



Clinical features of deep neck infection: analysis of 77 patients

Derin boyun enfeksiyonunun klinik özellikleri: 77 hastanın analizi

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ABSTRACT

Objectives: This retrospective study aims to detect the prognostic factors which affect the duration of hospital stay and evaluate the complications which develop in patients with deep neck infection.

Patients and Methods: The study included 77 patients (40 males, 37 females; mean age 42.4±20.1 years; range 11 to 88 years) treated with a diagnosis of deep neck infection in our clinic between November 2006 and November 2012. Patients' demographic and clinical features were analyzed to detect their associations with development of complications and hospitalization time.

Results: Odontogenic origin and submandibular localization were the most frequently observed clinical appearance. Of eight patients (10.4%) who developed serious complications, two (2.6%) died. Age, comorbidity, presence of anemia alone, Ludwig's angina and retropharyngeal involvement were associated with increased rate of complications ($p<0.05$); while sex, antibiotic usage prior to admittance and primary location of infection were not related ($p>0.05$). Submandibular localization and absence of leucopenia reduced the risk of complications ($p<0.05$). The mean duration of hospital stay was 12.9±8.7 days (range 2-59 days). Age, presence of comorbidity and development of complications extended the hospitalization period ($p<0.05$).

Conclusion: In spite of the improvements in diagnosis and treatment, deep neck infection may be an important cause of mortality if complications develop. Comorbid anemia, Ludwig's angina and retropharyngeal involvement were identified as the strongest predictors in terms of development of complications. Duration of hospital stay extended in patients who developed complications.

Keywords: Cervical necrotising fasciitis; deep neck infection; descending necrotizing mediastinitis.

ÖZ

Amaç: Bu retrospektif çalışmada derin boyun enfeksiyonlu hastalarda hastanede kalım süresini etkileyen prognostik faktörler belirlendi ve bu hastalarda ortaya çıkan komplikasyonlar değerlendirildi.

Hastalar ve Yöntemler: Kasım 2006 - Kasım 2012 tarihleri arasında derin boyun enfeksiyonu tanısıyla kliniğimizde tedavi gören 77 hasta (40 erkek, 37 kadın; ort. yaş 42.4±20.1 yıl; dağılım 11-88 yıl) çalışmaya alındı. Hastaların demografik ve klinik özellikleri komplikasyon gelişimi ve hastanede kalım süreleri ile ilişkilerinin belirlenmesi için incelendi.

Bulgular: Odontojenik orijin ve submandibüler yerleşim en sık görülen klinik görünümdü. Ciddi komplikasyon gelişen sekiz hastadan (%10.4) ikisi (%2.6) kaybedildi. Yaş, eşlik eden hastalık, yalnız anemi varlığı, Ludwig anjini ve retrofarengeal tutulum komplikasyon oranlarında artışla ilişkili iken ($p<0.05$); cinsiyet, başvurudan önce antibiyotik kullanımı ve enfeksiyonun primer odağı ilişkili değildi ($p>0.05$). Submandibüler yerleşim ve lökopeni yokluğu komplikasyon riskini azalttı ($p<0.05$). Hastanede kalım süresi ortalama 12.9±8.7 gündü (dağılım 2-59 gün). Yaş, eşlik eden hastalık varlığı ve komplikasyon gelişimi hastanede kalım süresini uzattı ($p<0.05$).

Sonuç: Tanı ve tedavideki gelişmelere rağmen, derin boyun enfeksiyonu komplikasyon geliştiğinde önemli bir mortalite nedeni olabilir. Eşlik eden anemi, Ludwig anjini ve retrofarengeal tutulum komplikasyon gelişimi açısından en güçlü öngörücüler olarak belirlendi. Komplikasyon gelişen hastalarda hastanede kalım süresi uzadı.

Anahtar Sözcükler: Servikal nekrotizan fasiit; derin boyun enfeksiyonu; desendan nekrotizan mediastinit.



Deep neck infection (DNI) is defined as cellulitis or abscess formation of the fascial planes and potential spaces of the neck. The incidence of DNI and development of complications associated with this disease have decreased significantly with the widespread use of antibiotics. However, DNI remains an important cause of morbidity and mortality due to the increasing frequency of antibiotic resistance, particularly in immunocompromised patients and those with low socioeconomic status.

Serious and life-threatening complications such as upper airway obstruction, cervical necrotizing fasciitis, descending necrotizing mediastinitis, aspiration pneumonia, pleural or pericardial effusion, dural sinus thrombosis, intracranial abscess and septic shock may occur.^[1] If complications develop, mortality can occur in up to 50% of cases despite aggressive antimicrobial and surgical treatment. Therefore, treatment should be initiated as soon as possible to reduce morbidity and mortality. The cornerstones of treatment are securing the airway, providing efficient drainage, appropriate antibiotics, and the improvement of immunologic status.^[2]

In recent years, the etiology and clinical features of DNI have differed greatly compared with those in the past, leading to innovations in diagnosis and treatment. In particular, the clinical course may vary depending on the infection location and microbial agents involved. The purpose of this study was to determine the predisposing factors for life-threatening complications and longer hospitalization duration in patients with DNI.

PATIENTS AND METHODS

In the current study, the medical records of 77 patients (40 males, 37 females; mean age 42.4 ± 20.1 years; range 11 to 88 years) who were treated for DNI at the Department of Otolaryngology and Head and Neck Surgery in Izmir Katip Çelebi University, Atatürk Training and Research Hospital between November 2006 and November 2012 were collected. The patient demographics and comorbidities, clinical features of present illness (location, infectious origin, initial symptoms and hospitalization time), diagnostic procedures (radiological and microbiological), treatment modalities (antibiotics and surgical drainage), and prognosis (complications, sequelae and mortality) were

reviewed. Cases were excluded if they had peritonsillar abscess, limited intraoral abscess, superficial infections, and infections related to penetrating or surgical neck trauma.

The initial evaluation of patients comprised a physical examination and laboratory tests, including a complete blood count, and biochemistry and coagulation studies. Odontogenic causes were identified by dental consultations. All patients were evaluated by computed tomography (CT) of the neck and thorax to assess the extent of the infections and distinguish cellulitis from an abscess. Cellulitis and small, self-limited abscesses were treated with medical therapy exclusively. If clinically required, surgical drainage was performed, and drainage materials were examined for bacterial growth.

Empirical intravenous antibiotics, including 1000 mg of ceftriaxone every 12h and 500 mg of metronidazole every 8h, were administered intravenously. The antibiotic regimen was modified according to the bacteriologic culture results.

The data were analyzed using the SPSS for Windows version 15.0 software program (SPSS Inc., Chicago, IL, USA, 2008). We used Pearson's chi-squared and Fisher's exact tests for categorical variables and the Mann-Whitney U test for analyzing the hospitalization duration according to the presence of complications. The effect of variables on the hospitalization duration and complications were analyzed by logistic regression analysis. Values were deemed to be statistically significant at a p value less than 0.05.

The research ethics committee approved the study on October 12, 2012 and assigned the number 105.

RESULTS

The age distribution of patients is given in Figure 1. Forty patients (51.9%) had received previous antibiotic therapy. The most common comorbid factor was anemia in 24 patients (31.2%), following by diabetes mellitus (DM) and smoking in 18 patients (23.4%). Neoplasms were observed in six patients (7.8%), five of them (6.5%) were malignant. Lymphoma was detected in two patients; other malignancies were recurrent laryngeal carcinoma, tongue cancer, and multiple myeloma. A benign neoplasm was

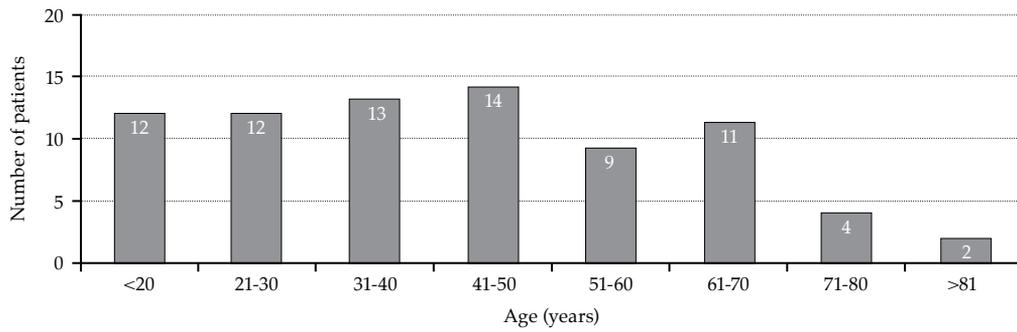


Figure 1. Age distribution of the cases.

Warthin tumor of the parotid gland. Twenty-five patients (32.5%) did not present with any risk factor. None of the patients was seropositive for human immunodeficiency virus, and none reported parenteral drug addiction. In the present study, comorbidity was found to be a statistically significant risk factor for the development of complications and prolonged hospitalization ($p<0.05$) (Table 1).

Presentations of the patients were neck or facial swelling in all the patients (100%), local pain in 64 patients (83.1%), fever in 42 patients (54.5%), trismus in 28 patients (36.4%), odynophagia in 22 patients (28.6%), and dyspnea in four patients (5.2%). The white blood count (WBC) ranged between 900 and 44,800 cells per mm^3 , and the mean WBC was $12,980 \pm 7,156$ cells per mm^3 . Leukocytosis (WBC $>11,000$) was detected in 44 patients (57.1%), and leukopenia (WBC $<4,000$) in three patients (3.9%). The absence of leukopenia was found to be a positive prognostic factor for the development of complications ($p<0.05$).

By far, the most common location of DNI was the submandibular space ($n=44$, 57.1%), followed by Ludwig’s angina ($n=14$, 18.2%).

Six patients (7.8%) had three involved spaces, including the submandibular, masseteric, and parotid spaces. Other locations of DNI were the parotid ($n=4$, 5.2%), masseteric, parapharyngeal, and retropharyngeal (three cases each, 3.9%) (Figure 2). Ludwig’s and retropharyngeal space involvement were found to be high risk for the development of complications. In contrast, submandibular localization was found to be a positive prognostic factor for the development of complications and duration of hospitalization ($p<0.05$) (Table 2).

The most frequent cause of DNI was dental infection ($n=42$, 54.5%). Tonsillopharyngeal infections occurred in 10 patients (13%), followed by sialadenitis in seven patients (9.1%). Lymphadenitis was found to be metastatic in five patients (6.5%), and tuberculosis occurred in two patients. Congenital neck cysts included a branchial cleft cyst in two patients and a thyroglossal duct cyst in one patient. The identified causes according to location are shown in Table 3. The origin of the infection could not be determined in six patients (7.8%). The primary focus of infection was not associated with an increased risk for the development of

Table 1. Risk factors for the development of complications and prolonged hospitalization duration

	Complication (n=8)			Hospitalization duration >11 days (n=40)		
	n	%	p	n	%	p
Comorbidity	8	100.0	0.045	31	77.5	0.016
Diabetes mellitus (n=18)	3	37.5	0.381	11	27.5	0.374
Anemia (n=24)	7	87.5	0.001	16	40.0	0.082
Hypertension (n=10)	2	25.0	0.277	8	20.0	0.089
Smoking (n=18)	1	12.5	0.672	10	25.0	0.726
Cancer (n=5)	–	–	1.000	3	7.5	1.000

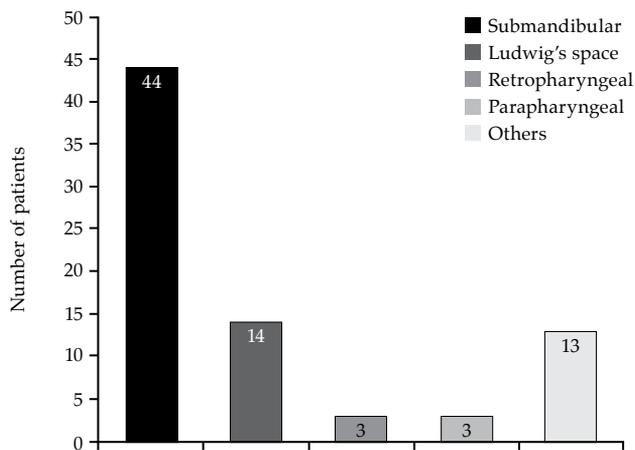


Figure 2. Infection locations.

complications and an extended hospitalization duration ($p > 0.05$). Twenty-seven patients with DNI were treated conservatively with medical therapy only. Surgical drainage and culture identification were performed in 50 patients (64.9%). Positive bacterial cultures were detected in 27 patients, 19 of whom displayed polymicrobial flora. Applications of surgical drainage and the bacterial culture results according to location are shown in Table 3. Because clinical progress could not be accessed in five patients and because bacterial cultures showed resistance to polyantibiotics in six patients, the drug regimen was changed to teicoplanin, tazocin and imipenem in consultation with the Infectious Diseases Clinic. Five of these 11 patients developed necrotizing fasciitis and one of them died due to this complication.

Eight patients (10.4%) had serious complications (Table 4). Six had Ludwig's angina,

and two had a retropharyngeal abscess. Age, comorbidity, the presence of anemia alone, and Ludwig's and retropharyngeal involvement, were associated with a significantly higher risk for the development of complications, whereas submandibular localization and absence of leukopenia indicated a low risk of complications ($p < 0.05$). The mortality rate was 2.6% ($n = 2$). Two patients who died on days 2 and 10 of hospitalization had Ludwig's angina, and were anemic and diabetic.

The mean hospitalization duration for all patients was 12.9 ± 8.7 days, and ranged from 2 to 59 days. Using logistic regression, although a submandibular localization decreased the hospitalization duration statistically, age and comorbidity extended the hospitalization duration ($p < 0.05$). The mean duration of hospitalization of six patients with complications (except two cases that died on days 2 and 10) was 31 ± 15.8 days (range, 16-59 days) (Table 5). The hospitalization duration of patients who had complications was significantly prolonged compared with that of the other patients ($p < 0.05$).

DISCUSSION

Deep neck infection is defined as cellulitis or abscess formation of the fascial planes and potential spaces of the neck. The incidence of DNI and the development of complications associated with this disease have decreased significantly with the widespread use of antibiotics. However, DNI remains an important cause of morbidity and mortality. Deep neck infection can cause acute respiratory failure, cervical necrotizing fasciitis, descending necrotizing mediastinitis, septic shock, dural

Table 2. Origins of infection: relationship with complications and the duration of hospitalization

	Complication (n=8)			Duration of hospitalization >11 days (n=40)		
	n	%	p	n	%	p
Localization	8	100.0	0.045	31	77.5	0.016
Submandibular zone (n=44)	–	–	0.001	16	40.0	0.002
Ludwig's space (n=14)	6	75	0.000	10	25.0	0.107
Parotid (n=4)	–	–	1.000	4	10.0	0.116
Masseteric (n=3)	–	–	1.000	3	7.5	0.241
Parapharyngeal space (n=3)	–	–	1.000	2	5.0	1.000
Retropharyngeal (n=3)	2	25	0.027	2	5.0	1.000
Combined (n=6)	–	–	1.000	3	7.5	1.000

Table 3. Treatment modalities

	Only medical	Surgical drainage (n=50)	
	Treatment (n=27)	Culture negativity (n=23)	Culture positivity (n=27)
Submandibular	18	14	12
Ludwig's	1	2	11
Retropharyngeal	-	-	2
Parapharyngeal	2	-	1
Others	6	6	1

sinus thrombosis, and intracranial abscess that are known to be life threatening. These manifestations are likely due to the increasing frequency of antibiotic resistance, particularly in immunocompromised patients or those of low socioeconomic status.

Cervical necrotizing fasciitis is a serious, devastating and rapidly progressive infection of subcutaneous tissue and deep cervical fascia.^[3] Prompt diagnosis, aggressive surgical debridement and appropriate antibiotic therapy contribute to improved survival. However, the progression of the disease to DNM and septic shock leads to a poor prognosis and high mortality rates.

Descending necrotizing mediastinitis is the most feared complication of DNI, and causes the spread of the infection to the posterior mediastinum via the retropharyngeal space. It is usually limited to the upper mediastinum and can be drained successfully by a transcervical approach,^[4] but can also lead to death by causing septic shock, pleural-pericardial effusion and cardiac tamponade.

Depending on the location and source of the infection and concomitant diseases, the mean hospitalization duration of DNI is 2-90 days.^[5] The mean hospitalization duration for all the patients in the present study was 12.9±8.7 days, and ranged from 2 to 59 days. Using logistic regression, although a submandibular localization decreased the hospitalization duration significantly, it was prolonged by age and comorbidity ($p<0.05$). The mean hospitalization duration of six patients with complications (excepting two who died on days 2 and 10) was 31±15.8 days (range, 16-59 days). The hospitalization duration of patients who had complications was significantly prolonged compared to that of the other patients ($p<0.05$).

Predisposing factors that can lead to DNI in the elderly are described in the literature. Daramola et al.^[6] reported 53% drug addiction, 9% hypertension, 5% DM and 6.6% head-neck cancer were associated with DNI. In our study, the most common comorbid factor was anemia in 24 patients (31.2%), following by DM and smoking in 18 patients (23.4%) each.

Table 4. General analysis of complicated cases

Age/gender	Comorbidity	Location	Origin	Bacteriology	Duration of hospitalization (day)	Outcome
84/F	Anemia, HT	Retropharyngeal	Tonsil	None	23	Pneumonia
32/F	Anemia	Retropharyngeal	Odontogenic	Mixed	20	CNF
39/F	Anemia	Ludwig's space	Odontogenic	Mixed	16	CNF, DNM
78/M	Anemia, DM	Ludwig's space	Odontogenic	None	2	CNF, DNM, exitus
67/F	Anemia, DM	Ludwig's space	Odontogenic	None	10	CNF, sepsis, exitus
40/F	Anemia	Ludwig's space	Odontogenic	Mixed	38	Pneumonia
48/M	DM, HT	Ludwig's space	Odontogenic	Mixed	30	CNF
77/M	Anemia, smoking	Ludwig's space	Unknown	Acinetobacter	59	Pleural effusion, sepsis

HT: Hypertension; CNF: Cervical necrotizing fasciitis; DNM: Descending necrotizing mediastinitis; DM: Diabetes mellitus.

Table 5. Hospitalization durations of patients with complications

Complication	Duration of hospitalization		p
	Mean±SD	Min.-Max.	
No (n=69)	11.5±5.8	3-27	0.001
Yes (n=6)	31±15.8	16-59	
Total (n=75)	13.1±8.7	3-59	

SD: Standard deviation; Min.: Minimum; Max.: Maximum.

The submandibular space is the most frequently encountered location of deep neck space infections.^[7] Dental infection is the most common cause, followed by pharyngotonsillitis.^[8] In our study, the most common location of DNI was the submandibular space (n=44, 57.1%), followed by the Ludwig's angina (n=14, 18.2%). Six patients had three involved spaces, including the submandibular, masseteric, and parotid spaces (7.8%). Other locations of DNI were the parotid (n=4, 5.2%), masseteric, parapharyngeal, and retropharyngeal spaces (three cases each, 3.9%) The most frequent cause of our DNI patients was dental infection (n=42, 54.5%). Tonsillopharyngeal infections were present in 10 patients (13%), followed by sialoadenitis in seven (9.1%). Lymphadenitis was found to be metastatic in five patients (6.5%) and tuberculosis in two. Congenital neck cysts included a branchial cleft cyst in two cases, and a thyroglossal duct cyst in one. The identified causes according to location are shown in Figure 2. The origin of the infection could not be determined in six patients (7.8%).

Maroldi et al.^[9] defined five critical roles of imaging methods in DNI patients: confirmation of the suspected diagnosis, determination of the spread of illness, definition of complications, differentiation of cellulitis and abscess, and determination of the progress of the illness.

Roentgen imaging, ultrasonography, computed tomography and magnetic resonance imaging can be used alone or in combination in the management of the infection. Lateral cervical radiography is useful for detecting a retropharyngeal abscess. Ultrasonography, which can differentiate between an abscess and cellulitis and define jugular vein thrombophlebitis, has a limited role because of ill-defined anatomic structures and inapplicability in some

compartments of the head and neck region. The main use of ultrasonography is as a guide for drainage of the superficial abscess areas; it can also be used in children for serial clinical follow-up to prevent exposure to the radiation associated with CT.

Computed tomography allows assessment of all anatomic compartments and facilitates diagnosis of the cause of the infection. MRI is preferred, particularly in complicated DNI, for suspected spread in the epidural, pre-paravertebral spaces and skull base, or if there is a suspicion of malignancy.

Although it is logical to select the antibiotic regimen in DNI based on culture results, an empirical antibiotic therapy regimen should be started at the beginning of treatment to control the disease and prevent complications. Because the bacteriologic culture results are not available for 48-72 hours, drainage cannot be applied in all DNI patients, and with 20-40% of culture results being negative, empiric antibiotic therapy becomes more important.^[10] At our institution, third-generation cephalosporins and metronidazole are the first-line drugs used for DNI.

Most pathogens isolated in DNI cultures are oropharyngeal flora bacteria, and two-thirds of infections are polymicrobial. The aerobic bacteria most commonly isolated are *Streptococcus pyogenes* and *Staphylococcus aureus*, whereas the most abundant anaerobic taxa are *Prevotella*, *Fusobacterium* and *Peptostreptococcus*.^[11] Thus, antibiotic choice must include agents with both aerobic and anaerobic effects.

Pathogens that cause DNI show various levels of antibiotic resistance-- thus, infection may not respond to therapy, and complications may occur. Boyanevo et al.^[12] reported 74% anaerobic reproduction and 2.5-58.3% resistance to clindamycin and metronidazole in these strains. Considering these high resistance rates, antibiotic regimens must be updated in the near future.

Primary head and neck cancers may present with DNI as an initial manifestation.^[13] The primary origins of malignancies are the nasopharynx, oropharynx, hypopharynx, larynx, parotid gland, thyroid, maxillary sinus and lymphoma.^[14] In the largest patient series in the literature (n=439), the incidence

of malignancy was ~2%.^[13] In our study, neoplasms were found in six patients (7.8%), five of which (6.5%) were malignant. Lymphoma was detected in two patients, and other malignancies were recurrent laryngeal carcinoma, tongue cancer, and multiple myeloma. One benign neoplasm was a Warthin tumor of the parotid gland.

Santos Gorjón et al.^[15] reported a mortality rate of ~6% in 286 adults and children with DNI. In their literature review, Sarna et al.^[16] reported mortality rates of cervical necrotizing fasciitis of 7-20%, depending on the spread in the neck. In those patients, the mortality rate increased to 41% in the presence of descending necrotizing mediastinitis, and 64% if sepsis occurred. In our study, eight patients (10.4%) had serious complications (Table 4). Six had Ludwig's angina, and two had a retropharyngeal abscess. The mortality rate was 2.6% (n=2). Two patients who died on days 2 and 10 of hospitalization had Ludwig's angina; these patients were anemic and diabetic.

Conclusion

The incidence of DNI and the development of complications associated with this disease have decreased significantly with the widespread use of antibiotics. However, DNI remains an important cause of morbidity and mortality, particularly because of the increasing frequency of antibiotic resistance in patients with concomitant diseases. Performance of further studies will likely reduce the mortality and morbidity rates in the near future.

Declaration of conflicting interests

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