Laboratory Risk Indicators for Necrotizing Fasciitis and Associations with Mortality

Nekrotizan Fasiitli Olgularda Laboratuvar Risk Belirteçleri ve Mortalite ile İlişkisi

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SUMMARY

Objectives

Necrotizing fasciitis (NF) is rare but life threatening soft tissue infection characterized by a necrotizing process of the subcutaneous tissues and fascial planes. The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been verified as a useful diagnostic tool for detecting necrotizing fasciitis. A certain LRINEC score might also be associated with mortality. The aims of this study are to determine risk factors affecting the prognosis and to evaluate the prognostic value of the LRINEC score in NF.

Methods

Twenty-five patients with necrotizing fasciitis treated in Samsun Education and Research Hospital between January 2008 and April 2013 were enrolled in the study. Surviving and non-surviving patient groups were compared regarding demographic data, co-morbidity, predisposing factors, causative agents, number of debridements and LRINEC score.

Results

Mean age was 55.6±16.79 years (min: 17-max: 84), and the female/male ratio was 16/9. Mortality was observed in 6 (24%) patients. The most frequent comorbid diseases were diabetes mellitus (52) and peripheral circulatory disorders (24%), and the most frequent etiologies were cutaneous (32%) and perianal abscess (20%). Pseudomonas aeruginosa infection was higher in the non-surviving group (p=0.006). The mean number of debridements and LRINEC score were higher in the non-surviving group than in the surviving group (p=0.003 and p=0.003, respectively).

Conclusions

Pseudomans aeruginosa infection and multiple debridements are related with mortality. The LRINEC score might help predict mortality in NF.

Key words: Fasciitis; mortality; necrotizing; prognosis.

ÖZET

Amaç

Nekrotizan fasiit (NF) cilt altı dokular ve fasyal planlarda nekrozla karakterize nadir görülen ama hayatı tehdit eden bir yumuşak doku enfeksiyonudur. Nekrotizan fasiit için laboratuvar risk indikatör (LRINEC) skor, NF teşhisinde kullanılan yararlı bir tanısal yöntemdir. Belirli bir LRINEC skor mortalite ile de ilişkili olabilir. Bu çalışmanın amacı NF için LRINEC skorun prognostik değerini ortaya koymak ve prognozu etkileyen risk faktörlerini belirlemektir.

Gereç ve Yöntem

Ocak 2008-Nisan 2013 tarihleri arasında Samsun Eğitim ve Araştırma Hastanesi'nde tedavi edilen nekrotizan fasiit tanılı 25 hasta çalışmaya dahil edildi. Yaşayan ve ölen hastalar; demografik özellikler, yandaş hastalıklar, presidpozan faktörler, enfeksiyon etkeni, debridman sayısı ve LRINEC skorlar açısından karşılaştırıldı.

Bulgular

Ortalama yaş 55.6±16.70 yıl (min: 17-maks: 84), kadın/erkek oranı 16/9 idi. Altı (%24) hasta kaybedildi. En sık eşlik eden hastalıklar diabetes mellitus (%52) ve periferik vasküler hastalıklar (%24) idi. En sık etiyoloji ise kutanöz apseler (%32) ve perianal abse (%20) idi. Pseudomanas aeruginosa enfeksiyonu ölen hastalarda daha fazlaydı (p=0.006). Debridman sayısı ortancası ve LRINEC skor ölen hastalarda yaşayan hastalardan anlamlı olarak daha yüksek idi (sırasıyla p=0.003, p=0.003).

Sonuç

Pseudomanas aeruginosa enfeksiyonu ve çoklu debridmanlar mortalite ile ilişkilidir. LRINEC skror NF için mortaliteyi tahmin etmede kullanılabilir.

Anahtar sözcükler: *Fasiit; mortalite; nekrotizan; prognoz.*

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Introduction

Necrotizing fasciitis (NF), which is characterized by progressive necrosis of the fascia, subcutaneous tissue and skin, is a life-threatening soft tissue infection. The disease was defined with its contemporary meaning in 1950 by Wilson, who observed that skin necrosis is a rare occurrence, but fascial necrosis is much more common.[1] Urogenital-anorectal infection and trauma plays an important role etiologically.[2-4] However, NF may be caused by minor injuries such as tissue abrasions and lacerations, insect bites, and intramuscular injection; it also should be considered that there may not always be a detectable cause.[5-8] Despite immediate surgical intervention and antibiotic therapy, the mortality rate is about 20-30%.[3,4,9]

Diagnosis is made by physical examination, but may be difficult since it is frequently confused with the other skin and soft tissue infections. For this reason, the scoring system called Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) was developed in 2004 by Wong and colleagues, and was shown to be helpful for distinguishing NF from other soft tissue infections.[10] It was reported in further studies that this scoring system can be used for early diagnosis of NF.[11-15] To calculate the LRINEC score, C-reactive protein, hemoglobin, blood leukocyte count, serum glucose, serum creatinine, and serum sodium values of patients were measured at admission and scored as shown in Table 1. Then a certain score value is obtained for each patient. Values of six or higher indicate the most likely diagnosis of NF.[10-15]

The aim of this study is the clinical evaluation of patients diagnosed with NF, for whom early diagnosis and intervention are vital, and to investigate the relationship between LRINEC score and mortality rate.

Materials and Methods

The study was approved by the ethics committee of our hospital. The files of 31 patients, who were diagnosed with necrotizing fasciitis (M72.5) and were operated for Fournier gangrene with debridement (621470) code from January 2008 to April 2013, were examined retrospectively on automation system. Four patients who were initially debrided in another hospital and then sent to our hospital for follow-up or intensive care support and two patients whose data were inaccessible were excluded from the study. It was found that patients with skin redness, swelling, tenderness, skin necrosis, and subcutaneous crepitus had been diagnosed with NF. All the patients received antibiotic therapy just after the diagnosis and underwent debridement within the first 24 hours. Antibiotic treatment, which caused patients to be responsive to the factors reproduced in the deep tissue culture taken during debridement, was continued. Repeated debridement was implemented for the necessary patients.

Table 1. LRINEC (Laboratory risk indicator for necrotising fasciitis) score

Parameters	Score
C-reactive protein (mg/dl)	
<150	0
>150	4
Leukocyte count (mm^3)	
<15	0
15-25	1
>25	2
Hemoglobin (gr/dl)	
>13.5	0
11-13.5	1
<11	2
Serum sodium (mmol/l)	
>135	0
<135	2
Serum creatinine (mmol/l)	
<141	0
>141	2
Serum glucose (mmol/L)	
<10	0
>10	1

Patient age, gender, co-morbidities, predisposing factors, number of debridement, and factors isolated in deep tissue culture were detected. The measured C-reactive protein, hemoglobin, blood leukocyte count, serum glucose, serum creatinine, and serum sodium values of patients were recorded to calculate LRINEC score for each patient.

Patients were divided into two groups, alive (Group 1, n=19) and deceased (Group 2, n=6). Both groups were compared in terms of age, gender, co-morbidities, predisposing factors, number of debridement, and factors isolated in deep tissue culture. The LRINEC score difference between the groups was investigated.

Statistical analysis

Data was recorded in the pre-prepared forms and was uploaded to SPSS (Version 16, SPSS Inc. Chicago, IL) software. Student's t-test and Mann-Whitney U-test were conducted for comparison of continuous variables, and chi-square test was used for categorical variables. Statistical significance was considered to be $p<0.05$.

Results

The distribution of the evaluation parameters included in this study is shown in Table 2. The average age is 55.6±16.79

Table 2. Comparison of the group

Parameters	Patients									*p*
	Group 1			Group 2			Total			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
Gender (Female)	11	68.7		5	31.2		16	64		0.364
Age (Mean)			54.79±17.74			58.17±14.47			55.6±16.79	0.722
Risk factor										
Soft tissue infection	6	75		2	25		8	32		0,936
Perianal apse	3	60		2	40		5	20		0.562
HVP	3	75		1	25		4	16		0.959
Number of debridement (Median)	1	1-3		3	1-4		1	1-4		0.003
LRINEC score (Mean)			4.6±2.7			9.6±2.87			5.8±3.49	0.003

HVP: Hollow Viscus Perforation; LRINEC: Laboratory risk indicator for necrotising fasciitis.

years old (min: 17, max: 84), and male/female ratio is 16/9. Six patients (24%) died and five of these patients (83.3%) were female. There was no statistically significant difference between groups in terms of average age and sex (p=0.722 and p=0.364, respectively). The most frequent co-morbid disease was diabetes mellitus (DM) in 13 patients (52%); the second most frequent disease was peripheral vascular disease (PVD) in 9 patients (24%). Other co-morbid diseases were chronic renal failure, chronic obstructive pulmonary disease, cerebrovascular disease, and hypertension. There was no difference between the groups in terms of DM as the most frequent co-morbid disease (p=0.645). The most common predisposing factors were as following: soft tissue infections (inguinal, femoral, parumbilical, and scrotal) in 8 patients (32%), perianal abscess in 5 patients (20%), and hollow organ perforation in 4 patients (16%). NF developed in the gluteal region after intramuscular injection in one patient; in the lower abdomen after wide skin, subcutaneous, and muscle laceration after vehicle traffic accident in another patient; and after arteriovenous fistula surgery conducted from the right femoral region in one other patient. Moreover, in the 17-year-old male patient, NF developed after orchitis in the scrotal area. Four (16%) patients did not show any predisposing factors (Table 3). There was no difference between the groups in terms of soft tissue infections and perianal abscesses as the most frequent etiologic factors (p=0.936 and p=0.562, respectively). The most frequently isolated microorganisms in deep tissue culture were *Pseudomanas aeruginos*a (32%), *Escherichia coli* (20%), and *Staphylococcus aureus* (16%). *Klebsiella pneumonia*, Proteus mirabilis and *Acinetobacter baumannii* were the other reproducing microorganisms. There was no reproduction in deep tissue culture of one patient, and another patient's culture results could not be obtained. The number of patients who had reproduction of *Pseudomanas aeruginosa* in their deep tissue culture was significantly high in the deceased group compared to alive group (p=0.006). The most commonly used antibiotics were Carbapenems (imipenem or meropenem) and beta-lactam-beta-lactamase inhibitors (piperacillin-tazobactam or cefoperazone-sulbactam).

LRINEC score averages were 4.6±2.75 in group 1, and 9.6±2.87 in group 2. LRINEC score average was significantly high in the deceased group compared to alive group (p=0.003). The median number of debridement implemented was 1 (min: 1, max: 4). Debridement median was 3 (min: 1, max: 4) in deceased patients and 1 (min: 1, max: 3) in alive patients. The difference was observed as significantly different (p=0.003). The defects were closed with fasciocutaneous flaps in 4 patients and with partial-thickness skin flap in 3 patients. Moreover, the defect of 4 patients was closed primarily. Images of a patient whose defect was closed with primary closure are shown in Figure 1.

Table 3. Predisposing factors

Etiology	n	%
Soft tissue infection	8	32
Perianal apse	5	20
Hollow viscus perforation	4	16
Unknown	4	16
Trauma	1	4
Gluteal injection	1	4
Surgery (A-V fistula)	1	4
Orchitis	1	4
Total	25	

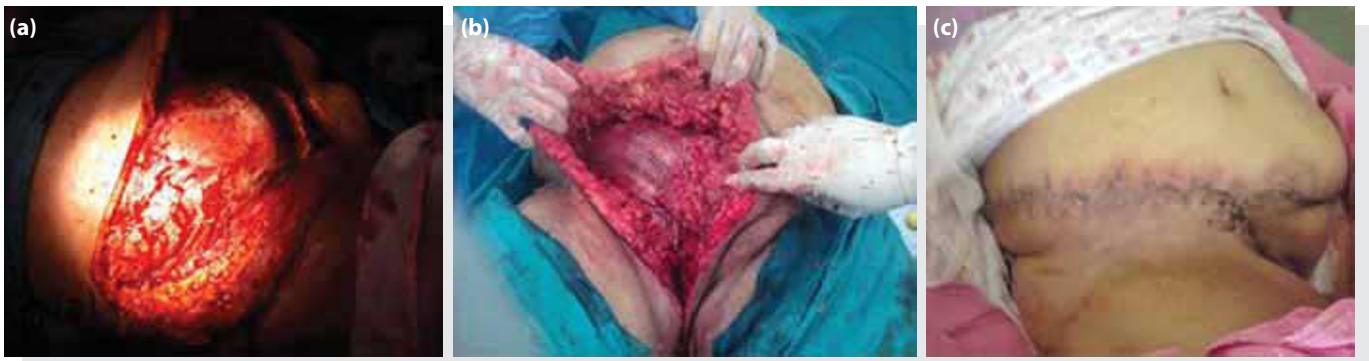

Figure 1. A 54-year-old female patient. **(a)** After debridement. **(b)** During daily wound care. **(c)** 15 days after primary closure.

Discussion

The studies show that NF is more common in males aged 50-60.[3,4,16] In our series, the average age of patients was 55.6; our study was found to be consistent with the literature. Although male patients' rates are higher in case series, female patient dominance was observed in the series of Tilkorn and colleagues, similar to our series.[15] The most common co-morbid diseases observed in NF are DM, immunosuppression, chronic renal failure, the underlying malignancy, atherosclerosis , chronic obstructive pulmonary disease, and obesity.[2-4,15,16] In our study, the most common co-morbid disease was DM (52%). The common predisposing factors are trauma, previous operations, and perianal abscess; in addition, perforated appendicitis, burns, insect bites, intravenous injection, and intramuscular injection seen after NF cases are also reported.[2-4,15-18] In our study, we also detected soft tissue infections, perianal abscess, perforation of hollow organs, previous surgery, and trauma as the most common predisposing factors. In 4 patients who did not have detectible predisposing factors, we found the co-morbid diseases DM and PVH. Undetectable microtraumas due to neuropathy and loss of sensation can cause NF in some patients. Diabetes is one of the important underlying factors for patients with NF, but there is no evidence that the disease is more fatal for patients with diabetes. Kalaivani et al.[19] showed in a 60-patient series that diabetes is not a predictor for mortality as in our patients.

According to the literature, the type and number of isolated microorganisms can vary. Factors are commonly polymicrobial, and the most common monomicrobial factors include *Streptococcus pyojenes, Staphylococcus aureus*, *E. coli*, *Klebsiella, Bacteriodes,* and *Pseudomanas aeruginosa*.[2-4,20] Pseudomanas aeruginosa was the most frequently detected factor in our study, is also the most common factor in the study by Özgenel and colleagues.[21]

The probability of having NF in patients with a LRINEC score of 6 or higher was calculated as 92% in the study of Wong et al.[10] Su et al.[13] reported that mortality also significantly increases in patients with LRINEC score of 6 or higher. Corbin[12] also showed in his study that the complication risk is higher in patients with LRINEC score of 6 or higher. Mortality is reported in the range of 20-30% in various series. The mortality rate in our study (24%) was consistent with the literature[3,4,9,20] Clayton et al.[22] presented that mortality is significantly lower in young patients, in patients with BUN of 50 mg/dl or below, and in patients without ongoing sepsis. Faucher et al.[5] proposed that co-morbid diseases do not affect mortality. On the other hand, Francis et al.[23] proposed that mortality is 50% in patients with 3 or more risk factors (being 50 years old or older, diabetes, malnutrition, hypertension, or intravenous drug abuse). As a result of this study, we propose that increased number of debridement due to severity of disease, factor grown in the deep tissue culture (*Pseudomonas aeruginosa*), and LRINEC scores might be relative to mortality.

Our study was limited by being a single centered and small volume study as well as a lack of anaerobic culture.

Conclusion

Emergency clinicians have a great responsibility in differentiating NF, which is seen rarely but is a surgical emergency with the highest morbidity and mortality, arising from simple soft tissue infections. The diagnosis can be supported and clinical course can be predicted using the LRINEC scoring system, allowing necessary precautions to be conducted to reduce the mortality rate of this disease.

Conflict of Interest

The authors declare that there is no potential conflicts of interest.

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