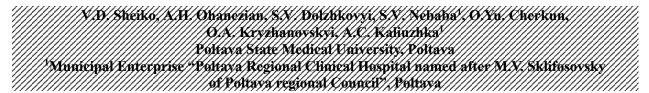
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THE COURSE OF DESCENDING NECROTIZING MEDIASTINITIS DEPENDING ON THE ETIOLOGY OF THE DISEASE

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Descending necrotizing mediastinitis is a rare complication of an oropharyngeal infection accompanied by phlegmon of the neck. The results of surgical treatment were analyzed depending on the etiology and dissemination of mediastinitis in order to improve the results of treatment of these patients. The treatment approach and course of the disease were studied in 27 patients with descending necrotizing mediastinitis, there were 22 men (81.5 %), 5 women (18.5 %); the mean age of patients was 48 years old (from 24 up to 71 years). Patients were divided into four groups: with parapharyngeal, odontogenic genesis, with perforations of the esophagus by foreign bodies and osteomyelitis of bones in the neck. Oropharyngeal infection was dominant amount etiological factors of descending necrotizing mediastinitis. It has been found that early patient seeking medical help and outpatient prescription of antibiotics improves treatment results; odontogenic mediastinitis is accompanied by the most severe course and high mortality; surgical treatment does not depend on the etiology of the disease, but understanding the ways of the infection dissemination may optimize surgical interventions and prevent the dissemination of the process in the mediastinum.

Key words: descending necrotizing mediastinitis, neck phlegmon; odontogenic mediastinitis, surgical treatment.

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ПЕРЕБІГ НИЗХІДНОГО НЕКРОТИЗУЮЧОГО МЕДІАСТИНІТУ В ЗАЛЕЖНОСТІ ВІД ЕТІОЛОГІЇ ЗАХВОРЮВАННЯ

Низхідний некротизуючий медіастиніт рідкісне ускладнення орофарингеальної інфекції, яка супроводжується флегмоною шиї. Проаналізовано результати хірургічного лікування залежно від етіології та поширення медіастиніту для покращення результатів лікування цієї категорії пацієнтів. Вивчено лікувальну тактику та перебіг захворювання у 27 пацієнтів з низхідним некротизуючим медіастинітом, чоловіків було 22 (81.5 %), жінок – 5 (18.5 %); середній вік пацієнтів – 48 років (від 24 до 71 року). Пацієнти були розподілені на чотири групи: з парафарингеальним, одонтогенним генезом, з перфораціями стравоходу сторонніми тілами та остеомієлітом кісток в ділянці шиї. У структурі низхідного некротизуючого медіастиніту домінувала орофарингеальна інфекція. З'ясовано, що раннє звернення пацієнта за медичною допомогою та амбулаторне призначення антибіотиків покращує результати лікування; одонтогенний медіастиніт супроводжується найбільш тяжким перебігом та високою летальністю; хірургічна тактика не залежить від етіології захворювання, але розуміння шляхів поширення інфекції може оптимізувати хірургічне втручання й попередити поширення процесу у межистіння.

Ключові слова: низхідний некротизуючий медіастиніт, флегмона шиї; одонтогенний медіастиніт, хірургічна тактика.

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Descending necrotizing mediastinitis (DNM) is a purulent-necrotic lesion of the mediastinum which occurs in case of dissemination of the phlegmon of the deep layers of the neck. Diagnostic criteria for this pathology were proposed in 1983 by Estrera A.S. et al. [5]: source of infection – purulent processes in the oral cavity and pharynx (1), clinical manifestations of intoxication (2), on CT scans – signs of edema, fluid and gas accumulation inside the neck and mediastinum (3), purulent-necrotic lesions of these areas in time of surgical intervention (4). Despite the possibilities of timely diagnosis and defined principles of treatment based on aggressive surgery and correct antibiotic therapy, mortality remains high and varies from 9 to 28 % in various studies, and in patients with sepsis and septic shock it reaches 60–80 % [8, 9].

In the structure of complications of oropharyngeal infection, which is accompanied by phlegmon of the neck, DNM is observed extremely rare. Most doctors in their practical work see single similar patients [8]. Even regional centers of maxillofacial and thoracic surgery have poor experience in the treatment of DNM. Scientific publications over the past decades are represented by treatment analysis of a small number of patients or systematic reviews and meta-analyses of previous studies [4, 8].

The purpose of the study was to analyze the results of surgical treatment depending on the aetiology and dissemination of descending necrotizing mediastinitis in order to improve the results of the treatment of these patients.

Materials and methods. A retrospective study of treatment and the course of the disease was done in 27 patients with DNM who were treated at the center of thoraco-abdominal surgery of the Poltava M.V. Sklifosovsky Regional Clinical Hospital in the period from 2012 to 2022. There were 22 men (81.5 %), 5 women (18.5 %); the mean age of patients was 48 years old (from 24 to 71 years).

The criteria for inclusion in the study were: signs of phlegmon of the neck and DNM, which complicated the course of inflammatory diseases of the oral cavity and pharynx, osteomyelitis C4 of the spinal cord and sternoclavicular joint, or were as a result of perforations of the pharyngeal sinuses and the cervical part of the esophagus by means of foreign bodies. The diagnosis of DNM was established in the presence of signs defined by Estrera et al. [5]. Patients with iatrogenic injuries of the pharynx and esophagus, mediastinitis due to spontaneous rupture of the esophagus (Boerhaave's syndrome) and diseases of the pleural cavity were not included in the study.

All patients underwent clinical and laboratory tests and CT scaning of the neck and chest at admission to hospital in accordance with the standard protocol in time of presence of an inflammatory process of oropharynx and neck.

Dissemination of mediastinal infection was determined based on CT scans of the neck and chest by visualizing tissue swelling, fluid and gas accumulation, clarified – in time of surgical revision. The dissemination of DNM was stratified according to the types which proposed by Endo S. et al. (1999) [4] in the modification of Sugio K. et al. (2021) (Fig. 1) [9]. Thus, type I was classified as DNM with damage to only the upper mediastinum (above the bifurcation of the trachea); to IIA type – when the process spreads to the retrosternal space, to IIB type – a total lesion of the upper and lower mediastinum, to IIC type – when the process spreads to the posterior mediastinum along the postpharyngeal and prevertebral spaces.

Based on data on the primary source of infectious-purulent inflammation, patients were divided into four groups. Group I included 11 patients (male -9 (81.8%); mean age -46 years) with parapharyngeal genesis of DNM; to the II group -8 patients (male -8 (100%); mean age -43 years) with odontogenic genesis; in the III group -6 patients (male -4 (66.7%); mean age -56 years) with DNM due to perforations of the pharyngeal sinuses and the cervical part of the esophagus by foreign bodies (fish and meat bones); to the IV group -2 patients (male and female; mean age -53 years) with DNM due to spondylodiscitis of the C4 spine and arthritis of the sternoclavicular joint.

The analysis of the course and results of treatment of DNM was carried out according to the following parameters: gender, age, etiological factor, comorbidity, duration of the disease before hospitalization, beginning of antibacterial therapy, type – prevalence of DNM, type of pathogen, severity of the condition at hospitalization (severe – 8–15, extremely severe – 16 or more points according to APACHE II), signs of sepsis (SIRS+organ dysfunction), type of surgical intervention, postoperative complications, duration of treatment in the intensive care unit (ICU), hospital stay or mortality.

Results of the study and their discussion. In group I according to the results of CT scaning and surgical revision, phlegmon of the deep layers of the neck was detected in all patients, and in 3 (27.3 %) observations spread to the upper mediastinal space (I type of DNM), in 8 (72.7 %) – to the lower one, with IIA type was not observed, IIB type was detected in 4 (36.4 %), IIC – also in 4 (36.4 %) patients. Thus, the ways of spreading of the infection into the mediastinum were mainly perivascular, retropharyngeal, and prevertebral. Duration of the disease from the beginning till administration to hospital was from 2 to 15 days (mean – 6 days). 5 (45.5 %) patients were administrated to hospital in extremely severe condition, 5 (45.5 %) in severe condition, and 1 (9.1%) in moderate condition. Signs of systemic inflammation (SIRS) were in 9 patients (81.8 %); sepsis – in 4 (36.4 %), one (9.1 %) of them had septic shock, and he has died. At the pre-hospital stage 10 (90.9 %) patients got treatment with antibiotics, all of them recovered. Clinically significant concomitant pathology (disseminated pulmonary tuberculosis) was observed in 1 (9.1 %) who died; diabetes – in 2 (18.2 %). Phlegmon of the neck was verified in all patients, but DNM initially only in 7 (63.6 %), in 4 (36.4 %) – during dynamic monitoring for 2–8 days (on average – 4 days) after opening the phlegmon of the neck, according to the repeated CT scaning in time of the absence of clinical effect.

All patients underwent cervicotomy and neck phlegmon draining. The kind of the intervention in the mediastinum depended on the dissemination of DNM. Thus, in type I (3 patients), transcervical drainage of mediastinitis was performed; with IIB type (4 patients) – combined transcervical and right-side transthoracic, in 2 cases the opposite pleural cavity was additional drained; with IIC type (4 patients) – combined in 2 cases, combined with bilateral thoracotomy in 2 cases; transcervical with

drainage of the pleural cavity – in 1 case. Postoperative complications developed in 1 (9.1 %) – stenosis of the larynx and paresis of n. recurens. Microbiological study revealed mono-infection (S. epidermidis (3 cases), Enterobacter, E. coli) in 5 (45.5 %) patients, in 3 (27.3 %) no culture was detected, in 3 (27, 3 %) – mixed culture (E.faecalis, Kl.pneumoniae, Acinetobacter, Ps.aeruginosa, Candida). The average duration of treatment for patients who recovered was 29 days (from 12 to 45 days); the average duration of treatment in the ICU was 11 days (from 1 to 33 days); mortality – 9.1 % (1 patient, male, 51 years old).

In patients of group II phlegmon of the neck was verified in all patients, while DNM was primary – in 6 (75.0 %), in 2 (25.0 %) – on the second day after the draining of the phlegmon due to the progression of the disease. Type I of DNM was detected in only 1 (12.5 %) patient, type II in all others: IIA – in 3 (37.5 %), IIB – in 4 (50.0 %), IIC – was not observed. Hydrothorax was observed in 4 (50.0 %) patients, in half of them it was bilateral. Thus, the ways of infection dissemination in the mediastinum were mainly pretracheal and perivascular. Duration of the disease before hospitalization was from 3 till 5 days (average – 4 days). 4 (50.0 %) were hospitalized in extremely severe condition, and all of them died; in severe condition – 4 (50.0 %). Signs of systemic inflammation (SIRS) were present in 6 (75.0 %); sepsis – in 4 (50.0 %), of them in 3 (37.3 %) – septic shock, all 4 patients with sepsis and septic shock died. Before administration to hospital only 50.0 % of patients got outpatient treatment with antibiotics, and all of them have recovered. Concomitant pathology – heart rhythm disorder (1), peptic ulcer of the stomach with impaired evacuation and bleeding episode (1) was observed in 2 (25.0 %), both have died; diabetes – in 1 (12.5 %), who also has died.

All patients underwent cervicotomy due to phlegmon of the neck and mediastinotomy, in type I (1 patient) this intervention was final; with IIA (3 patients) and IIB type (4 patients) – interventions were combined, in 2 the opposite pleural cavity was additionally drained. Postoperative complications developed in 2 (25.0 %): PE followed by stroke (1), the patient died, and occlusive empyema of the pleura, which required rethoracotomy, the patient recovered. Microbiological examination revealed monoinfection in 2 (25.0 %) patients (S.epidermidis (1) and St.aureus (1)); in majority of patients – 6 (75.0 %) mixed microflora was predominant (E.faecalis, Kl.pneumoniae, Acinetobacter, S.epidermidis, Candida). The average duration of treatment in patients who recovered was 26 days (from 15 to 40 days); the average duration of treatment in the ICU was 7 days (from 3 to 9 days); mortality rate – 50.0 % (4 patients, all of them were men, average age – 50 years old).

All patients of the III group associated the onset of the disease with having meal, in time of it they felt a fish or meat bone stuck "in their throat". Phlegmon of the neck was found in 4 (66.7 %) patients and was combined with upper (33.3 %) and anterior (33.3 %) mediastinitis (I and IIA types of DNM), in other 2 (33.3 %) observations the impression of the base of the neck was combined with a total lesion – IIB type DNM. Hydrothorax was detected in 4 (66.6 %) patients, of which 3 (50.0 %) had bilateral hydrothorax. The ways of spreading the infection in the mediastinum were central – perivascular and anterior-pretracheal. The mean duration of the disease was 5 days (from 3 to 7 days). Half of these patients were hospitalized in an extremely severe condition, the others in a severe condition. Signs of systemic inflammation (SIRS) were present in 4 (66.7 %); sepsis – in 2 (33.3 %), one of them had septic shock, the patient died. Before administration to hospital, 6 (66.7 %) patients got outpatient treatment with antibiotics, all of them recovered. Clinically significant concomitant pathology – infantile cerebral palsy with disability of I group (1), HIV infection (1), compensated cirrhosis of the liver and heart rhythm disorders (1) were observed in 3 (50.0 %), 2 of them died; one of the patients had diabetes – 1 (16.7 %).

Transcervical mediastinotomy was performed in 4 (66.7%), in 3 of them transthoracic mediastinotomy was additionally performed for I and IIA types of DNM, in one of them drainage of the opposite pleural cavity was performed. For 2 (33.3%) patients without signs of phlegmon of the neck with IIB type DNM, an isolated right-sided transthoracic mediastinotomy was performed, in 1 of them the opposite pleural cavity was additionally drained. Suturing of the perforation hole in the cervical part of the esophagus was performed in 2 (33.3%) patients, the rest, did not have any perforation hole in time of revision. Nutrition after surgery – through a nasal tube in one case, gastrostomy – in 2 cases. Postoperative complications developed in 3 (50.0%) patients: subcutaneous emphysema (1), external esophageal fistula, which closed on the 27th day (1), cervical-pleural atmospheric fistula with failure of esophageal sutures, which required delayed gastrostomy for a disabled patient, and this patient died. Streptococcal monoinfection was detected in 4 (66.7%) cases (Str.viridans (3), Acinetobacter (1)), in others – mixed microflora (Str.viridans, E.faecalis, Kl.pneumoniae, Acinetobacter). The mean duration of treatment was 29 days

(from 26 to 33 days); treatment in ICU - 10 days (from 3 to 17 days); mortality - 33.3 % (2 patients, men, mean age - 62 years).

Phlegmon of the neck in patients with DNM due to spondylodiscitis of the C4 spine and arthritis of the sternoclavicular joint (IV group) was accompanied by I and IIA types of DNM, in one patient there was additionally phlegmon of the frontal chest wall. The ways of spreading the infection were perivascular and pretracheal. The mean duration of the disease was 7 days (2 and 12 days). Patients were hospitalized in extremely severe (1) and severe (1) condition. Signs of systemic inflammation (SIRS) were present in both patients, sepsis in 1 (50.0 %). Before hospitalization, patients were treated with antibiotics. There was no clinically significant concomitant pathology; diabetes – in both patients. Combined mediastinotomy was performed for both patients, in addition, phlegmon of the chest wall was drainaged for one of them. A postoperative complication occurred in 1 patient with spondylodiscitis – bacterial myelitis with tetraparesis (long-term treatment in the intensive care unit). St. aureus was found in both observations at microbiological examination. The duration of treatment was 32 days (35 and 28 days); treatment in ICU – 15 days (3 and 27 days); all the patients have survived.

The spreading of neck phlegmon to the mediastinum is often diagnosed late for objective reasons, often against the background of pronounced intoxication and the patient's severe condition. Prescribing of non-steroid anti-inflammatory drugs and antibiotics in the early stages of treatment significantly distorts typical clinical manifestations. Only CT scanning of neck and chest permits to diagnose DNM, and also to determine surgical approach [8, 9]. Previous studies indicated that regardless of the typical clinical signs and CT imaging data, the course of the disease mainly depended on the etiology of DNM. The genesis of the disease determined the differences in pathogens and their virulence, ways of infection spreading in the deep layers of the neck and mediastinum [1–3]. In some publications, attention is focused on more severe course of DNM, on odontogenic infections, which are accompanied by higher mortality [1, 2, 6]. However, the most significant factors for the adverse course of DNM of any etiology are: the senile age of the patient, which is associated with concomitant diseases and diabetes, the virulence of the microorganisms and the inability of the body to localize it with the early development of sepsis and multiple organ failure [6].

Analysis of the disease duration from the onset of disease manifestation, which determines the etiology, till admission to hospital for DNM shows certain differences that may indicate the severity of the course of the infectious process. Unfortunately, these differences are not statistically significant. The most severe course is demonstrated at odontogenic DNM, the mildest – at purulent bone diseases. Thus, at odontogenic genesis of DNM, the mean duration of the disease before hospitalization was 3.9 (3-5) days, perforating genesis – 5.0 (3-7) days, parapharyngeal genesis – 5.5 (2-15) days, bone genesis – 7.0 (2 and 12) days. It should be noted that in total mass of patients with DNM those who were hospitalized in the first 3 days, the mortality rate was 18.2 %, in later terms – 31.3 % (p<0,05). All patients who recovered had got preliminary treatment with the appointment of antibiotics for the primary disease; and vice versa, those who died regarding treatment due to the main disease had not got antibiotic therapy for DNM before admission to hospital. Genesis of the disease has an impact on the early referral of patients for medical help. Thus, 90.9 % of patients received outpatient treatment for parapharyngeal ENT, 66.7 % for perforating, only 50 % for odontogenic, and 100 % for osseous one (p<0,05).

In majority of published studies, severity of phlegmon of the neck and DNM were associated with high virulence of the microorgsnisms [1, 3, 7, 8]. The spectrum of microflora in our study was highly variable, but dependent on the etiology of the disease. Thus, mono-infection prevailed at parapharyngeal, perforative and bone genesis of the disease, respectively 45.5 %, 66.7 % and 100 %; poly-microbial – at odontogenic – 75.0 % (p<0,05). Streptococci and staphylococci predominated at parapharyngeal, perforative, and bony etiology of ENT, while E. faecalis, E. faecium, Kl.pneumoniae, Acinetobacter, and Candida dominated at odontogenic ones. Part of patients with parapharyngeal infection (45.5 %), for whom the diagnosis of DNM and treatment were postponed from the onset of the disease on 5 or more days, due to unclear clinical manifestations in time of outpatient treatment, had a slow flowing course of infection and favorable the course of the disease. On the contrary, patients with odontogenic genesis of DNM (50.0 %), despite early admission to hospital, have an unfavorable course with rapid progression of infection with early development of sepsis and septic shock, which confirms the high virulence of microbial associations typical for the oral cavity.

The senile age of the patient and the concomitant pathology associated with it have a significant impair on the adverse course of DNM [6]. In our study, there were 29.6 % of patients of senile age groups (60 years and over) and young age (under 40 years), but the distribution of mortality in these age groups

was different – 37.5 % and 25.0 %; which confirms the data of previous studies (p<0,05). But in groups of patients with different origin of DNM, such pattern is not seen, only in case of perforating origin, the number of senile patients is exaggerated (50.0 %), with a mortality rate of 66.7 % in this age group. In total only 22.2 % had concomitant pathology that had an impact on the severity of the patient's condition, but most of them died – 74.1 %, and this criterion did not depend on the etiology of the disease and age (the mean age of these patients was 57 years old). Diabetes mellitus, which is cited in many studies as an important factor in the adverse course [6, 9], did not show such dependence. Thus, diabetes was observed at 22.2 % of patients with DNM, 28.6 % of them died, while the presence of diabetes with different etiologies of DNM did not have a statistically significant effect on the consequences of treatment.

The severity of the patients' condition in time of hospitalization demonstrates significant influence on the course of DNM. Thus, 96.3 % of these patients were hospitalized in a severe or extremely severe condition, while severe condition was established in 48.2 %, extremely severe – also in 48.2 %, but the mortality rate in these categories of patients differed significantly – 14, 3 % and 85.7 %, respectively (p<0.05). It should be noted that the etiology of DNM had no significant effect on the severity of these patient's condition. Thus, 45.5 %–50.0 % of patients with DNM of various origin were hospitalized in an extremely severe condition. At the same time, the genesis of the disease had an effect on the frequency of sepsis and septic shock: in case of parapharyngeal and perforating etiology sepsis was diagnosed at 36.4 % and 33.3 % patients, and septic shock at 9.1 % and 16.7 %, respectively, in case of odontogenic etiology, sepsis and septic shock developed at 50.0 % and 37.3 % of these patients, respectively (p<0.05), in case of bone genesis, sepsis developed at 1 (50 %) patient. All patients with septic shock, regardless of the etiology of DNM, died; at the same time, paratonsillar sepsis was accompanied by a mortality rate of 25.0 %, perforative sepsis – of 50.0 %, odontogenic sepsis – of 100 %, bone - all patient recovered (p<0.05). The total mortality in group of patients with DNM and sepsis was 85.7 %, septic shock – 100 %. This agrees with the data of previous studies [5].

Surgical approach for DNM depended on the dissemination of the purulent-necrotic process in mediastinum and did not depend on its etiology. However, the etiology of the disease determined the ways of spreading in the spaces of the neck and mediastinum, which was sufficiently demonstrated in previous studies [5, 7, 9]. In our observations, in case of parapharyngeal etiology of DNM, infection spreads through the retrovisceral and retropharyngeal route with damage to the upper and posterior spaces and total mediastinitis (type 1 – 27.3 %; IIS – 36.4 %, IIB – 36.4 %). For odontogenic etiology – pretracheal, previsceral and retrovisceral ways, with type I mediastinal lesion in 12.5 %, IIA – 37.5 %, IIB – 50.0 %. In case of perforation of the pharynx and esophagus infection spreads by previsceral and retrovisceral routes with lesions of mediastinum according to type I at 33.3 %, IIA – 33.3 %, IIB – 33.3 %. In case of spondylodiscitis of the cervical vertebrae infection spreads retroviscerally with type I DNM; at infection of the sternoclavicular joint – retrosternal with IIA type DNM. It has been noted extremely rapid dissemination of the purulent-necrotic process at odontogenic DNM to the lower mediastinum: in the first three days, type I was not detected, only types IIA and IIB. Similar dynamics is absent at other etiology of DNM.

The purpose of surgery for DNM is to achieve control over the source of infection [4, 8, 9]. In our study, all patients underwent unilateral or bilateral cervicotomy for debridment and drainage of the deep spaces of the neck with an upper mediastinotomy, but if, in time of intraoperative revision, additional collection of exudate inside mediastinal pleura, had not visualized on CT before, was detected, transthoracic access to the upper mediastinum was additionally performed. In all cases of lesions of the lower mediastinum (types II A, B, C) combined transcervical and right-sided transthoracic mediastinotomy was used. In the presence of ipsilateral hydrothorax, the pleural cavity was drained. The main stages of surgical intervention at mediastinotomy were debridement, lavage and drainage of the relevant departments of the infected mediastinum. Therefore, we used thoracoscopy only as a diagnostic procedure, based on the results of which, if debridement was necessary, thoracotomy was performed. It should be noted that in recent year publications, thoracoscopic intervention for DNM demonstrates treatment results comparable to thoracotomy [9, 10]. Postoperative complications developed in 33.3 % of the total number of patients with DNM, while only at the group with parapharyngeal etiology this indicator was 9.1 %, in other groups – 50.0 %.

The mean hospital stay period in groups with different etiologies of DNM ranges from 26 days for odontogenic to 32 days for osseous, but does not have significant difference in values. Similar data shows duration of treatment in the ICU. But the mortality rate clearly demonstrates the dependence of the course

of DNM on its etiology. Thus, mortality at odontogenic DNM was 50.0 % (mean age of patients was 50 % years old), at perforating DNM -33.3 % (mean age was 62 % years old), at parapharyngeal DNM -9.1 % (51 % years old), and there were no deaths due to spondylodiscitis and arthritis (p<0.05).

- 1. The analysis of the course of DNM for different etiology has certain limitations due to the small number of observations and the absence of statistically significant differences in the compared groups according to some criteria. Meanwhile, the rarity of the pathology and the small number of studies make it useful for further study of the problem.
- 2. Most patients with DNM who have oropharyngeal infections in time of early seeking medical help for the initial disease and outpatient treatment with the appointment of antibiotics improves treatment results.
- 3. Odontogenic DNM has the most severe course and high mortality, which is a consequence of untimely seeking medical help for diseases of the oral cavity, high virulence of the mix of pathogens that are inherent in odontogenic pathology, and cause the early development of sepsis and septic shock.
- 4. Factors that negatively affect the course of DNM and do not depend on the etiology are the senile age of patients, clinically significant concomitant pathology, and the severity of the condition in time of hospitalization. Surgical approach does not depend on the etiology of DNM, but understanding the ways of infection's dissemination at phlegmon of the neck may impact surgical intervention and prevent the dissemination of the process in the mediastinum.

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