CLINICAL STUDY

THE DELTA NEUTROPHIL INDEX AS A PREDICTIVE MARKER IN DEEP NECK SPACE INFECTIONS

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SUMMARY

Background: Delta neutrophil index (DNI) has recently been introduced as a useful marker for predicting infection and sepsis. No study has yet evaluated DNI as an inflammation marker in deep neck infections

Aims: The aim to investigate DNI as an early predictive marker for distinguishing abscess and phlegmon in patients with deep neck space infections.

Methods: Totally 43 patients with DNSI divided into two groups (abscess (N:23) and phlegmon (N:20)) according to the presence of the pus after drainage. Length of hospital stay(LOS), laboratory tests such as white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM) counts, neutrophil-lymphocyte ratio (NLR), delta neutrophil index (DNI) and inflammatory markers; procalcitonin (PCT), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) of the groups were compared.

Results: DNI and LOS were significantly higher in the abscess group ($p<0,05$). Other inflammatory markers (CRP, PCT, ESR) were higher in the abscess group compared to phlegmon but the difference between these values was not statistically significant($p>0,05$). The optimum cut-off value of DNI was 0,95% to predict the presence of an abscess. The sensitivity and specificity of DNI were 60,9% and 75% respectively.

Conclusion: DNI stands out as an effective parameter in determining the presence of an abscess in patients with deep neck infection and evaluating the prognosis of the disease. DNI can help in clinical diagnosis with acceptable sensitivity and specificity in the process of differentiating between abscess and phlegmon in patients with deep neck infection and making the decision to perform surgery.

Keywords: Deep Neck Infection, Abscess, Phlegmon, Delta Neutrophil Index

DERİN BOYUN ENFEKSİYONLARINDA DELTA NÖTROFİL İNDEKSİN PREDİKTİF MARKER OLARAK KULLANILMASI

ÖZET

Giriş: Delta nötrofil indeksi (DNİ), enfeksiyon ve sepsis tanısında yararlı bir belirteç olarak kullanılmaktadır ancak derin boyun enfeksiyonlarında DNİ'yi inflamasyon belirteci olarak değerlendiren bir çalışma henüz bulunmamaktadır. Amacımız DNİ'nin derin boyun enfeksiyonlu (DNE) hastalarda apse ve flegmonu ayırt etmede erken prediktif bir belirteç olarak etkinliğini belirlemektir.

Materyal ve method: DNE'li toplam 43 hasta drenaj sonrası püy varlığına göre iki gruba (apse (N:23) ve flegmon (N:20)) ayrıldı. Grupların hastanede kalış süresi (LOS) ve laboratuvar parametreleri; lökosit (WBC), nötrofil (NEU), lenfosit (LYM) sayıları, nötrofil-lenfosit oranı (NLR), delta nötrofil indeksi (DNİ), prokalsitonin (PCT), C-reaktif protein (CRP), eritrosit sedimantasyon hızı (ESR) karşılaştırıldı.

Bulgular: DNİ ve LOS apse grubunda anlamlı olarak yüksekti ($p<0,05$). Diğer inflamatuar belirteçler (CRP, PCT, ESR) abse grubunda flegmondan daha yüksekti ancak bu değerler arasındaki fark istatistiksel olarak anlamlı değildi($p>0,05$). Apse varlığını tahmin etmek için DNI'nin optimum eşik değeri %0,95 idi. DNİ'nin duyarlılığı ve özgüllüğü sırasıyla %60,9 ve %75 idi.

Sonuç: DNİ derin boyun enfeksiyonu olan hastalarda apse varlığını belirlemede ve hastalığın prognozunu değerlendirmede etkili bir parametre olarak öne çıkmaktadır. DNI, derin boyun enfeksiyonu olan hastalarda apse ve flegmonu ayırt etme ve ameliyat kararı verme sürecinde kabul edilebilir duyarlılık ve özgüllük ile klinik tanıya yardımcı olabilir.

Anahtar Sözcükler: Derin boyun enfeksiyonu, abse, flegmon, delta nötrofil index

INTRODUCTION

Deep neck space infection (DNSI) is a life-threatening situation localized in the compartments between the layers of deep cervical fascia[1]. While the incidence of deep neck infections has decreased dramatically since the dawn of the antibiotic era, these infections continue to cause significant morbidity and mortality.

Even with antibiotic treatment, early surgical drainage has an important role in the treatment modality of DNSI, especially with the presence of abscess. Detecting cases that require surgical drainage during hospitalization is important to prevent life-threatening complications, such as mediastinitis, and avoid unnecessary surgical interventions in patients with cellulite or phlegmon[2,3]. Physical examination and radiologic evaluation are used to diagnose DNSI.

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Computed tomography (CT) is the most common method used to differentiate between abscess and cellulite because of its high sensitivity; however, its low specificity can lead to unnecessary neck explorations[4]. Several laboratory tests, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and neutrophil-lymphocyte ratio (NLR), can also be used to decide the appropriate treatment[3,5].

Delta neutrophil index (DNI) measures the fraction of immature granulocytes in the circulation. It can be detected simultaneously with a routine complete blood count test and has recently been introduced in many studies as a useful marker for predicting infection and sepsis[6-8]. To the best of our knowledge, no study has yet evaluated DNI as an inflammation marker in deep neck infections.

In this study, we aim to investigate DNI as an early predictive marker for distinguishing abscess and phlegmon in patients with deep neck infection.

MATERIAL and METHODS

We retrospectively reviewed the medical records of patients treated at the Otolaryngology Department of Ankara City Hospital for deep neck space infection(DNSI) for the years 2019 and 2020. All of the researchers who participated in the study signed the most recent version of the Helsinki Declaration.

The subjects were included if their blood sampling and radiological imaging were performed before surgical drainage and the analyzes were based on the first examination performed during hospitalization. Patients with a known immunologic deficiency state or hematologic disorders and patients with a head and neck malignancy and trauma were excluded.

The demographic data including age, sex, length of hospital stay (LOS), pre-hospitalization antibiotic use, presence or absence of pus intraoperatively, laboratory tests such as white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM) counts, neutrophil-lymphocyte ratio (NLR), delta neutrophil index (DNI) and inflammatory markers; procalcitonin (PCT), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) were recorded.

Neck CT scans performed at the time of admission were used to evaluate the location of the abscess or phlegmon.

The patients were divided into 2 groups according to the presence or absence of the pus after drainage. Patients with pus were included in the abscess group, and those without pus were included in the phlegmon group.

All patients received intravenous antibiotics. Puncture for drainage of pus was performed on all patients. If pus was detected, incision and drainage were performed either under local or general anesthesia. Postoperative period was uneventful, no complication was observed.

Statistical analysis

Statistical analysis was performed using Social Package for the Social Sciences (SPSS) version 1.0.0.1508 for macOS (SPSS Inc., Chicago, IL, USA). For continuous variables, the significance of differences between groups was analyzed with the independent t-test or the Mann-Whitney U test. Pearson's chi-squared test was applied for categorical variables. The Pearson correlation test was used for correlation analysis. Receiver operating characteristics (ROC) curve analysis was used to assess the predictive effect of DNI on the presence of an abscess. The area under the ROC curve (AUC) was calculated with 95% confidence interval. P-values less than 0.05 were considered statistically significant.

RESULTS

Totally, 43 patients with DNSI were included in the study according to our criteria. Their ages ranged from 6 to 87 (mean, 34,6) years. There were 24 (55,8%) males and 19 (44,2%) females. Their LOS ranged from 1 to 30 days (mean, 6,8).

Of the patients with DNSI, 23 (%53,5) had abscess confirmed by puncture and included in the abscess group, other 20 (%46,5) patients were included in the phlegmon group. Demographic and laboratory data of study groups were summarized in Table 1. DNI and LOS was significantly higher in abscess group (p=0,021, p=0,005; respectively). Other inflammatory markers (CRP, PCT, ESR) were higher in the abscess group compared to phlegmon but the difference between these values was not statistically significant.(p>0,05)

Laboratory markers affecting the LOS were examined with Pearson's correlation test. There was a positive correlation between DNI

and LOS. (r:0,321,p=0,036) There was no significant correlation between LOS and other examined parameters.

Pre-hospitalization antibiotic use in abscess and phlegmon groups was 13(56,5%) and 7(35%), respectively. Table 2 shows the anatomical sites of DNSI in our series. The most common primary site of DNSI was peritonsillar space followed by submandibular space.

The ROC curve was used to assess the ability of DNI to predict the presence of abscess. The optimum cut-off value of DNI was 0,95%. The sensitivity and specificity of DNI were 60,9% and 75% respectively (AUC=0,689, p=0,034) (Fig.1).

Table 1. Comparison of demographic characteristics and hematologic markers between study groups

N:43	Abscess (n:23)	Phlegmon (n:20)	P
Age, years	32,3± 15,2	37,2± 18,7	0,350
Gender n(%)			
Female	10(43,5)	9(45)	0,920
Male	13(56,5)	11(55)	
LOS, days	9,1± 6,7	4,2± 4	**0,005**
WBC (x10^9/L)	12,24 ± 3,05	13,51 ± 5,01	0,333
NEU (x10^9/L)	9,64 ± 2,69	10,3 ± 5,11	0,607
LYM (x10^9/L)	1,64 ± 0,51	2,07 ± 1,99	0,322
NLR	6,95 ± 4,83	8,15 ± 8,66	0,571
DNI (%)	2,42 ± 3,56	0,55 ± 0,71	**0,021**
PCT (µg/L)	1,70 ± 6,33	0,29 ± 0,74	0,401
CRP (mg/L)	105,57± 57,93	91,85 ± 72,43	0,494
ESR (mm/hr)	31,33 ± 17,74	25,39 ± 18,28	0,329

Data are presented as means ± SD or number (percentage)

LOS, length of hospital stay; WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; NLR, neutrophil lymphocyte ratio; DNI, delta neutrophil index ; PCT, procalcitonin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 2. Sites of infection

Involved spaces	Total (%) (N=43)	Abscess (n=23)	Phlegmon (n=20)
Peritonsillar	22 (51,2)	8	14
Submandibular	11 (25,6)	7	4
Parotid	3 (7)	1	2
Masticatory	3 (7)	3	0
Parapharyngeal	2 (4,7)	2	0
Retropharyngeal	1 (2,3)	1	0
Submental	1 (2,3)	1	0

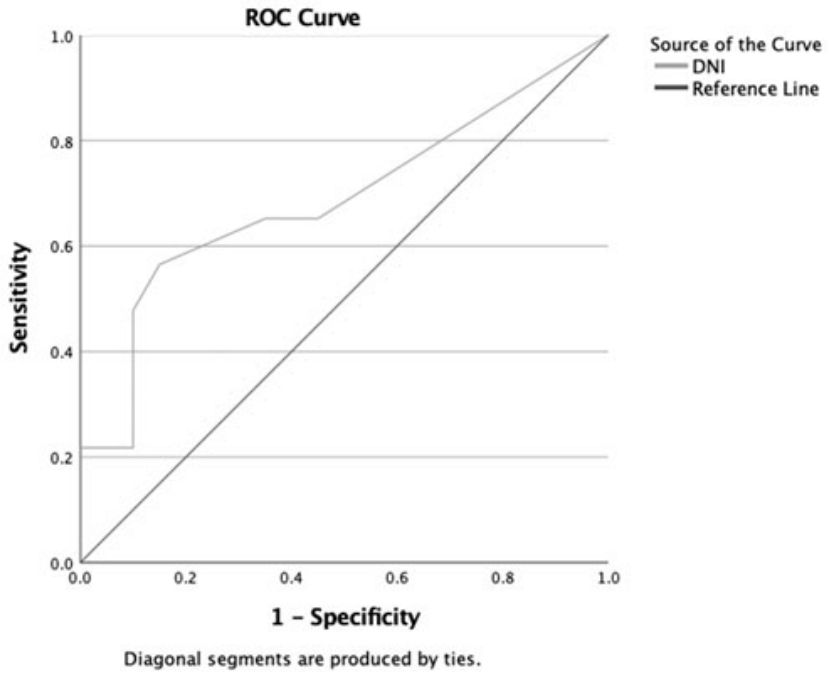

Fig 1: *ROC analysis graph of DNI in the prediction of abcsess, the area under the curve and 95% confidence intervals for indicator was 0,689 (0,528-0,850)*

DISCUSSION

It is important to choose a suitable and effective treatment in the early stage of deep neck infections. Most DNSIs can be successfully treated with antibiotherapy and drainage, and studies are showing that intravenous antibiotics alone can be effective in the treatment of DNSI, especially in selected patients[9-11]. However, delayed drainage or inaccurate antibiotics can lead to life-threatening complications[12]. Therefore, the early detection of cases requiring urgent surgical drainage is important.

Surgical exploration decisions should be made by considering all clinical, laboratory, and

radiological evaluations. Although CT is one of the most important diagnostic tests in determining the presence of DNSI, it may not be sufficient to differentiate between abscess and phlegmon. Pus may not be observed in 25% of surgeries performed with the diagnosis of abscess[2]. In the present study, pus was not detected by puncture in 46.5% of patients with the diagnosis of deep neck infection and suspicion of abscess.

Therefore, the need to benefit from laboratory tests in addition to clinical symptoms and imaging methods has emerged. Ban et al. showed that CRP, ESR, and NLR can be used as predictive parameters for successful surgery in addition to CT in patients with abscess drainage, and they established a clinical scoring system for drainage by determining the cut-off value for each parameter[3]. In another large DNSI series, it was shown that a high CRP (> 100 mg/L) value is associated with the development of complications and prolonged hospital stay[13] In the present study, although WBC, CRP, and ESR parameters were found to be higher in the group with abscess, no statistically significant difference was found.

NLR can be used an inflammation marker for determining DNSIs that develop after acute bacterial tonsillitis in the pediatric population[5]. Clinical use of LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) and NLR value was useful for early detection of the risk of sepsis and necrotizing fasciitis, which are life-threatening complications, in a DNSI case series of 118 patients[14]. However, data are available in the literature regarding the use of NLR as a predictive value in the presence of abscess, and in the present study, no significant difference was found between abscess and phlegmon groups in terms of NLR values. Although NLR has been reported as a valuable parameter in detecting the development of DNSI, it has not been evaluated as an auxiliary parameter in the differentiation of abscess and phlegmon and the selection of treatment.

Apart from the laboratory parameters mentioned above, DNI is another marker with proven clinical value in case of infection. DNI measures the fraction of immature granulocytes in the circulation and has recently been used in numerous studies as a new inflammatory marker[15]. The low cost of DNI and its direct measurement in complete blood count have increased its usage. Another feature of DNI is its short half-life (approximately 3-5 hours). As it may reflect the reaction of immature granulocytes in the circulation immediately after treatment, DNI can be used to monitor the effects of the treatment[16]. In literature, DNI is used to monitor the infectious process (e.g., sepsis, cholecystitis, pancreatitis, pneumonia, etc.) and determine the prognosis[6-18] Many studies are using DNI as a marker in non-infectious diseases, such as cardiac arrest and thyroid malignancies[19]. DNI has also been used as a prognostic marker to determine intensive care mortality in patients with COVİD-19[20].

In this study, we compared the values of DNI between the abscess and phlegmon groups in terms of its effect on the course of the disease in patients with deep neck infection. The value of DNI was found to be significantly higher in the abscess group (2.42 ± 3.56%) than in the phlegmon group (0.55 ± 0.71%) (p = 0.021). It was observed that DNI can be used in clinical diagnosis with 60.9% sensitivity and 75% specificity to determine the presence of abscess with a cut-off value of 0.95%. When the parameters affecting the hospitalization process-one of the important indicators of the prognosis of the disease-were examined, the laboratory parameter that showed a positive correlation with length of hospital stay was DNI (r: 0.321, p = 0.036).

CONCLUSION

DNI stands out as an effective parameter in determining the presence of abscess in patients with deep neck infection and evaluating the prognosis of the disease. DNI can help in clinical diagnosis with acceptable sensitivity and specificity in the process of differentiating between abscess and phlegmon in patients with deep neck infection and making the decision to perform surgery. This study is considered a preliminary work, and DNI, which is a laboratory test that can be easily evaluated with studies having a larger number of cases, can

contribute to the early diagnosis and treatment of deep neck infection patients.

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