaluation of colonizing bacteria or flora elements as agents. In non-purulent SSTI, skin biopsies and skin aspirations for microbiological examination are not practical and are not used much in the clinic. Treatments are mainly organized empirically. This study aimed to review the results of the microbiological examination in groups with a chance of detecting the causative agent, evaluate their susceptibility to shed light on empirical treatments, and compare them with the literature.

Material and Methods

In this study, which is a cross-sectional retrospective study, patients with community-acquired infections who were followed up in the outpatient clinic or hospitalized in the service-intensive care unit between August 2018 and August 2022 were determined by file scanning following the inclusion and exclusion criteria. The patients were evaluated in age, gender, mechanism of infection, site of infection, presence of diabetes, need for spontaneous drainage or surgery, culture results, treatments given, and outcome (amputation, exitus, recovery).

Patients 18 years of age or older who had community-acquired necrotizing or suppurative skin and appendage infections, pus or deep tissue biopsy for culture, or had pathogen growth in blood culture were included in the study. Patients with foreign body infections, cellulitis, erysipelas, and lymphangitis patients without abscess and purulation or with no growth in blood culture, patients under 18 years of age, HIV-positive patients, and hospital-acquired infections were excluded from the study.

Ethics Committee Approval: Permission was obtained from the local ethics committee of Ordu University Faculty of Medicine (Date: 05.08.2022, No: 2022/196).

Statistical Analysis

Statistical Package for Social Sciences (IBM SPSS for Mac) version 26 and Jamovi software version 2.2.3 were used for statistical analysis. Chi-square analysis and Fisher's exact test were used to compare categorical variables. Univariate and multivariate binominal logistic regression analyzes were performed for the effects of gender, site of infection, agents, and presence of diabetes on mortality and severe morbidity. P<0.05 was accepted as the statistical significance level.

Results

A total of 57 patients, 38 (66.7%) male and 19 (33.3%) female were included in the study. The median age was 58 (range: 27-90). Thirty-nine patients (68.4%) had diabetes.

In 43 (75.5%) of the patients, the infection was in the lower extremity and gluteal region, and its distribution was as follows;

foot 21 (36.8%), tibial region 11 (19.3%), gluteal region 5 (8.8%), femoral region 5 (8.8%), knee 1 (1.8%). Infection focus was found in the upper extremity in 6 patients (10.5%), the torso in 4 patients (7%), and in the head and neck region in 4 patients (7%). Nine patients (15.7%) had a history of significant trauma causing infection. It was observed that 7 (12.3%) of them were in the lower extremities.

As a result of the cultures taken, the agent could not be produced in 8 patients (14%). The causative agent was isolated in blood, pus, or tissue cultures in 49 patients, with three (5.3%) in blood cultures. Gram-positive agents were detected in 35 patients (61.4%), Gram-negative agents were found in 13 patients (22.8%), and Gram-positive and Gram-negative mixed growth was detected in 1 patient (1.8%). Of the 21 *Staphylococcus aureus* produced, 4 (19%) were methicillin-resistant (MRSA).

Although Gram-negative growth was detected at a rate of 28.2% (11/39) in diabetic patients and 11.1% (2/18) in non-diabetic patients, this difference was not statistically significant (P= 0.318). The distribution of the agents is shown in Table 1. Bacteria isolated from blood cultures were *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Streptococcus disgalactiae*.

Table 1. Distribution of pathogens

PATHOGEN	N (%)
Gram-positive	35 (%61.4)
Staphylococci	18 (%31.6)
MSSA	15 (%26.3)
MRSA	3 (%5.3)
Streptococci	11 (%19.2)
Streptococcus spp.	4 (%7)
S.pyogenes	3 (%5.3)
S. agalactia	1 (%1.8)
S.disgalactiae	1 (%1.8)
S. pneumoniae	1 (%1.8)
S. intermedius	1 (%1.8)
<i>Enterococcus faecalis</i>	2 (%3.5)
<i>Corynebacterium striatum</i>	1 (%1.8)
Gram-positive polymicrobial	3 (%5.3)
MSSA + Streptococcus	2 (%3.5)
MRSA + Enterococcus	1 (%1.8)
Gram-negative	13 (%22.8)
<i>E.coli</i>	5 (%8.8)
ESBL (-)	4 (%7)
ESBL (+)	1(1.8)
<i>Paeruginosa</i>	2 (%3.5)
Proteus	2 (%3.5)
<i>P.vulgaris</i>	1 (1.8)
<i>P.mirabilis</i>	1 (1.8)
Gram-negative polymicrobial	3 (%5.3)
<i>E.coli</i> + <i>Morganella</i>	1 (%1.8)
<i>Serratia</i> + <i>Morganella</i>	1 (%1.8)
<i>Alcaligenes faecalis</i> + <i>Providencia</i> spp.	1 (%1.8)
<i>Citrobacter freundii</i>	1 (%1.8)
Mixed Gram-positive + Gram-negative	1 (%1.8)
No growth	8 (%14)
Total	57 (%100)

Surgical intervention such as drainage, aspiration, debridement, or amputation was required in 29 patients (50.8%). Adequous

spontaneous purulent drainage occurred in 22 (38.6%) of them, which did not require additional surgical intervention. It was observed that 31 patients (54.4%) required hospitalization for their treatment, and 26 patients (45.6%) were followed up and treated on an outpatient basis. The follow-up results of the patients are shown in Table 2.

Table 2. Follow-up and treatment results of the patients

Result	N	%
Death	3	5.3
Amputation ¹	4	7
Partial recovery ²	2	3.5
Recovery	48	84.2

¹All-foot amputation ²Chronic ulcerated lesions on the leg

Although severe morbidity and mortality (amputation and death) were observed at a rate of 15.4% (6/39) in patients with diabetes and 5.6% (1/18) in non-diabetic patients, this difference was not statistically significant (P=0.280). In the binominal logistic regression analysis (Cox & Snell R²=0.125, Nagelkerke R²= 0.238, Hosmer and Lemeshow test P=0.924), none of the variables of diabetes, site of infection, type of causative agent and gender had a significant effect on severe morbidity and mortality.

Discussion

There is not enough data on the frequency of SSTIs in our country. A study conducted in the United States found that the incidence reached 3.3 million, with an increase of 40% in 2012 compared to 2000, and the cost reached 13.8 billion dollars, with a threefold increase [2]. In another study conducted in the USA, 471550 SSTI attacks of 376262 individuals were examined in the three years between 2009 and 2011, and the annual incidence was calculated as 496 for 10000 individuals [3].

Various classifications have been made for SSTI according to the depth of inflammation in the affected skin, the clinical picture it causes, the surface area involved, the pathogenic microorganism, and the mechanism of infection [4]. Infectious Diseases Society of America (IDSA) updated the skin and soft tissue infections guideline in 2014, divided the SSTI into purulent and non-purulent, mild, moderate, and severe in severity, and necrotizing and non-necrotizing in terms of tissue necrosis [5]. The U.S. Food and Drug Administration proposed a new classification and terminology describing complicated skin and soft tissue infections in 2013. acute bacterial skin and skin structure infections (ABSSSI) The guideline defined ABSSSI as cellulitis/erysipelas, wound infection, and cutaneous abscess with a minimum surface area of 75 cm², and did not include less serious skin infections such as impetigo and minor cutaneous abscess, as well as infections from animal or human bites, necrotizing fasciitis, diabetic foot infection, decubitus ulcer infection, infections requiring more complex treatment regimens such as myonecrosis and ecthyma gangrenosum in the definition [6].

In our study, Gram-positive bacteria were found to be the causative agent in the majority (61.4%) of purulent and complicated skin

and soft tissue infections, and *S.aureus* was the causative agent in more than half of them. The share of *S.aureus* among the total causative agents was 36.8%, and the share among Gr-positive bacteria was 60%. Four (19%) of 21 *S.aureus* strains produced from clinical isolates were found to be methicillin-resistant. Gram-negative bacteria were isolated in 22.8% of the patients. More than one agent was isolated in seven patients (12.2%). In purulent and non-purulent SSTIs, Gram-positive bacteria, mainly *S.aureus* and streptococci, are the causative agents [7]. In a study conducted in the United States between 2009 and 2011, 471550 SSTIs were examined, and it was observed that only 23% of them could be cultured, and the pathogen was produced in 54% of the cultures. It was determined that 81% of the growing bacteria were *S.aureus*, and 46% were MRSA. In this study by Ray et al., Gram-negative agents were 14%, beta-hemolytic streptococci 10%, polymicrobial growth 6%, and blood culture growth 14% [3]. In our study, the causative agent was obtained from blood cultures only in 5% of the patients.

In another study in which 11705 hospitalized patients with a diagnosis of SSTI were evaluated, it was observed that half of the patients were obese, 30.9% had diabetes, and 56% were not cultured. It was determined that 63.9% of the bacteria produced were Gram-positive, 11.9% were Gram-negative, and 24.2% were mixed growth [8]. Although the share of Gram-negative bacteria in SSTIs is generally less than Gram-positive bacteria, there is an increase in this rate all over the world. Risk factors for developing SSTI with multidrug-resistant and pan-resistant Gram-negative bacteria include diabetes, burns, pressure sores, neutropenia, immunosuppression, previous antibiotic use, hospitalization, and long-term residence in a healthcare facility. Unfortunately, Gram-negative and mixed-infection SSTI with multi-drug resistance have a worse prognosis [9]. Gram-negative and mixed polymicrobial growths may be encountered in SSTIs, mostly in complicated and healthcare-associated infections, and may pose a risk for inappropriate initial antibiotic therapy. Risk factors for developing complicated SSTI with mixed polymicrobial and Gram-negative bacteria were the presence of comorbidities such as surgical site infections, intensive care, nursing home stay, diabetes mellitus, cirrhosis, and intravenous-subcutaneous drug use [10,11].

Since it is more difficult to take culture in SSTIs than in other clinical conditions and the rate of agent detection in the samples is low, clinicians mostly turn to empirical treatments. Taking culture is even more difficult in cellulite and erysipelas because there is no pus to aspirate and when there is a diffuse inflammation of the skin itself. In these clinical pictures, blood culture positivity is detected only at a rate of 5% or less. In the aspiration of inflamed skin, growth is detected in only 5-40% of the cases, while this rate remains in 20-30% of skin biopsy cultures. In light of these data, the microbiological etiology of most SSTIs is unclear [5]. In the study of Zervos et al., in which they examined 1096 SSTI patients requiring hospitalization between 2005 and 2008, the rate of Gram-negative factors, including those in polymicrobial

growth, was 19.4%, *S.aureus* 66.4% and streptococcal species 26.1%. This study found that approximately half of the patients had healthcare-associated SSTIs, and 74.8% of *S.aureus* were methicillin-resistant [12].

In the SENTRY program, in which the antimicrobial susceptibility of 191460 *S.aureus* isolates obtained between 1997 and 2016 from 427 centers from 45 countries was evaluated, 40.3% of the total isolates were found to be MRSA. This study found methicillin resistance in 41% of *S.aureus* isolated from SSTIs. The highest rates of MRSA were found in nosocomial isolates, urinary tract infections, patients with hospital-acquired pneumonia, and those over 80 years of age. Geographically, variability was found between continents and regions, and the rate of MRSA was 26.8% in European isolates, while it was 47% in North America [13]. Methicillin resistance in *S.aureus*, which we found at 19% in our study, was consistent with European data and was found to be relatively low due to the inclusion of community-acquired infections in the study.

In the study conducted by Parlak et al. in our country, in which 163 SSTI cases were included, growth was found in the culture at a rate of 63%; Gram-negative bacteria were isolated from only 7.8% of the patients with growth. In the study in which *S.aureus* was found at a rate of 65% and *S.pyogenes* at a rate of 9.7% in the produced agents, methicillin resistance was found to be 25.4% in *S.aureus* [14]. In the study of Turhanoğlu et al., the bacteria produced in 693 wound cultures and their susceptibility were evaluated in 5 years; Gram-positive bacteria were found to be 52% (88% of them were staphylococci), Gram-negative bacteria were found to be 42.9%. The share of *S.aureus* in all growths was 19%, and methicillin resistance was 35.8% [15]. The fact that this study included all wound cultures and hospital-acquired infections may explain the higher rates of non-*S.aureus* staphylococci, Gram-negative rods, and MRSA than our data.

The cause of death of SSTIs is usually sepsis due to necrotizing infections. There is not much data on the overall mortality rate in SSTIs. A study evaluating 275 million hospitalizations between 2005 and 2011 in the USA found that the primary diagnosis was SSTI in 1.8% of hospital admissions, and diabetes was the most common comorbidity. In the study of Kaye et al., the overall mortality was 0.45%, and it was observed that it decreased from 0.49% to %0.41 from 2005 to 2011 [16]. In a study in which 115 patients with necrotizing fasciitis (NF) were examined, the mortality was 20.9%, and the most common comorbidities were cirrhosis (47%) and diabetes mellitus (39%) [17]. In another study in which 88 patients with NF were evaluated, it was observed that the rate of concomitant diabetes was 70.8%, mortality was 21.3%, and amputation had to be performed in 22.5% [18].

In an NF series of 44 cases from our country, it was reported that 52% of the patients had diabetes, 27% polymicrobial growth, 9% *S.aureus*, 9% *Streptococcus* spp, 6.8% *P.aeruginosa* were found in cultures, and mortality was 25% [19]. In a series of 14 cases, it was reported that 71% of the patients had diabetes, and 14.3%

died [20]. In our study, three deaths (5.3%) and four amputations (7%) were detected, and our study did not include only necrotizing infections, making it difficult to compare with the literature. In all cases that resulted in death, the causative agent was *streptococcus* (*S. pneumoniae*, *S. disgalactiae*, *S. pyogenes*), and effective and broad-spectrum antibiotic treatments were started early in all of them. Thirty-nine (68.4%) of our cases had diabetes. Although the Gram-negative growth rate and severe morbidity-mortality rate were found to be higher in diabetic patients, these differences were not statistically significant. In the logistic regression analysis, diabetes was not a risk factor for death and severe morbidity (amputation). It is known that diabetes mellitus is a frequent comorbidity that accompanies infectious diseases and adversely affects the prognosis. It is more common and severe in diabetic patients than non-diabetic patients and is the leading cause of hospitalizations in SSTI [21].

In a study of 10063 people followed for seven years in Denmark, the risk of pneumonia (adjusted hazard ratio [aHR] 1.75, 95% confidence interval [CI] 1.23–2.48) was increased in diabetic patients compared to patients without urinary tract infection (aHR 3.03, 95% CI 2.04–4.49) and skin infection (aHR 2.43, 95% CI 1.49–3.95). At baseline, each 1 mmol/l increase in plasma glucose was associated with a 6-10% relative risk increase for pneumonia, urinary tract infection, and skin infection after adjusting for other possible confounding agents. In patients hospitalized for urinary tract infections, people with diabetes were found to have a higher risk of death 28 days after admission (HR 3.90, 95% CI 1.20-12.66) compared to non-diabetic patients [22]. In the study of Lipsky et al., 3030 hospitalized, culture-positive, diabetic patients were examined in 4 years in the USA, and it was determined that 1.4% of the patients died. It was observed that 73.2% of the cases had foot infection, 26.8% had non-foot SSTI, approximately half of the cases had polymicrobial growth, and Gram-negative monomicrobial growth was only in 6.8%. Those with non-foot infections were more seriously ill than those with foot infections, and mortality was two times higher than those with foot infections. Severe disease at the time of admission, non-foot infection site, polymicrobial growth containing *Paeruginosa*, and Gram-negative growth were associated with mortality [23].

The limitations of our study are that the data were obtained retrospectively, limited to the information in the electronic database, and possible data losses. This study only covers some SSTIs. Only purulent, complicated infections in which tissue samples could be cultured and growth in blood culture were included in the study. It does not reflect infections such as cellulitis, erysipelas, impetigo, ecthyma. Therefore, although there were mild uncomplicated cases in our study, mortality and morbidity rates were higher than the general SSTI rates but lower than those of complicated conditions such as NF. In some patients, antibiotic treatment was started before the culture was taken, resulting in no growth in the culture. Only routine aerobic cultures were studied; anaerobic cultures could not be done.

The exclusion of hospital-acquired infections and surgical site infections makes the microbiological results more meaningful in terms of the microbiology of community-acquired SSTIs. Necrotizing and purulent SSTIs are less common among SSTIs treated as outpatients and inpatients. Some clinicians initiate empirical antibiotic therapy without needing culture, even if drainage and aspiration are performed in typical cases. Time passes from the onset of the infection to abscess and suppuration, during which the patient is started on antibiotics. Early antibiotic treatment prevents complications and progression to an abscess and prevents microbiological identification even if suppuration develops. The rate of detection of growth in blood culture in hospitalized patients is low. For these reasons, although cellulitis, erysipelas, and SSTI secondary to trauma are common, the number of patients who met the inclusion criteria remained limited even over four years. Culture facilities should be forced in all community and hospital-acquired SSTIs; blood cultures in patients with fever, aspirated or drained pus cultures in suppurative infections, and intraoperative tissue cultures should not be neglected and should be obtained before antibiotics if possible. Studies reflecting the SSTI microbiology, antibiotic resistance, and susceptibility of agents need to continue on a regional and global scale. Thus, it can be possible to determine the differences in the agents and resistance profiles caused by the patient characteristics changing due to immunosuppression treatments, chemotherapies, frequent foreign body use, increasing age, and chronic diseases. These studies will guide empirical treatments initiated in emergencies when cultures cannot be obtained, or results are awaited.

Conclusion

As a result, our study provided an up-to-date overview of the microbiological characteristics of rarer varieties of SSTIs with community-based data from our region. Although our data contain different data and rates specific to the study design, they are generally compatible with the literature of the world and our country. It can be said that it is not necessary to consider MRSA and *P.aeruginosa* in every patient for the initial empirical treatment because it was detected at a low rate in our cases, Gram-negative rods can be taken into account, especially in diabetics, and broad-spectrum and combined antibiotics are not needed in the vast majority of patients. It is seen that the severity of the clinical picture, the development of sepsis, and the occurrence of surgical indication are responsible rather than resistant bacteria and inappropriate antibiotic treatments in patients who died and underwent amputation.

Conflict of interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

Permission was obtained from the local ethics committee of Ordu University Faculty of Medicine (Date: 05.08.2022, No: 2022/196).

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