International Journal of Infectious Diseases 60 (2017) 44–48

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Staphylococcus aureus soft tissue infection may increase the risk of subsequent staphylococcal soft tissue infections☆

Cindy Bouvet[a], Shpresa Gjoni[b], Besa Zenelaj[a], Benjamin A. Lipsky[c,d], Elif Hakko[f], Ilker Uçkay[a,c,e,*]

[a] *Orthopaedic Surgery Service, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland*
[b] *Division of General Medical Rehabilitation, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland*
[c] *Service of Infectious Diseases, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland*
[d] *Division of Medical Sciences, Green Templeton College, University of Oxford, Oxford, United Kingdom*
[e] *Infection Control Program, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland*
[f] *Anadolu Sağlık Hospital, Istanbul, Turkey*

ARTICLE INFO

Article history:
Received 9 January 2017
Received in revised form 3 April 2017
Accepted 2 May 2017
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Soft tissue infections
epidemiology
Staphylococcus aureus
new episodes

SUMMARY

Background: Staphylococcus aureus is the most common cause of soft tissue infections. It is unknown, however, if a patient who has had such an infection is at greater risk for future soft tissue infections with *S. aureus*.

Methods: We conducted an epidemiological survey of adult patients hospitalized in the only public hospital in Geneva for treatment (usually combined surgical and medical) of a soft tissue infection caused by *S. aureus*. By reviewing nursing and medical records from the emergency department and hospital wards, we assessed whether or not they developed any other soft tissue infections (excluding a recurrence) after or before the index one.

Results: Among 1023 index episodes of soft tissue infections, 670 (65%) were caused by *S. aureus*, of which 47 were caused by methicillin-resistant strains (30 healthcare-associated and 17 community-acquired). The patients' median age was 51 years and 334 (34%) were immune-compromised. The median time span between the patient's first and last consultation (for any reason) in our hospital was 21.4 years (interquartile range, 10-30 years). In addition to their index infection, 124 patients (12%) developed a new nosocomial or community-acquired soft tissue infection. Among the index cases with an *S. aureus* infection, 92 (14%) had another soft tissue infection, compared to 32 (9%) who had a non-staphylococcal index infection (Pearson-χ^2-test; $p = 0.03$). Similarly, patients with an index *S. aureus* infection, compared to those with a non-*S. aureus* infection, had a higher rate of another soft tissue infection caused by *S. aureus* (χ^2-test; $p < 0.01$). In multivariate analysis, an index infection due to *S. aureus* shows a high association to further *S. aureus* soft tissue infections (logistic regression; odds ratio 2.5, 95% confidence interval 1.4-4.6).

Conclusion: Among adult patients hospitalised for a soft tissue infection, those infected with *S. aureus* (compared with other pathogens) may be at higher risk of a subsequent soft tissue infection, particularly with *S. aureus*.

Introduction

Staphylococcus aureus is the most common cause of skin and soft tissue infections. Carriage of *S. aureus* in the anterior nares or elsewhere, which is found in 20% to 30% of all humans (Sollid et al., 2014; Brown et al., 2014), is an established risk factor for developing a surgical site infection with this organism (Bertrand et al., 2010; Uçkay et al., 2013; van Rijen et al., 2012). There are no published data on whether or not long-term *S. aureus* carriage increases the risk of subsequent infection *S. aureus* other than in

☆ All authors declare no financial support, grants, financial interests or consultancy that could lead to conflicts of interest. The information has been presented in part at the 6th Oxford Bone and Joint Infection Conference (OBIC), September 2016, Oxford, United Kingdom, and the Swiss Annual Meeting of Infectious Diseases, September 2016, Montreux, Switzerland.

* Corresponding author at: Geneva University Hospitals and Faculty of Medicine 4, rue Gabrielle Perret-Gentil, 1211 Geneva 14, Switzerland. Tel: +41 22 372 9828, Fax: +41 22 372 3987.
E-mail address: ilker.uckay@hcuge.ch (I. Uçkay).

http://dx.doi.org/10.1016/j.ijid.2017.05.002

the perioperative setting or with the unusual entity of recurrent furunculosis (Sollid et al., 2014; Tzermpos et al., 2013). Specifically, it is unknown if a patient who has a soft tissue infection caused by *S. aureus* (as opposed to another pathogen) is at greater risk for another soft tissue infection (caused by *S. aureus* or another pathogen) during his or her lifetime. To address this issue, we conducted a single-center cohort study of all patients hopitalised for a soft tissue infection on our orthopaedic ward. Our main objective was to investigate how many developed another soft tissue infection that requires inpatient or outpatient treatment during their lifetime. In contrast, we did not investigate the outcome of these soft tissue infections, which we already published (Reber et al., 2012; Perez et al., 2010; Chargui et al., 2014; Müller et al., 2015; Uçkay et al., 2015).

Methods

Geneva University Hospitals are the only public hospital in Geneva Canton and some parts of neighboring France. The covered area has an estimated population of 600,000 habitants. The prevalence of community-acquired methicillin-resistant *S. aureus* (MRSA) is lower than 1% in our region (Longtin et al., 2009).

Data sampling

We performed a retrospective single-center, mixed cohort study of adult patients with healthcare and community-acquired soft tissue infections who were treated with surgery as part of their management. We noted the date, the microbiological results, patients' sex and age, and the anatomic localisation of each of these infections. Additional variables were the origin of these infections, the antibiotic susceptibility pattern of the *S. aureus* isolates, the profession of the patients, and their immune status. The database stems from the hospital's clinical pathway for diabetic foot infections, the Orthopedic Infectious Diseases consultations and different Orthopaedic Infection Cohorts (Uçkay et al., 2009a) as well as databases from several ongoing studies (septic bursitis, three studies regarding diabetic foot infections) or past investigations (soft tissue abscesses, phlegmonas of the hand) (Reber et al., 2012; Perez et al., 2010; Chargui et al., 2014; Müller et al., 2015; Uçkay et al., 2015). For roughly 40% of these studies, we consulted the hospital's coding office, while approximately 60% of case findings originated from ongoing studies. For each patient with a soft tissue infection, we recorded when they were first seen in our hospital (which has been electronically recorded since 1990) and their last visit as of 29 February 2016. This time span during which the patient was followed up in our hospital served as a surrogate for the individual observation period.

Study definitions and criteria

We only enrolled patients in this study who had a soft tissue infection, which we defined as the presence of intraoperative pus, together with other symptoms (new onset of fever or local pain, warmth, redness or discharge). In seeking evidence of subsequent soft tissue infections after the index case, we excluded recurrent infection episodes, recurrent furunculosis (Sollid et al., 2014; Tzermpos et al., 2013), implant-related infections, and osteoarticular infections (Ferry et al., 2010; Post et al., 2014). A recurrence was defined has the clinical re-apparition of the same infection by the same pathogen at the same anatomical place due to failure of initial therapy. Subsequent soft tissue infections were new infections at any body site, any pathogen, at any time or reason and not due to failure of initial therapy. The reason for the exclusion of recurrent episodes was avoiding "recurrence biases", because in our epidemiologic analysis, microbiological recurrences due to the same pathogens belonged to the same episode that was not healed, and were not considered as new episodes, which is a different situation.

We defined a patient as being chronically immune-compromised if they had any one of the following conditions: diabetes mellitus, solid organ or bone marrow transplants, untreated HIV disease, chronic immune-suppressive medication, active cancer, cirrhosis of CHILD class C, renal dialysis, or splenectomy. Transient immune suppression such as polytrauma, sepsis, agranulocytosis without hematologic malignancy, limited steroid medication, cancer in remission, denutrition or advanced age were not counted as chronic immune suppression. A healthcare-associated infection was defined as due to an invasive medical or nursing procedure within the last 30 days prior to the onset of infection. Auto-injections or traumatic wounds within the hospital were not regarded as healthcare-associated.

Microbiological analyses

We processed all microbiologic specimens according to CLSI (Clinical and Laboratory Standard's Institute) recommendations (Performance Standards for Antimicrobial Susceptibility Testing, 2007), before switching to EUCAST criteria (European Committee on Antimicrobial Susceptibility Testing) in 2014 (European Committee on Antimicrobial Susceptibility Testing, 2014). In our hospital, we keep only pathogens of bacteremia. Due to the retrospective and composite nature of our database, we lack typisation data comparing the *S. aureus* between subsequent and index episodes. As a surrogate we assessed differences in the antibiotic susceptibility testing of the different *S. aureus* isolates. Our laboratory routinely tested all clinical *S. aureus* isolates for penicillin, flucloxacillin, cefuroxime, ciprofloxacin, clindamycin, erythromycin, fusidic acid, co-trimoxazole, tetracycline, and rifampicin.

Statistical analyses

For group comparisons we used the Pearson χ^2 test, the Fisher exact test or the Wilcoxon rank sum test. An unmatched logistic regression analysis with the outcome "*subsequent S. aureus soft tissue infection*" adjusted for the case-mix. We included 8 to 10 predictor variables per outcome event and checked key variables for collinearity and for interaction (by Mantel-Haenszel estimates and interaction terms). We considered p values ≤ 0.05 as significant, and used STATA™ software (9.0; College Station, Texas, USA).

Results

We found a total of 1023 index episodes of soft tissue infection without variation in the rate of index cases over the study period, or detected outbreak situations. The median age of enrolled patients was 51 years and 334 (34%) were chronically immune-compromised. Twenty-one patients were known intravenous drug abusers and nine indicated their profession as healthcare workers in close contact of somatic patients. Almost all infections were associated to abscesses of various diameters (948/1023; 93%), including 401 septic bursitis cases. There were 27 necrotizing fasciitis and 48 solely phlegmonous infections requiring surgical intervention. Only a minority of episodes (48/1023; 5%) were clearly healthcare-associated.

Microbiology

Among the index episodes of soft tissue infections, 670 (65%) were caused by *S. aureus,* of which 36 were due to healthcare-