Journal of Infection (2015) 71, 312–316

BIA
British Infection Association

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Necrotizing soft tissue infections after injection therapy: Higher mortality and worse outcome compared to other entry mechanisms

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Accepted 11 May 2015
Available online 3 June 2015

KEYWORDS
Necrotizing soft tissue infection;
Necrotizing fasciitis;
Injection therapy

Summary *Objectives:* Necrotizing Soft Tissue Infections represent a rare entity of infection associated with a high mortality. The aim of this retrospective study was to analyze patients with an iatrogenic etiology of injection or infiltration to compare the outcome with other etiologies.
Methods: The study group consisted of 21 patients treated with a Necrotizing Fasciitis caused by injection or infiltration. Risk factors and outcome were compared to 134 patients with a Necrotizing Fasciitis caused by other entry mechanisms.
Results: Overall mortality in our study group was 14 of 21 (67%) with an amputation rate of 11 of 15 (73%) if an extremity was involved. The survival rate was significantly worse after injection or infiltration ($p < 0.001$) as was the amputation rate ($p = 0.013$), the percentage of patients requiring intensive care (100% vs. 83%, $p = 0.038$) and vasopressors (81% vs. 54%, $p = 0.02$). Injection or infiltration therapy proved to be the strongest prognostic factor ($p = 0.003$) besides the known risk factors obesity (0.007) and renal insufficiency (0.025).
Conclusions: Our results demonstrate that patients with a Necrotizing Soft Tissue Infection after injection or infiltration therapy have a significantly worse prognosis.

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http://dx.doi.org/10.1016/j.jinf.2015.05.013

Introduction

Necrotizing Soft Tissue Infection (NSTIs) or Necrotizing Fasciitis are often characterized by a rapid progression and although they represent a rare entity of infection are associated with a high mortality. Reported mortality rates have improved over the last decades from up to 32% between 1980 and 1998 to less than 20% in recent publications.[1–4] Determinants for this increase in survival rates are radical surgical treatment, a better antibiotic therapy and improvements in intensive care treatment. However, the diagnosis and a rapid, aggressive and adequate treatment are still challenging and many questions as the role of different microorganisms, patient risk factors, adjuvant treatment options, localization and source of infection and other prognostic factors still remain open or are controversially discussed.[4–8]

It is commonly agreed, that early aggressive surgical treatment is a strong prognostic factor for a positive outcome and that delayed surgery results in a higher mortality.[1,7,9] Other factors influencing the outcome of Necrotizing Soft Tissue Infections have been described including age, female gender, extent of infection, diabetes, elevated serum creatinine and lactate level.[3,6,8,10] However, there are still many questions about the role of different causative infectious agents, monomicrobial and polymicrobial infections and predisposing host factors. It has been reported that diabetes and shock are associated with a higher rate of limb loss.[11,12] An advanced APACHE II score[1,2] and the evidence of sepsis and shock upon admission[10,12] are strong predictors of a negative outcome. Despite advanced treatment options and the importance of a radical initial surgical debridement the limb amputation rate remains up to 20%[1] and although several prognostic markers for a successful surgical and overall outcome have been described,[9–11,13,14] many decisions have to be based on clinical parameters and the experience of the surgeon.

Whereas the body surface area involved with the infection has been shown to correlate with overall outcome[10] and a higher mortality has been reported for truncal and perineal infections,[15] the source of infection has not described to be significantly correlated with outcome. Besides the common etiologies of necrotizing infections as insect bites, chronic wounds, trauma or idiopathic origin, several possible sources are iatrogenic, for example injections or infections of surgical wounds. So far no study was able to compare large series of these specific ways of causing a Necrotizing Soft Tissue Infection. Postoperative wound infections have been reported to have a significantly higher survival in one study[10] while the use of injection drugs could be identified as a predisposing risk factor for NSTIs.[4] However, several small studies and cases reports have been published describing fulminant Necrotizing Soft Tissue Infections after the intramuscular injection of ampicillin[16] or bath salts,[17] the local injection of corticosteroids to treat a trigger finger[18] or after a Bacilli-Calmette-Guerin vaccination of a newborn.[19]

The aim of this study was to analyze a specific subgroup of patients with an iatrogenic etiology of Necrotizing Soft Tissue Infections and compare them with other sources of infections in order to identify risk profiles or prognostic factors.

Material and methods

The study population of 21 patients with the diagnosis of a Necrotizing Soft Tissue Infection (NSTI) after injection therapy was acquired out of an established database. The database consists of more than 150 patients treated for the diagnosis of a Necrotizing Soft Tissue Infection in our Level 1 Trauma Center between November 2003 and December 2013. The initial diagnosis of necrotizing fasciitis was based on clinical characteristics[1–5] and intraoperative findings, in all patients the diagnosis was confirmed through intraoperative histopathological examination. Patients who in the later follow-up did not meet the criteria of a Necrotizing Soft Tissue Infection were excluded from the study. The etiology of injection therapy was verified and other sources of entry were excluded, only patients with doubtless etiology were included in the study. Injection therapy was defined as subcutaneous, intramuscular and intravenous injections as well as infiltration therapy for various reasons in the area of fasciitis prior to first signs of infection. A total of 21 patients who met the inclusion criteria could be identified out of our database. 134 patients met the inclusion criteria to serve as a control group without history of recent injections of infiltrations.

All patients were operated at least once, microbiological and histological samples were acquired from all patients. For microbiological examinations tissue samples and cultures were obtained with every operative procedure. All patients received necessary critical care support, antibiotic therapy and in absence of contraindications hyperbaric oxygen therapy (HBO). Medical records of all treated patients were acquired and entered into an established database. The variables examined in the present study included age, gender, body mass index (BMI), comorbidities, duration of hospitalization and intensive care, site of injection or infiltration, site and cause of infection, microbiological results, number and type of surgical procedures, rate of amputation, surgical eradication of the septic focus and mortality.

To compare the study group of patients with the specific etiology of injection or infiltration therapy with Necrotizing Soft Tissue Infections caused by other entry mechanisms, a control group of 134 patients was formed out of the database. Continuous variables were expressed as median with ranges. Depending on the distribution of the data the Student T test or Mann–Whitney U test was performed for independent variables to investigate differences between patient groups (injection versus others groups). Nominal data were analyzed using the chi-square test and survival curves using the log rank test. For risk factor groups a factor reduction analysis was performed prior to the analysis. The effect of these risk factors was analyzed with univariate covariance analysis (ANCOVA). Analyses were performed using the Statistical Package for the Social Sciences (SPSS 19, IBM SPSS Corp, NY, USA).