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Blood cultures in the evaluation of uncomplicated cellulitis

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ABSTRACT

Purpose: The frequency of bacteremia and the array of microorganisms involved in cellulitis vary greatly among studies. Although current guidelines do not recommend routine blood culture in uncomplicated cellulitis, their implementation in clinical practice remains challenging. We therefore aimed to assess the frequency, determinants and microbiology of bacteremia in hospitalized patients with uncomplicated cellulitis.
Methods: We retrospectively reviewed the medical records of all adult patients admitted at a primary-care hospital with a diagnosis of community-acquired uncomplicated cellulitis during a 4-year period. We looked at the factors associated with blood cultures sampling and at the incidence, determinants and microbiology of bacteremia in this population.
Results: Among the 476 patients hospitalized with a diagnosis of cellulitis, 250 (52.5%) had blood cultures. Fever, high C-reactive protein and lymphatic insufficiency were significantly associated with the sampling of blood cultures. Twelve (4.8%) patients had bacteremia. Alcoholism and duration of hospitalization were associated with bacteremia in multivariate analysis. Among the 12 patients with bacteremia, 9 had Streptococcus sp. and 3 had *Staphylococcus aureus* infection.
Conclusion: In our study population with uncomplicated cellulitis, representative of unselected population admitted at primary-care hospitals, bacteremia was uncommon and not associated with discriminant patient characteristics, except for alcohol abuse. Episodes of bacteremia were exclusively due to gram-positive cocci susceptible to co-amoxicilin, a common first-line empirical therapy. In accordance with existing guidelines, we do not recommend to collect blood for cultures in uncomplicated cellulitis. Clinicians' awareness of guidelines and of the poor yield of blood cultures could reduce useless investigation.

1. Introduction

Cellulitis is commonly seen in clinical practice. Most of the cases are due to gram-positive bacteria such as β-hemolytic streptococci and *Staphylococcus aureus* [1–4]. The utility of blood cultures remains equivocate in the literature with wide rates of bacteremia ranging from 2.0% [5] to 18.5% [6], related to the severity of the disease, the condition of the patient and the number of blood cultures drawn. The mortality associated with bacteremic infections is high, particularly in specific settings such as intensive care units, or nosocomial or gram-negative infections [7]. Identifying the right clinical indications for blood culture is necessary to avoid false-positive results from contamination that can lead to inappropriate antibiotic therapy, longer hospitalization stay and higher costs [8,9]. Current guidelines do not recommend ordering blood cultures routinely in immunocompetent patients with uncomplicated cellulitis [10,11], but their clinical implementation remains unclear. The aims of this retrospective study in patients hospitalized with a diagnosis of community-acquired uncomplicated cellulitis were to observe the local prevalence and factors associated with blood cultures samplings, and to describe the incidence and microbiology of positive blood cultures.

2. Material and methods

2.1. Setting and population

This retrospective study was conducted in 6 different sites of Fribourg Hospital Network in Switzerland, which includes 600

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beds of acute care, intensive care and rehabilitation. This hospital serves urban and rural areas with a population of 300,000 inhabitants and has approximately 71,000 admissions per year though the emergency department. A list of all adult patients hospitalized with a diagnosis of cellulitis or erysipelas at admission from January 2011 to December 2014 was obtained from computerized chart records. According to Swiss law about retrospective studies, no consent was needed. A standard protocol was used to collect medical information for each case. Cellulitis was defined as a superficial spreading infection of the skin. Distinction between cellulitis and erysipelas was not made because of the frequently confusing ways to separate these two entities, including depth of the infection, delimitation of the border and lymphatic involvement [4,12]. The presence of comorbidity was considered if mentioned in the clinician's notes or in the list of comorbidities included in computerized chart records. Venous and lymphatic insufficiencies were also considered if typical clinical signs (varicosis, lymphedema) were described in the clinician's notes. Patients with complicated cellulitis, defined as nosocomial infection (consequence of a medical intervention or infection ≥48 h after admission), fluctuant or purulent infection, necrotizing soft tissue infection or a concomitant infection, were excluded. As retrospective data may be limited and to explore rates of bacteremia in the less ill patients, we performed a sensitivity analysis after excluding patients with admission at an intensive care unit (ICU), or with an indication for blood cultures according to the 2014 guidelines of the Infectious Diseases Society of America (IDSA), i.e. high fever (that we defined as ≥39 °C), hypotension (that we defined as a systolic blood pressure < 90 mm Hg and/or a diastolic blood pressure < 60 mm Hg), malignancy, neutropenia, immunosuppression, animal bites and/or immersion injury [11]. Contamination of the blood cultures was considered in the presence of skin flora microorganisms in a single blood culture without any clinical sign of systemic infection, after discussion with an infectious disease specialist. Bacteremia was defined as positive blood cultures without contamination. Only blood cultures drawn on the day of admission or the previous day in an ambulatory setting were included. Each pair of aerobic and anaerobic bottles was defined as a set.

2.2. Microbiological studies

According to the institutional guidelines for blood cultures, 20 ml of blood was drawn and inoculated into one aerobic and one anaerobic media. Recommendations made to the trained nurses in charge of the blood drawing were to sample blood twice with an interval of 30 min, from two different peripheral veins. Blood samples obtained from each patient were transported immediately to the microbiology laboratory and incubated into the BACTEC® 9240 System (Becton Dickinson, Sparks, MD) for up to 5 days. Samples from positive culture bottles were investigated by gram stain and acridine if the gram stain remained negative. Subcultures were performed onto 5% sheep blood, and chocolate agars in aerobic and anaerobic atmospheres, 5% CO_2 at 35 °C, and Brucella agars with 5% sheep blood in anaerobic atmospheres. Standard bacteriological procedures were used to identify the microorganisms isolated, mostly with the MALDI-TOF technology (Bruker Corporation, XXX).

2.3. Statistical analyses

Categorical variables were described as frequency (percentage) and continuous variables as mean with standard deviation (SD). Data were compared using Fisher's test, Student's test, χ^2 analysis, or ANOVA, as appropriate. Univariate logistic regression analysis was performed to study variables associated with the request of blood cultures and with bacteremia, respectively. All variables with a p-value < 0.20 in univariate analysis, as well as variables supposed to be related with the outcome of interest, were included in the multivariate regression analysis. All tests were conducted as two-sided at a 0.05 level of significance. Statistical analysis was performed using computer software Epi Info Version 7.1.4 (Center for Disease Control and Prevention, Atlanta, GA).

3. Results

3.1. Study population

During the 4-year study period, 476 patients hospitalized with a diagnosis of community-acquired uncomplicated cellulitis were

Table 1
General characteristic of the population.

Variable	Distribution
Total, n	456
Basal characteristic	
Male, n (%)	276 (58.0)
Age (years), mean ± SD	62.7 ± 17.6
Age 0–45 years, n (%)	84 (17.6)
Age 46–65 years, n (%)	164 (34.5)
Age > 65 years, n (%)	228 (47.9)
Duration of hospitalization (days), mean) ± SD	10.0 ± 13.3
Duration of symptoms <2 days, n (%)	143 (30.0)
White blood cell count (G/l), mean[a] ± SD	11.6 ± 5.0
White blood cell count >12 G/l, n[a] (%)	180 (38.1)
C-reactive protein (mg/l), mean[a] ± SD	99.1 ± 93.6
Fever[b], n (%)	118 (24.8)
Comorbid factors	
Obesity (BMI > 30), n (%)	170 (35.7)
Recent local trauma[c], n (%)	152 (31.9)
Recurrence[d], n (%)	98 (20.6)
Diabetes mellitus, n (%)	91 (19.1)
Past local trauma[e], n (%)	79 (16.6)
Previous or concomitant deep venous thrombosis, n (%)	68 (14.3)
Alcoholism, n (%)	49 (10.3)
Solid tumor, n (%)	27 (5.7)
Immunosuppression[f], n (%)	25 (5.3)
Active toxicomania, n (%)	7 (1.5)
Renal insufficiency with hemodialysis, n (%)	2 (0.4)
Cirrhosis Child C, n (%)	2 (0.4)
Hematological malignancies, n (%)	5 (1.0)
Arterial insufficiency, n (%)	43 (9.0)
Venous insufficiency, n (%)	109 (22.9)
Lymph insufficiency, n (%)	38 (8.0)
Edema, n (%)	182 (38.2)
Location	479
Lower extremities, n (%)	386 (81.1)
Others[g], n (%)	93 (19.5)
Portal of entry	
Not known, n (%)	188 (39.5)
Trauma, n (%)	146 (30.7)
Tinea pedis, n (%)	66 (13.9)
Chronic ulcer on limb, n (%)	51 (10.7)
Others, n (%)	25 (5.3)
Pretreatment with antibiotics[h], n (%)	122 (25.6)

[a] As measured in the emergency department on day of admission.
[b] Fever: central temperature ≥ 38.4 °C in the hour before blood cultures were taken or on admission for patients without blood cultures.
[c] Recent local trauma: trauma in the last month including dermabrasion, erosion, superficial burn, recent tattoo, drug injection site, cut, sting, bite, and scratching lesion.
[d] Recurrence: ≥1 episode of cellulitis in the history.
[e] Past local trauma: trauma or intervention >1 month ago including saphenectomy, chronic wound, skin graft, lymphadenectomy, and abdominal surgery.
[f] Immunosuppression: drug immunosuppression with chemotherapy, immunotherapy or corticotherapy, HIV infection with CD4 count <200 G/L, lymphomas, leukemias, myelodysplastic syndromes, asplenia, and severe neutropenia (<500 G/L).
[g] Including upper extremities, face, neck, and abdomen.
[h] Pretreatment with antibiotics: antibiotics <72 h before admission.

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