Original research article

ROLE OF PRE-OPERATIVE SERUM PROCALCITONIN IN EARLY DISCRIMINATION OF NECROTISING FASCIITIS FROM CELLULITIS

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Abstract

Necrotising fasciitis is a fatal and rapidly progressing soft tissue infection which requires early diagnosis and treatment to avoid morbidity and mortality, however cellulitis which presents similar in clinical presentation can be managed conservatively with IV antibiotics and supportive care and can avoid surgical debridement, hence LRINEC scoring suggested by Wong *et al*. was used earlier to differentiate and diagnose NF from cellulitis. In our study we studied serum PROCALCITONIN as a new and non-invasive marker to differentiate and diagnose NF from cellulitis, and also compared its efficacy with relation to LRINEC scoring system. We did a cross-sectional study on 35 patients including both NF and cellulitis. We used laboratory parameters like CBC, CRP, RFT, RBS and PROCALCITONIN when patient presented with soft tissue inflammation in emergency room and then patient was operated for surgical debridement and tissue was sent for tissue culture and histopathology. Patient was diagnosed as NF or cellulitis based on HPE report. And final diagnosis was compared with pre-operative PCT value and its sensitivity, specificity, PPV, NPV, cut-off value to diagnose NF was studied and also it was compared with LRINEC scoring system. In our study 46% were NF positive and 54% were diagnosed as cellulitis by HPE. 51% patients had PCT >2.6 ng/ml and majority were in high risk group according to LRINEC scoring system 85%. PCT showed 100% sensitivity and 84% specificity for NF with cut-of value of 2.4 ng/ml. Our study showed that pre-operative serum PCT can be used as a single and non-invasive marker to diagnose and differentiate NF from cellulitis as an alternative or in combination with LRINEC scoring system.

Keywords: Necrotising fasciitis, cellulitis, lrinec scoring, procalcitonin

Introduction

Necrotizing fasciitis (NF) is a severe and life-threatening soft tissue infection characterized by progressive necrosis of the fascia and subcutaneous tissue occurring along the fascial planes. It is more prevalent among those having diabetes mellitus, the immunodeficient status, malnutrition, and illicit drug usage [1] necrotising fasciitis is fatal disease which warrants immediate diagnosis and surgical debridement [2]. The mortality can reach up to 100% if not diagnosed and treated [3]. Patient's clinical characteristics, surgical exploration, microbiological and histopathological analysis of soft tissue are the gold standard for the diagnosis of NF. These tests can be invasive and time-consuming and delay the treatment, increasing the chances of mortality [3]. Majority of infections were polymicrobial (87.5%). Early and aggressive surgical debridement, often in multiple sittings, supplemented by appropriate antibiotics and supportive therapy, forms the key to a successful outcome in necrotizing fasciitis [5].

Cellulitis is spreading inflammation of skin and subcutaneous tissue which can be managed conservatively if the infection level is not severe and may not need the surgical exploration. However, it is difficult to differentiate NF and cellulitis at the first visit, since the clinical presentation of both disease entities appears similar in the early phase [2].

The availability of the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score to diagnose NF was proposed by Wong *et al*. in 2004 [1].They compared a set of laboratory risk indicators between NF and other soft tissue infections. The total score of the LRINEC ranges from 0 to 13, and the cut off score of 6 was found to have a positive predictive value of 92% and a negative predictive value of 96%.

Procalcitonin (PCT) is a peptide precursor of the hormone Calcitonin, which is involved in calcium homeostasis. The level of PCT increases in response to a proinflammatory stimulus, Especially of bacterial origin [4]. During a bacterial infection, PCT is Produced mainly by the cells of the lungs and intestines, which is a reliable marker in the diagnosis and treatment of serious bacterial infections and sepsis [5, 6]. Therefore aim of this study is to use pre-operative serum procalcitonin as a new non-invasive marker for early diagnosis and discrimination of necrotising fasciitis from cellulitis as compared to LRINEC scoring to differentiate the same and to reduce the time delay in treatment of the disease.

Methodology

This study was a cross-sectional study. Patients who came under inclusion criteria was subjected to the investigations to support the diagnosis. The investigations done was CBC, RFT, CRP, serum electrolytes, random blood sugars, serum procalcitonin. All Patient was taken for surgery like wound debridement or fasciotomy and the tissue sample was sent for culture and sensitivity and histopathology.

Study Period: 2019 to 2021

Sampling Procedure

The serum procalcitonin level was analyzed in Ramaiah hospitals laboratories using the "ECLIA" (electrochemiluminescence immunoassay) test.

Sampling Size

The sample for the present study consisted of of 35 samples including both the cases of necrotising fasciitis and cellulitis.

Inclusion criteria for sampling
- Patients above 18 years of age.
- History of acute onset of fever.
- History of acute increase in pain and swelling of the infected area with signs of inflammation.
- History of diabetes mellitus.

Exclusion Criteria for sampling
- Patients in sepsis Q-sofa score more than 2.
- Patient with renal disease.
- Patient with burns.
- Patient in cardiac shock.
- Pregnant women.
- Pediatric age group <18 years.
- Recent history of other systemic infections.

Data collection method

All the patients who came to hospital with history of sudden onset of fever, pain, edema at the affected area was admitted and patient was explained about the condition and after taking consent was subjected for the investigations to check the infection level in blood like CBC, RFT, serum electrolytes, CRP, serum procalcitonin. Serum procalcitonin levels was checked using "ECLIA" (electrochemiluminescence) test. It is based on antigen and antibody reaction test. Then the patient was taken for surgery for wound debridement or fasciotomy and the tissue was sent for culture and sensitivity. And histopathology, the confiramtional diagnosis from culture and sensitivity and histopathology report was compared with pre-operative serum procalcitonin and values were analyzed, the range of value for true positivity for the disease was studied.

Cases with positive histopathology for necrosis was diagnosed as Necrotising Fascitis and histopathology with no necrosis or negative report was diagnosed as cellulitis, and this report was compared with pre-operative serum procalcitonin value and its true positivity and true negativity to differentiate Necrotising fasciitis from cellulitis was studied and also its efficacy was compared with LRINEC scoring system to diagnose NF.

Results

Table 1: Procalcitonin - distribution of patients studied

Procalcitonin	No. of Patients	%
<2.6	17	48.6
>2.6	18	51.4
Total	35	100.0

In our study 51.4% (18) patient's serum pre-op PCT was more than 2.6 ng/ml and 48.6% (17) was below 2.6 ng/ml

Table 2: Procalcitonin – correlation with total composite score of patients studied

Procalcitonin	Total Composite Score			Total
	Low Risk	Intermediate Risk	High Risk	
<2.6	13 (59.1%)	3 (50%)	1 (14.3%)	17 (48.6%)
>2.6	9 (40.9%)	3 (50%)	6 (85.7%)	18 (51.4%)
Total	22 (100%)	6 (100%)	7 (100%)	35 (100%)
Mean ± SD	1.68±1.63	2.88±0.86	3.87±2.07	2.32±1.82

P=0.011*, Significant, Student t Test

In our study, relationship between serum PCT and LRINEC scoring was as follows. In low risk group majority had serum PCT <2.6 ng/ml 59.1% (13) and in high risk group majority patient's PCT was >2.6 ng/ml 85.7% (6).

Table 3: ROC curve analysis

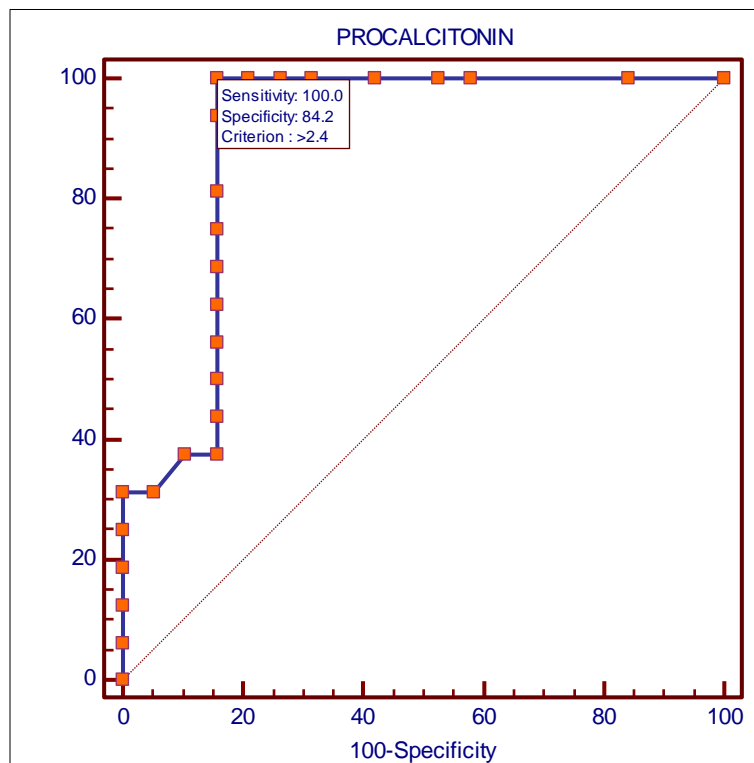| Variables	ROC results to predict Procalcitonin				Cut-off	AUROC	SE	P value
	Sensitivity	Specificity	LR+	LR-				
Procalcitonin	100.0	84.21	6.33	0.00	>2.4	89.6%	0.059	<0.001**

Fig 1: ROC results to predict Procalcitonin

In our study, pre-operative serum PCT had 100% sensitivity and 84.2% specificity for histopathologically positive Necrotising Fascitis with cut off value of 2.4 ng/ml.

Table 4: Correlation of procalcitonin with necrotising fascitis of patients studied

Procalcitonin	Necrotising Fascitis		Total
	Negative	Positive	
<2.6	16(84.2%)	1(6.3%)	17(48.6%)
>2.6	3(15.8%)	15(93.8%)	18(51.4%)
Total	19(100%)	16(100%)	35(100%)
Mean ± SD	1.15±1.42	3.71±1.16	2.32±1.82

$p \leq 0.001^{**}$, Significant, Student t Test

In our study, patients with PCT <2.6 ng/ml only 6.3% (1) were positive for NF, and patients with PCT > 2.6 ng/ml, 93.8% (15) were positive for NF.

Discussion

PCT as a new invasive marker to differentiate same between NF and cellulitis. And we also compared the efficacy of PCT with LRINEC scoring.

Retrospective observational study conducted by Wong et al. [1] showed the cutoff value for the LRINEC score was 6 points with a positive predictive value of 92.0% and negative predictive value of 96.0%. and the study conducted by Lance J. Johnson et al. [7] showed LRINEC score was associated with Necrotizing Soft Tissue Infection diagnosis in patients with Sensitivity, specificity, positive predictive value, and negative predictive value were 100%, 69%, 16.6%, and 100% respectively.

In our study LRINEC scoring, showed majority of patients were in low risk group 62.9% (22) patients and only 17.1% (6) in intermediate and 20% (7) in low risk group and it showed around 50% sensitivity and 73% specificity with positive predictive value of 61% and negative predictive value of 63%.with cut-off LRINEC score of 6.

Another similar study conducted by Cheng-Ting Hsiao et al. [8] in 106 patients with necrotizing fasciitis and 825 patients with cellulitis, With an Laboratory Risk Indicator for Necrotizing Fasciitis cut-off score 6, the sensitivity was 43% specificity was 83% positive predictive value was 25% and negative predictive value was 92%. Hence there was a significant statistical relationship between our and previous studies.

In our study 51.4% (18) patient's serum pre-op PCT was more than 2.6 ng/ml and 48.6% (17) was below 2.6 ng/ml, In low risk group majority had serum PCT <2.6 ng/ml 59.1% (13) and in high risk group majority patient's PCT was >2.6 ng/ml 85.7% (6) which implied that PCT > 2.6 ng/ml had more positivity rate for NF. And pre-operative serum PCT had 100% sensitivity and 84.2% specificity, 80% PPV and 100% NPV for histopathologically positive Necrotising Fascitis with cut off value of 2.4 ng/ml.

In a study conducted by Hassan Al-Thani et al. [9] in 62 cases of NF based on the initial procalcitonin concentrations (Group I: <0.5 low risk, Group II: ‡0.5–<2 moderate risk, Group III: ‡2-<10 high risk, and Group IV: ‡10 ng/mL, study showed common affected regions were thigh and chest in Group II (46% and 9%, respectively), lower limbs in Group III (46%), and perineum and abdomen in Group IV (25% and 21%,

respectively). And the cut off procalcitonin value for septic shock was 5.6 ng/mL. Another similar Retrospective study s conducted by Jayant Wadhwani et al. [10] in 23 patients showed that the cut-off point for the PCT level with the highest AUC under the curve was from 0.87 ng/ml with sensitivity 90.9% and specificity 82.6%, whereas it was a score of 5 on the LRINEC scale with sensitivity 72.7% and specificity 82.6% for NF and concluded that PCT measurement was a more effective method than the LRINEC score for early discrimination between NF and cellulitis.

And another study conducted by Manoj Gowda Avalahalli et al. [11] on 50 patients also concluded that LRINEC score with PCT had better predictability for severity and duration of hospital stay in NF infections [12].

Hence by our study we came to a conclusion that pre-operative serum PCT as a non-invasive marker for early discrimination between NF and cellulitis can be used in an emergency as an alternative or in combination with LRINEC scoring in order to provide adequate early treatment and reduce morbidity and mortality in NF patients.

Conclusion

Use of pre-operative serum PROCALCITONIN (PCT) as a new and single non-invasive marker in combination or as alternative to LRINEC score can help in early discrimination of NF from cellulitis and can help in timely intervention of NF to reduce mortality and morbidity.

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