Diagnostic value of laboratory parameters for the discrimination between erysipelas and limited cellulitis

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Summary

Background and objectives: Erysipelas, caused by beta-hemolytic streptococci, and limited cellulitis, frequently caused by Staphylococcus aureus or other bacteria, are skin and soft tissue infections characterized by typical clinical signs. However, despite the therapeutical relevance they are often not differentiated (e.g. in clinical trials). Erysipelas are efficiently treated with penicillin, while limited cellulitis is treated with more wide-spectrum antibiotics. This study investigates whether parameters such as CRP, blood counts or novel parameters like immature granulocytes could serve as biomarkers to distinguish between these entities.

Patients and methods: For this retrospective analysis 163 patients were included. We compared laboratory markers in patients with erysipelas (n = 68) to those with limited cellulitis (n = 41) of the leg. Both erysipelas and limited cellulitis were defined clinically, with an additional aspect for erysipelas being a prompt response to penicillin.

Results: Erysipelas were characterized by higher levels of inflammation. CRP and leukocyte counts are the best parameters to discriminate between both infections. A CRP value ≥ 3.27 mg/dl indicated the diagnosis of erysipelas with 75% sensitivity and 73.2% specificity.

Conclusions: Our results support the thesis that erysipelas and limited cellulitis are distinct infections as defined in the German guidelines and that an assessment of CRP and leukocytes is useful for differential diagnosis.

Introduction

Bacterial skin and soft tissue infections (SSTI) are the most common infections worldwide and among them erysipelas and limited cellulitis are the most frequent forms encounted in dermatology.

In this context erysipelas is an acute bacterial, non-purulent infection of the dermis, involving the lymphatic spaces and usually starting from small entry sites (for example interdigital mycosis). It is clinically characterized by i) an acute, overheated, slightly painful, bright red erythema with a shiny surface, sharply defined margins and tongue-shaped processes, ii) usually a systemic inflammatory reaction, consisting of fever or at least shivering [1]. Beta-hemolytic streptococci, mostly group A (Streptococcus pyogenes) are considered the underlying pathogens [1–6].

In contrast, limited cellulitis, the other frequent, clinically distinguishable SSTI in immunocompetent individuals is frequently caused by Staphylococcus aureus (Sunderkötter, Becker et al., unpublished) [1, 7–10]. It is clinically characterized as a warm, slightly painful erythema, which is more edematous than erysipelas, has a darker red hue and duller and less distinct margins. It usually develops around larger entry sites, such as wounds or ulcers. It is remarkable that the initial systemic signs seen in erysipelas, such as shivers or fever, are less frequently described in initial limited cellulitis; this point, however, has never been systematically analyzed.
If not adequately treated, limited cellulitis can proceed to severe cellulitis, an often purulent infection extending to the fascia. Its requirement of surgical intervention (in addition to antibiotics) has been introduced as a distinctive criterion [11]. In contrast, necrotizing soft tissue infections, the most severe form of SSTI, is a rare entity in its own, leading to rapid and life threatening ischemic necrosis as well as shock due to bacterial toxins [12].

Unfortunately, the clear distinction between erysipelas and limited cellulitis, especially with respect to the causative infectious agents, is not reflected by many nomenclatures or classification systems of SSTI. Thus, clinical studies on SSTI usually include both patients with erysipelas and those with limited cellulitis within the same group of diseases. We believe that a differentiation between streptococcal infections and infections which can be caused by other pathogens, such as staphylococci, should be mandatory and should be stringent for when making a diagnosis and deciding on treatment. For beta-hemolytic streptococci penicillin is the treatment of choice, since up to now streptococci have not acquired penicillin resistance [1]. The majority of staphylococci, however, are resistant to penicillin by beta-lactamase, requiring at least penicillinase-resistant beta-lactam antibiotics or even more broad-spectrum antibiotics.

Thus, further diagnostic criteria for differentiation between erysipelas and limited cellulitis are desirable since – despite the existence of typical clinical signs – the clinical differentiation alone can be challenging in some patients. Laboratory markers of inflammation could be helpful to distinguish erysipelas from limited cellulitis. Although laboratory variability between these types of infection has been postulated, to our knowledge no studies have yet systematically addressed this question.

Therefore, this study investigated whether standard laboratory parameters of inflammation such as C-reactive protein (CRP) and differential blood counts or the recently introduced parameters immature granulocytes or platelet volume, could be reliable biomarkers to differentiate between both conditions. Our analysis should also help to further establish a separation of these two diagnoses and result in more rational antibiotic treatment [13].

Patients and methods

Patients from the department of dermatology at the university of Muenster with the clinical diagnosis “limited cellulitis” or “erysipelas” were identified with the administration software “Orbis” by using the International Classification of Disease 2010 (ICD-10) codes “A46” for limited cellulitis/erysipelas and by reviewing the physicians’ letters. A diagnosis was established according to clinical criteria, following a standard operating procedure (SOP) established in our clinic 2011. According to this SOP typical erysipelas were defined as acute non-purulent infections presenting with strongly overheated, bright red erythema with a shiny surface, sharply defined margins and/or tongue-shaped processes and were always treated with penicillin G monotherapy. Limited cellulitis was defined as non-purulent infection presenting with moderately overheated, edematous dull red erythema without sharply defined margins (mostly around an ulcer) and treated with cephalosporines or aminopenicillins. The recruitment period was between 1st of January 2013 and 31st of December 2017. We excluded patients suffering from surgical site infections, cutaneous abscesses or severe, deep-seated (gangrene, necrotizing fasciitis) SSTI requiring surgical debridement and unclear differential diagnosis limited cellulitis/erysipelas. Patients with immunosuppressive therapy (e.g. glucocorticoids), chemotherapy and active cancer were not included. In total 163 patients were enrolled. Patient information was screened for type of infection, age, sex, body temperature (Celsius, measured auricular), CRP, complete blood counts, immature granulocytes (metamyelocytes, myelocytes, promyelocytes but not band cells and blasts) and mean platelet volume. Patient data were entered pseudonymously into an Excel spreadsheet. Statistical analyses were performed using IBM SPSS® Statistics Version 25 for Windows (IBM Corporation, Somers, NY, USA) and R version 3.6.0. To evaluate differences between two groups, the Mann-Whitney U test was used. Inter-group comparisons concerning categorical data were made by Chi-Square tests. The diagnostic values of the laboratory parameters for differentiating between limited cellulitis and erysipelas were compared by receiver operating characteristics (ROC) analysis. The area under the ROC curve (AUC) is a measure to compare the performance of the laboratory markers to distinguish between these two entities. Youden’s Index (YI) was used to determine cut-off values. A random forest analysis using the R package randomForest was applied to assess the importance of the predictors for the distinction between erysipelas and limited cellulitis. Based on the results of the univariable analysis and the random forest analysis, a multivariable logistic regression was performed. The accuracy of classification of this model was determined using leave-one-out cross validation (LOO-CV). Two-sided p-values are given but all inferential analyses are considered explorative. A p-value ≤ 0.05 was considered statistically noticeable. The study (AZ 2018-763-f-S) was approved by the ethics committee of the medical association of Westfalen-Lippe (Germany).

Results

In this study 122 subjects with erysipelas and 41 with limited cellulitis were enrolled (Figure 1). Erysipelas was found in
55.7 % (68/122) on legs. We did not observe ulcers within this group whereas limited cellulitis always affected legs with ulcers. We further compared only infections on the leg to exclude effects caused by the site of infection. The two groups differed only in age (Table 1). Patients with erysipelas, with a median age of 55.71 years (interquartile range (IQR): 42.8–69.8), were younger than patients with limited cellulitis, where the median age was 66.13 years (IQR: 47.8–78.8) (Table 1).

The median values of body temperature and the recorded laboratory markers for patients with erysipelas and limited cellulitis are shown in Table 2.

Compared with limited cellulitis, erysipelas had higher values ($p \leq 0.05$) for body temperature, CRP, leukocytes, erythrocytes, monocytes and immature granulocytes. Eosinophil levels were higher in patients with limited cellulitis ($p = 0.05$).

In univariate analysis we used ROC analysis to identify the discriminatory ability of these parameters (Figure 2, Table 3). Compared to the clinical parameter body temperature (AUC 0.668 [95% confidence interval (CI) 0.560, 0.777]) the laboratory markers CRP (AUC 0.767 [95% CI 0.672, 0.862]), leukocytes (AUC 0.730 [95% CI 0.652, 0.848]), neutrophils (AUC 0.744, [95% CI 0.627, 0.860]) and monocytes (AUC 0.668 [95% CI 0.559, 0.817]) showed higher discriminative values.

### Table 1 Demographic distribution of patients with skin or soft tissue infections on the leg.

|                      | Erysipelas | Limited cellulitis | p-value |
|----------------------|------------|--------------------|---------|
| Number of patients   | 68         | 41                 |         |
| Sex (female in %)    | 47 (n = 32)| 56.1 (n = 23)      | 0.43    |
| Age (years, mean ± SD)| 55.71 ± 18.52 | 66.13 ± 18.98       | ≤ 0.05  |
| BMI (in kg/m², mean ± SD) | 31.78 ± 6.88 | 28.4 ± 5.88        | 0.071   |

Abbr.: SD, standard deviation, BMI, body mass index.

### Table 2 Body temperature and laboratory markers in patients with skin or soft tissue infections on the leg.

|                      | Limited cellulitis (n = 41) | Erysipelas (n = 68) | p-value |
|----------------------|----------------------------|--------------------|---------|
| **Body temperature (°C)** | 36.8 (36.6–37.2, n = 29) | 37.3 (36.7–38.0, n = 64) | ≤ 0.05 |
| **C-reactive protein (< 0.5 mg/dl)** | 1.70 (0.65–4.1, n = 41) | 6.65 (2.95–12.63, n = 68) | ≤ 0.05 |
| **Leukocytes (3.91–10.9 × 10⁹/L)** | 7.48 (6.37–8.69, n = 41) | 10.80 (8.2–13.19, n = 68) | ≤ 0.05 |
| **Erythrocytes (4.44–5.61 × 10⁹/L)** | 4.18 (3.83–4.52, n = 41) | 4.33 (4.09–4.69, n = 68) | ≤ 0.05 |
| **Blood platelets (166–308 × 10⁹/L)** | 235 (216–280, n = 41) | 246 (191–307, n = 68) | 0.717 |
| **Neutrophils (1.8–6.98 × 10⁹/L)** | 5.05 (3.68–6.47, n = 28) | 8.16 (5.31–11.14, n = 49) | ≤ 0.05 |
| **Lymphocytes (1.26–3.35 × 10⁹/L)** | 1.38 (1.05–1.86, n = 28) | 1.46 (1.03–1.80, n = 49) | 0.767 |
| **Monocytes (0.29–0.96 × 10⁹/L)** | 0.61 (0.41–0.85, n = 28) | 0.85 (0.63–1.03, n = 49) | ≤ 0.05 |
| **Eosinophils (0.03–0.59 × 10⁹/L)** | 0.17 (0.07–0.32, n = 28) | 0.11 (0.03–0.22, n = 49) | 0.050 |
| **Basophils (0.01–0.07 × 10⁹/L)** | 0.04 (0.02–0.06, n = 28) | 0.03 (0.02–0.07, n = 49) | 0.418 |
| **Immature granulocytes (≤ 0.06 × 10⁹/L)** | 0.03 (0.01–0.06, n = 28) | 0.05 (0.03–0.09, n = 49) | ≤ 0.05 |
| **Mean platelet volume (9.3–12.1 fl)** | 10.95 (9.98–11.35, n = 28) | 10.5 (10.1–11.2, n = 49) | 0.238 |
We identified threshold values with optimal sensitivity and specificity to discriminate between erysipelas and limited cellulitis. At a CRP threshold of 3.27 mg/dl or more the sensitivity for the diagnosis erysipelas versus limited cellulitis was 75 % and specificity was 73.2 % (YI 0.48), the positive predictive value (PPV) was 82.5 % and the negative predictive value (NPV) was 65.2 % respectively. At CRP ≥ 5.65 mg/dl the sensitivity decreases to 56 % but specificity rises to 85.4 %. Vice versa the sensitivity for the diagnosis limited cellulitis versus erysipelas at this CRP threshold was 73.2 % (values below the threshold) and the specificity was 75 % according to a PPV of 65.2 % (values below threshold) and NPV (values above this threshold) of 82.5 %.

At a leukocyte threshold of 8.12 × 10^9/L the sensitivity for the diagnosis erysipelas versus limited cellulitis was 77.9 % and specificity was 68.3 % (YI 0.46) respectively. This threshold lies within the normal range for leukocytes. The PPV for erysipelas at or above this threshold is 80.3 % and the NPV is 65.1 %. A leukocyte count above the threshold for the normal range ≥ 12.68 × 10^9/L shows a sensitivity of only 29.4 % but a high specificity of 90.2 % (YI 0.2). Vice versa the sensitivity for the diagnosis limited cellulitis versus erysipelas at this leukocyte threshold was 68.3 % (values below threshold) and specificity was 77.9 % according to a PPV of 65.1 % (values below threshold) and a NPV (values above threshold) of 80.3 %. A neutrophil threshold ≥ 6.73 × 10^9/L, which lies close to the upper limit of normal (6.98 × 10^9/L), yielded the cut-off value with the best combination of sensitivity (71.4 %) and specificity (78.6 %) (YI 0.5) and a PPV of 85.4 % and NPV of 61.1 %. The optimal cut-off value for the clinical parameter body temperature was 37.5°C (auricular).

Table 3 Area under the ROC curve (AUC) for significant parameters to discriminate erysipelas and limited cellulitis.

| Parameter              | AUC for erysipelas (95 % CI) | Cut off for erysipelas | Sensitivity | Specificity | Youden-Index |
|------------------------|-----------------------------|------------------------|-------------|-------------|--------------|
| Body temperature       | 0.668 (0.560–0.777)         | ≥ 37.5°C               | 73.4 %      | 51.7 %      | 0.25         |
| CRP                    | 0.767 (0.672–0.862)         | ≥ 3.27 mg/dl           | 75.0 %      | 73.2 %      | 0.48         |
| Leukocytes             | 0.750 (0.652–0.848)         | ≥ 8.12 × 10^9/L        | 77.9 %      | 68.3 %      | 0.46         |
| Erythrocytes           | 0.627 (0.516–0.739)         | ≥ 4.43 × 10^9/L        | 47.1 %      | 75.6 %      | 0.23         |
| Neutrophils            | 0.744 (0.627–0.860)         | ≥ 6.73 × 10^9/L        | 71.4 %      | 78.6 %      | 0.50         |
| Immature granulocytes  | 0.653 (0.522–0.784)         | ≥ 0.03 × 10^9/L        | 81.3 %      | 46.4 %      | 0.28         |
| Eosinophils            | 0.634 (0.506–0.763)         | ≤0.24 × 10^9/L         | 83.7 %      | 39.3 %      | 0.23         |
| Monocytes              | 0.688 (0.559–0.817)         | ≥ 0.58 × 10^9/L        | 83.7 %      | 50.0 %      | 0.34         |

Abbr.: CRP, C-reactive protein; AUC, area under the curve.
which had a low sensitivity (42.2 %) but a high specificity of 86.2 % (YI 0.28). The more recently introduced parameter immature granulocytes and the parameters eosinophils and monocytes all yielded cut-off values with high sensitivity > 80 % but low specificity < 60 %.

In multivariable analysis we used different statistical approaches to identify the best independent predictors for an optimal separation of the two diagnoses. In the random forest analysis, the parameters mentioned in Figure 2 and age as potential confounding parameter were tested. Despite the significant difference in age, the values of CRP, leukocytes and neutrophil counts were identified as relevant parameters to differentiate between erysipelas and limited cellulitis. To determine parameter-specific odds ratios (ORs) we used logistic regression as another multivariable statistical approach. We included CRP values and leukocytes in this approach. Since the values for leukocytes and neutrophils were highly correlated (Pearson correlation coefficient 0.91) and there were more missing values for neutrophil counts we used only leukocytes for this analysis. We also included body temperature, an important clinical parameter. As with the random forest analysis we adjusted the logistic regression for age. We found that higher values for body temperature, CRP and leukocytes indicated a higher probability for the diagnosis erysipelas. The age-adjusted OR for the diagnosis erysipelas versus limited cellulitis is 1.13 (95 % CI 1.013, 1.262, p ≤ 0.05) with every increase of 1 mg/dl CRP. The OR of leukocytes for the diagnosis erysipelas versus limited cellulitis is 1.12 (95 % CI 0.962, 1.305, p = 0.144) with every increase of 1000 leukocytes/μl. For body temperature the OR was 1.66 for every°C (95 % CI 0.858, 3.227, p = 0.132). Moreover, a leave-one-out cross validation (LOO-CV) was used to estimate the classification accuracy of the multivariable model to classify each patient with an estimated probability for erysipelas > 0.5 (accuracy 75.27 %, sensitivity 85.94 %, specificity 51.72 %). This analysis confirmed the random forest analysis: the age-adjusted accuracy in prediction of the diagnosis erysipelas was highest for a combination of CRP, leukocytes, and body temperature.

Thus, the combination of all three parameters results in the best differentiation between these two skin infections.

Discussion

Erysipelas and limited cellulitis are accountable for a large percentage of infections seen by general practitioners, dermatologists, pediatricians and in emergency rooms.

Erysipelas and limited cellulitis do not only differ in their clinical presentation but also in their microbial cause: Group A streptococci are the infectious agents in erysipelas while limited cellulitis is frequently caused by *Staphylococcus aureus* and less frequently by other bacteria [7–10]. Unfortunately, many classifications of skin infections do not reflect these clinically important differences very well [14] and the use of not well-defined technical terms in the German or English literature makes it difficult to find evidence-based statements on diagnostic criteria and therapy recommendations [1]. The Food and Drug administration (FDA) has recently defined the term acute bacterial skin and skin structure infections (ABSSSI) to generate criteria for clinical studies on antibiotics [15]. This includes both erysipelas and limited cellulitis if the involved area of infection comprises 75 cm². Differentiation between both conditions, however, is therapeutically important. Beta-hemolytic streptococci have not acquired penicillin resistance and thus erysipelas are always efficiently treated with usually well-tolerated and narrow spectrum penicillin [1, 3, 4, 6], which has only minimal potential for selecting resistant strains or for causing collateral damage to the microbiome of other organs [16]. Instead, limited cellulitis is treated with a more broad-spectrum antibiotic approach since *Staphylococcus aureus*, which is mostly resistant to penicillin, is a frequent infectious agent and in some cases, gram-negative bacteria cannot be excluded as causative agents. While in most cases flucloxacillin or 1st generation cephalosporines are sufficient [12], many physicians prescribe more wide spectrum antibiotics to also cover gram-negative bacteria. So, when a distinction between limited cellulitis and erysipelas is not made, erysipelas are frequently overtreated.

Despite the described different appearances, the clinical diagnosis of erysipelas versus limited cellulitis can be challenging in some patients, especially when the infected site is altered by non-infectious inflammations (e.g. stasis dermatitis). Therefore, additional diagnostic criteria are warranted. Unfortunately, direct detection of the infectious agent in tissue has a reported low sensitivity and was only done in single patients in our collective, while the determination of specific antibody responses is not helpful in the acute situation. [2, 6–8, 17] In review articles it has been described that limited cellulitis is associated with a lower clinical inflammatory response (fever, shivers) and lower laboratory markers of inflammation compared to erysipelas [18]. Yet, there is no study addressing this point, probably because the two infections are frequently not kept apart [6, 19, 20, 21].

CRP and leukocyte counts are well-established markers for bacterial infection in general [22–24], but there are only limited data on their relevance in the differential diagnosis of SSTI [6, 8]. There are only some studies on the laboratory differences between acute and recurrent erysipelas and as predictors of treatment response [9, 25]. Moreover, there are only two studies reporting values of novel inflammatory markers like immature granulocytes and platelet volume in SSTI [26, 27], but no study has addressed the diagnostic setting erysipelas versus limited cellulitis.
We now demonstrate that patients with erysipelas and limited cellulitis indeed differ in both laboratory and clinical inflammatory parameters. A CRP threshold ≥ 3.27 mg/dl indicated the diagnosis of erysipelas versus limited cellulitis with a sensitivity of 75% and a specificity of 73.2%. Only 1.5% (1/68) of patients with erysipelas versus 12.2% (5/41) of patients with limited cellulitis showed CRP levels < 0.5 mg/dl at admission. These data are comparable to previous reports which demonstrate normal CRP levels in 3–12% of patients with SSTI [9, 28]. Compared to CRP levels, leukocyte and highly correlated neutrophilic granulocyte counts yielded only slightly lower AUCs in the ROC analysis and the optimal cut-off values for the diagnosis erysipelas for leukocytes (8.12 × 10⁹/L) and neutrophils (≥ 6.73 × 10⁹/L) showed similar sensitivity and specificity. The other determined laboratory markers and body temperature had a lower discriminatory ability.

Since patients with limited cellulitis were older than patients with erysipelas, we performed different multivariable statistical approaches to exclude age related effects. This could be ruled out by all applied statistical methods. The multivariable approaches confirmed that the CRP level was the most important parameter to differentiate between erysipelas and limited cellulitis with a higher probability of erysipelas at higher CRP levels (age adjusted OR 1.13/1 mg/dl CRP in logistic regression). However, both random forest analysis and logistic regression indicated that a combination of CRP, leukocytes and body temperature had the best ability to differentiate between both diagnoses. Higher numbers of leukocytes and increased body temperature indicated an increased probability for the diagnosis erysipelas.

Thus, the results of this study demonstrate for the first time that clinically diagnosed erysipelas is indeed accompanied by a higher grade of systemic inflammation compared to limited cellulitis.

We only analyzed patients with SSTI in the leg, thus predications for other anatomical regions are difficult. However, the leg is most frequently affected making our data relevant for clinical practice [4, 6, 8, 9]. Moreover, the skin of the leg is often altered due to chronic venous stasis, thus obscuring some of the clinical diagnostic criteria such as bright and distinct erythema. Our results also support the assessment that erysipelas and limited cellulitis are distinct diagnoses as defined in the recent German guidelines [1].

Highly elevated parameters of inflammation usually result in the choice of a broader antibiotic treatment regime, especially if no dermatologist is involved in the treatment decision [29–31]. Our data indicate that higher levels of inflammation are rather typical for streptococcal infection. This is in agreement with limited data obtained from mixed patient collectives in which the causative infectious agent has been identified by microbiology [8] or by serial serological analysis [6].

Patients with detected beta-hemolytic streptococci in tissue biopsies had higher leukocyte counts and body temperature than patients with detected *Staphylococcus aureus* [8]. Similarly, patients with serologic evidence for streptococcal infections had higher leukocyte counts and CRP levels than patients without [6]. Since streptococcal infections can be efficiently treated with penicillin, highly elevated inflammation markers should not prevent the use of penicillin in clinically typical erysipelas, as successfully done in all our patients. Elevated CRP and leukocyte levels rather argue for using penicillin as initial treatment when the clinical diagnosis is difficult. This proceeding can be supported by high NPVs for the diagnosis limited cellulitis for CRP (82.5%) and leukocytes (80.3%) above the defined thresholds.

In line with this, it has been reported that even procalcitonin (PCT) levels, usually regarded as an indicator for sepsis, can be markedly increased in patients with erysipelas [6, 24]. However, these recommendations only apply when there are no signs of necrotizing SSTI (like severe pain) which are characterized by exceptionally increased laboratory parameters of inflammation [32–35].

Our data indicate that CRP levels are most useful for differentiation between erysipelas and limited cellulitis. Measuring body temperature and determining leukocyte counts may provide additional help, whereas neither the differential blood count nor additional novel markers like immature granulocytes or platelet volume are helpful in this diagnostic setting. Thus, our results also have economic implications.

Our study has the following limitations: i) It presents a retrospective review of medical records. We did not include other inflammatory markers like erythrocyte sedimentation rate (ESR), procalcitonin and ferritin [28, 36] since they were not regularly determined in our patients; ii) since sufficient microbiological data were lacking streptococcal infections in our limited cellulitis group cannot be ruled out, while the response to penicillin therapy in the erysipelas group makes staphylococcal infection in this group highly unlikely; iii) no data on the time course of laboratory parameters were accessible for a sufficiently high number of our patients; iv) these questions should be addressed in a prospective analysis.

**Conclusions**

Measuring fever and laboratory parameters of inflammation is helpful in differentiating between erysipelas and limited cellulitis localized to the leg. High levels of CRP, increased body temperature and numbers of leukocytes indicate a higher probability for the diagnosis erysipelas and thus justify a therapy with penicillin given there is no indication for a necrotizing SSTI.
References
1. Sunderkötter C, Becker K, Eckmann C et al. S2k Guideline Skin-and Soft tissue infection – Excerpt from S2k Guidelines Calculated initial parenteral therapy of bacterial infections in adults. J Dtsch Dermatol Ges 2019; 17(3): 345–69.
2. Bernard P, Bedane C, Mounier M et al. Streptococcal cause of erysipelas and cellulitis in adults. A microbiologic study using a direct immunofluorescence technique. Arch Dermatol 1989; 125(6): 779–82.
3. Karppelin M, Sijlander T, Haapala A-M et al. Evidence of streptococcal origin of acute non-necrotising cellulitis: a serological study. Eur J Clin Microbiol Infect Dis 2015; 34(4): 669–72.
4. Jeng A, Beheshi M, Li J, Nathan R. The role of beta-hemolytic streptococci in causing diffuse, nonculturable cellulitis: a prospective investigation. Medicine (Baltimore) 2010; 89(4): 217–26.
5. Eriksson BKG, Karkkonen K, Jorup-Rönström C, Wretlind B. Determination of initial parenteral therapy for bacterial skin and soft tissue infections in patients with limb cellulitis. Infection 2018; 46(4): 466–72.
6. Bruun T, Oppegaard O, Kittang BR et al. Etiology of cellulitis and clinical prediction of streptococcal disease: a prospective study. Open Forum Infect Dis 2016; 3(1): ofv181.
7. Duvanel T. Quantitative cultures of biopsy specimens from cutaneous cellulitis. Arch Intern Med 1989; 149(2): 293.
8. Hook EW. Microbiologic evaluation of cutaneous cellulitis in adults. Arch Intern Med 1986; 146(2): 295.
9. Lazzarini L, Conti E, Tositti G, de Lalla F. Erysipelas and cellulitis. Infect Dis (Lond) 2019; 51(7): 534–40.
10. Bruun T, Oppegaard O, Kittang BR et al. Etiology of cellulitis and clinical prediction of streptococcal disease: a prospective study. Open Forum Infect Dis 2016; 3(1): ofv181.
11. Chalupa P, Beran O, Herwald H et al. Evaluation of potential biomarkers for the discrimination of bacterial and viral infections. Infection 2011; 39(5): 411–7.
12. Brunn T, Oppegaard O, Hufthammer KO et al. Early response in cellulitis: a prospective study of dynamics and predictors. Clin Infect Dis 2016; 63(8): 1034–41.
13. Brindle RJ, Ijaz A, Davies P. Procalcitonin and cellulitis: correlation of procalcitonin blood levels with measurements of severity and outcome in patients with limb cellulitis. Biomarkers 2019; 24(2): 127–30.
14. Brishkoska-Boshkovski V, Dimitrovskova I, Kondova-Topuzovska I. Clinical presentation and laboratory characteristics in acute and recurrent erysipelas. Open Access Maced J Med Sci 2019; 7(5): 771–4.
15. Erturk A, Cure E, Cure MC et al. The association between serum YKL-40 levels, mean platelet volume, and c-reactive protein in patients with cellulitis. Indian J Med Microbiol 2015; 33 (Suppl): 61–6.
16. Pyo JY, Ha Y-J, Song JJ et al. Delta neutrophil index contributes to the differential diagnosis between acute gout attack and cellulitis within 24 hours after hospitalization. Rheumatology (Oxford) 2017; 56(5): 795–801.
17. Noh SH, Park SD, Kim EJ. Serum procalcitonin level reflects the severity of cellulitis. Ann Dermatol 2016; 28(6): 704–10.
18. Li DG, Di Xia F, Khosravi H et al. Outcomes of early dermatology consultation for inpatients diagnosed with cellulitis. JAMA Dermatol 2018; 154(5): 532–43.
19. Arakaki RY, Strazzula L, Woo E, Kroshinsky D. The impact of dermatology consultation on diagnostic accuracy and antibiotic use among patients with suspected cellulitis seen at outpatient internal medicine offices: a randomized clinical trial. JAMA Dermatol 2014; 150(10): 1056–61.
31 Jenkins TC, Knepper BC, Moore SJ et al. Antibiotic prescribing practices in a multicenter cohort of patients hospitalized for acute bacterial skin and skin structure infection. Infect Control Hosp Epidemiol 2014; 35(10): 1241–50.
32 Borschitz T, Schlicht S, Siegel E et al. Improvement of a clinical score for necrotizing fasciitis: “pain out of proportion” and high CRP levels aid the diagnosis. PLoS ONE 2015; 10(7): e0132775.
33 Goh T, Goh LG, Ang CH, Wong CH. Early diagnosis of necrotizing fasciitis. Br J Surg 2014; 101(1): e119–25.
34 Zil-E-Ali A, Fayyaz M, Fatima A, Ahmed Z. Diagnosing necrotizing fasciitis using procalcitonin and a laboratory risk indicator: brief overview. Cureus 2018; 10(6): e2754.
35 Kato T, Fujimoto N, Honda S et al. Usefulness of serum procalcitonin for early discrimination between necrotizing fasciitis and cellulitis. Acta Derm Venereol 2017; 97(1): 141–2.
36 Simon L, Gauvin F, Amre DK et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 2004; 39(2): 206–17.