Deep Neck Space Infections: A Case Series and Review of the Literature

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ABSTRACT: Deep neck spaces are regions of loose connective tissue filling areas between the 3 layers of deep cervical fascia, namely, superficial, middle, and deep layers. The superficial layer is the investing layer, The pretracheal layer is the intermediate layer and the prevertebral layer is the deepest layer. Deep neck space infection (DNI) is defined as an infection in the potential spaces and actual fascial planes of the neck. Once the natural resistance of fascial planes is overcome, spread of infection occurs along communicating fascial boundaries. More recent trends include the increasing prevalence of resistant bacterial strains, a decline in DNIs caused by pharyngitis or tonsillitis, and a relative increase in DNIs of odontogenic origin. Most DNIs are polymicrobial. Only 5% are purely aerobic and 25% with isolated anaerobes. The epidemiology of DNIs needs to be monitored for changing trends and the impact of underlying host immunity and developing microbial multidrug resistance is established. Surveillance at laboratory level should include mandatory susceptibility testing of all empiric antibiotics against microbes commonly identified in adult DNI microscopy, culture, and sensitivity (MC&S) specimens. The role of susceptibility testing of microbes not commonly identified in adult DNI MC&S specimens needs further review, on a clinical case-by-case basis.

KEYWORDS: Deep neck soace infections, antibiotics, microbiology

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Introduction

The contents of the neck are enveloped by fascia known as cervical fascia. The fascia has potential spaces that may be divided into superficial, middle, and deep layers. The superficial layer is the investing layer, the pretracheal layer is the intermediate layer, and the prevertebral layer is the deep layer.[1]

These deep neck spaces may be further classified into 3 anatomic groups, relative to the hyoid bone:

1. Those located above the level of the hyoid (peritonsillar, submandibular, parapharyngeal, masticator/temporal, buccal, and parotid spaces);
2. Those that involve the entire length of the neck (retropharyngeal, prevertebral, and carotid spaces);
3. The anterior visceral or pretracheal space located below the hyoid.[2]

A deep neck space infection (DNI) is defined as an infection in the potential spaces and actual fascial planes of the neck.[3]

Once the natural resistance of fascial planes is overcome, spread of infection occurs along communicating fascial boundries.[2]

The patterns of infection may include abscess formation, cellulitis, and necrotizing fasciitis.[4]

Antibiotics and surgical drainage form the mainstay of treatment.[5]

Traditionally, broad-spectrum antibiotic therapy was initiated; however, with changing patterns of disease, it has become more important to determine the microbiology of the neck infections seen in our population.

The aim of this study is to review the microbiology of the neck infections based on the pus aspirates.

Methodology

This study is a 7-year (from July 1, 2008 to June 30, 2015) retrospective review of the microbiology of DNIs in 52 adult patients at an academic hospital. Microorganisms isolated from patients with DNIs were analyzed, including their antibiotic susceptibility patterns. The effectiveness of empiric usage of amoxicillin-clavulanic acid against commonly identified microbes and recommended alternative antibiotic usage were reviewed.

The register records of 70 microscopy, culture, and antibiotic sensitivity results of specimens taken intraoperatively, in patients with DNIs who underwent surgical intervention, were analyzed.

Ethical considerations

All patient information was kept strictly confidential, being a retrospective study.

Data analysis

Standard statistical methods were used for the analysis. To determine the statistical significance of findings, the probability values were calculated. A probability value of $P \leq .05$ was regarded as significant. Statistical values such as mean, median, range, minimum, maximum, standard deviation (SD), and standard error were calculated for age, sex, and antibiotic

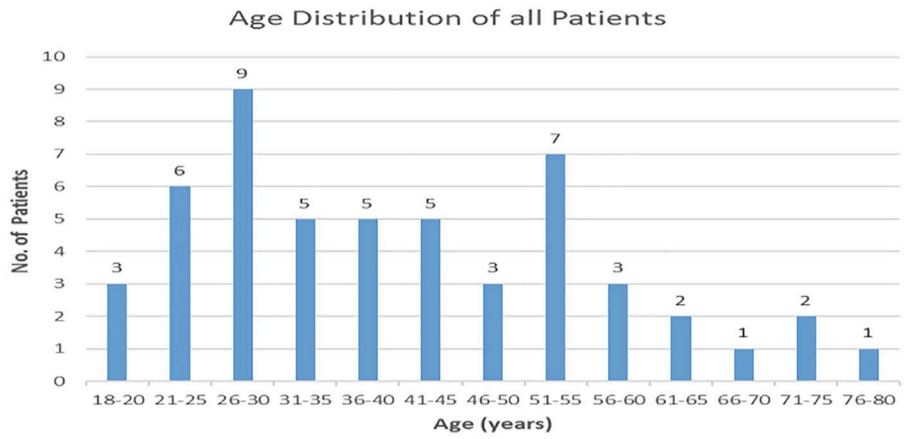

Figure 1. Age distribution of patients (N = 52).

Antibiotics	Reactive Microorganisms	Sensitivity	Resistance	Total
Ceftazidime	ACIBA	3 [43%]	4 [57%]	7 [100%]
Cefotaxime/ Ceftriaxone	KLESP	2 [67%]	1 [33%]	3 [100%]
Penicillin/ Ampicillin	CNS	2 [67%]	1 [33%]	3 [100%]
Amoxicillin-Clavulanic acid	KLESP	2 [67%]	1 [33%]	3 [100%]
Ciprofloxacin	ACIBA	2 [33%]	4 [67%]	6 [100%]

Figure 2. Antibiotic sensitivity and resistance.

sensitivity/resistance patterns, for which histograms were drawn. The bacterial profile in male patients was compared with that of female patients for various variables as shown in the tables, and its statistical significance was determined. Chi-square test and Student *t*-test were used to determine statistical significance.

Results

The age distribution of patients ranged from 19 to 77 years with a mean of 40.9 (±15.5) years (Figure 1).

The study population comprised 63% (n = 33) men and 37% (n = 19) women. The male:female ratio was 1.74:1 (Figure 2).

The distribution of positive cultures is 69% (n = 36) and that of negative cultures is 31% (n = 16), per absolute count of 52 patients with DNIs.

The duration of hospital stay varied from 1 day, for very sick patients that demised within 24 hours despite medical and surgical management, to 67 days for a patient that had a prolonged intensive care unit (ICU) stay and needed 2 surgical procedures.

The mean overall length of hospital stay was 18 days (SD = 20 days).

Immunocompromised patients in our study had a significantly longer duration of hospital stay compared with immunocompetent patients (21 vs 13 days).

Regarding the influence of the patient's age on DNIs, the odontogenic and salivary origins are the most common sources of infection for the elderly (>65 years of age). Compared with the adult group (>18 years of age), elderly patients with DNIs had more multiple space involvement, complications, surgical interventions, and longer hospital stays.

All 52 patients underwent an open surgical drainage under general anesthesia. An external transcervical approach was necessary in 42 cases (81.0%), transoral in 3 cases (7%), and a combined approach in 7 cases (12%).

Three patients needed surgery more than once. This was due to a recollection of pus within the neck spaces following initial surgery. All these 3 patients had underlying immunocompromised states.

There were 26 different microorganisms isolated and identified on culture. Of these, 92% (n = 24) of microorganisms were aerobic and 8% (n = 2) anaerobic. The most frequently isolated aerobic microorganisms, in descending order, were *Acinetobacter baumannii* (ACIBA), *Streptococcus pyogenes* (STRPY), *Streptococcus anginosus* (STRAN), *Enterococcus faecalis/Enterococcus faecium* (ENTFA/ENCFE), coagulase-negative staphylococcus (CNS), group F streptococcus (STRGF), *Streptococcus milleri* (STRMI), and Klebsiella (KLESP). Prevotella was the most frequently isolated anaerobic microorganism, in keeping with the literature.

The reported sensitivity trend of microorganisms—specifically Klebsiella and *Escherichia coli* (ESCCO)—to amoxicillin-clavulanic acid has been fairly consistent over the 7-year study period, with per year 100% sensitivity inferred. Extended-spectrum beta-lactamase-producing Klebsiella (ESBL KLESP), *Enterobacter cloacae* (ENTCL), *Serratia marcescens* (SERMA), *Citrobacter freundii* (CITFR), and *Morganella morganii* (MOGMO) were the 5 of 26 identified microbial subtypes (19%), resistant to amoxicillin-clavulanic acid, 7 of 57 microbes (12%), when all microorganisms were considered (Figure 3).

Discussion

The widespread use of antibiotics, particularly penicillin, has dramatically reduced the incidence of DNIs.[6]

Microorganisms	No.	% of Total
Aerobes		
ACIBA	6	10.5
STRPY	4	7
STRAN	4	7
CNS	3	5.3
STRGF	3	5.3
ENTFA/ENCFE	4	7
STRSP	2	3.5
STRMI	3	5.3
STAHA	2	3.5
MOGMO	1	1.8
KLESP	3	5.3
STRVI	2	3.5
ENTCL	2	3.5
CANAL	1	1.8
CITFR	1	1.8
CORSP	1	1.8
ESCCO	1	1.8
HAEPA	1	1.8
SALSP	2	3.5
SERSP/SERMA	2	3.5
AFB	1	1.8
STAEP	1	1.8
STAAU	2	3.5
STEMA	1	1.8
Anaerobes		
Prevotella	3	5.3
CORSP	1	1.8
TOTAL	57	100
Summary:		
Aerobes	53	93
Anaerobes	4	7

Figure 3. Sex distribution of microorganisms.

The current literature reveals trends that include the increasing prevalence of resistant bacterial strains, a decline in DNIs caused by pharyngitis or tonsillitis, and a relative increase in DNIs of odontogenic origin.[7]

Low socioeconomic status and poor oral hygiene, as seen in our study group, have been associated with higher rates of odontogenic infections, including cellulitis of the floor of the mouth (Ludwig angina).[2]

As there is an increase in global obesity as part of the metabolic syndrome, patients with diabetes mellitus and HIV infection are at risk for atypical and more complicated DNIs.[2]

Hence, the prevalence pattern of bacteria is possibly changing, and if so, the initial empiric antibiotic therapy for DNIs must appropriately be changed, to remain effective.

Studies conducted in urban centers revealed highly virulent bacteria such as *Staphylococcus aureus* and Porphyromonas/Prevotella that are responsible for the infection that develops in Ludwig angina. Anaerobic bacteria isolated from Ludwig angina were resistant to erythromycin and aerobic bacteria, to carbinicillin.[8]

Anatomic sites

The most frequent DNI is the peritonsillar abscess, followed by submandibular, parotid, parapharyngeal, retropharyngeal, masseteric, and pterygomaxillary abscesses and finally Ludwig angina.[9]

This is in contrast to a report of a decline in DNIs caused by tonsillitis or pharyngitis.[2] Nevertheless, in most cases, the source of the infection is a periapical infection of the mandibular second or third tooth, ie, of odontogenic origin, or tonsillitis.[1]

The microbiology of DNIs is similar, reflecting normal endogenous upper aerodigestive tract flora.[10]

An infection in the prevertebral space can be primarily hematogenous and thus their pathogenesis and microbiology are different, usually a predominance of *S aureus* and anaerobes playing a minor role. Special mention of tuberculosis (TB) infection in Pott disease can result in complications such as local vertebrae or disk destruction with spinal instability or a psoas abscess distally.[11]

Bacteria

Most DNIs are polymicrobial. Only 5% are purely aerobic and 25% with isolated anaerobes. From a resource perspective, the

utility of cultures has been questioned, with some reports indicating that culture and sensitivity data do not lead to a change in antibiotic selection or treatment.

The recommendations for cultures include extensive or rapidly spreading infections, necrotizing and gas-forming infections, nosocomial or recurrent infections, and in the immunocompromised host.[4]

The number of negative or contaminated cultures varies in the literature.

One study reported 18.8% of cultures as negative and 1.1% as contaminated.[9]

These negative cultures may be due to a high dose of IV antibiotics prior to surgical drainage of DNIs.[3] Sampling errors during collection, as occurred with anaerobes when the sample is taken using a syringe containing air, may also be a contributing factor.[9] Of note, anaerobes are fastidious and thus difficult to culture and are often overlooked.

Their exact role in the disease is difficult to ascertain due to inconsistent methods used for isolation and identification.[4] In an analysis of 233 patients with DNIs, gram-positive anaerobic cocci were most often isolated.[12]

Blood cultures have a low positive rate of 15.5% and are thus assumed to have little impact on the management of deep neck abscesses, in particular, compared with pus cultures.[3]

Molecular techniques, eg, sequence-based analysis, such as 16S rRNA, have been advocated for organisms that are poorly cultivable or for identification when traditional phenotypic methods have failed.[13]

In the past studies, *S pyogenes, S aureus*, and anaerobes were emphasized as predominant organisms in DNIs.[14] Although anaerobic cultures were not performed in all cases, 1 study reported that gram-negative organisms have replaced hemolytic streptococcus as the dominant pathogen in deep neck abscesses.[15]

In a study of 365 cases of DNIs, *Streptococcus viridans*, coagulase-negative staphylococcus, *S aureus*, and *Klebsiella pneumoniae* were found to be the most prevalent aerobic organisms. Bacteroides, Peptostreptococcus, Fusobacterium, and Prevotella were the most prevalent anaerobes, in descending order.[16]

Another study reported similar results in an analysis of 634 patients.[16] Factors predictive of severe DNIs are streptococcus infections, presence of tonsils, education level, and geographic location.[14]

Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) isolation is increasingly common, especially in intravenous (IV) drug abusers and immunocompromised patients.[1] In our study, there were immunocompromised patients, but no patients with a history of IV drug abuse. We propose that this may be the reason as to why there was no reported MRSA in our study.

K pneumoniae is the most common causative pathogen in diabetic patients with DNIs.[3] Diabetes mellitus and multiple deep neck space involvement are the strongest independent predictors of complications in this group.[1]

In another study, the *Streptococcus milleri* group (SMG) was identified in 33% of DNIs. Of note, the SMG infection spreads rapidly and is also suspected to be involved in systematic purulent diseases, eg, empyema, hepatic, and cerebral abscesses.[5,6]

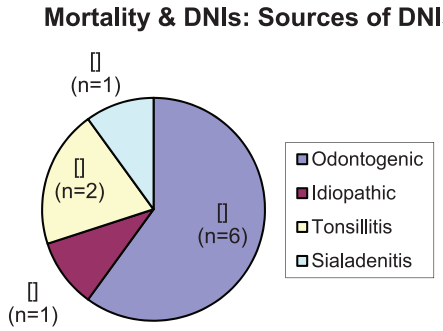

Figure 4. Source of deep neck space infections in patients that demised. DNIs indicates deep neck space infections.

An analysis of 118 case reports found that the commonest metastatic focus is the lung followed by joints. The overall mortality was 6%.[17] In patients with deep neck abscesses, factors related to mortality were: multiple deep neck space involvement ($P < .01$), bilateral involvement ($P < .05$), and reoperation ($P < .001$); 40% of these patients had comorbidities, with diabetes mellitus being the commonest, found in 34% of patients.[18]

In our study, the risk factors for poor outcomes included HIV infection, age > 50 years, and underlying diabetes. The source of DNI in survivors was idiopathic (52%) in most instances, followed by odontogenic origin (26%). In patients who demised, secondary to DNIs, odontogenic sources (60%) were most frequently encountered (Figure 4).

There were 32% of survivors of DNI of idiopathic sources who were retroviral disease positive. One survivor of DNI of idiopathic source was a patient with granulomatosis with polyangiitis (GPA) in remission, secondary to iatrogenic immunosuppressive steroid therapy. Salmonella from idiopathic sources was identified in 4% (n = 2) of patients with DNIs who were interestingly also newly diagnosed with diabetes mellitus type II, in keeping with the literature.

There were 31% (n = 10) of patients with "no growth" on DNI cultures and 30% (n = 3) of patients with DNIs who demised also had "no growth" on DNI cultures. In elderly patients with idiopathic DNIs, with or without other immune-compromising comorbidities, sterile microscopy, culture, and sensitivity (MC&S) results should not be taken at face value, especially in the context of empiric antibiotic therapy duration of less than 24 to 48 hours.

Age

Regarding the influence of the patient's age on DNIs, the odontogenic and salivary origins are the most common sources of infection in the elderly (>65 years of age). Compared with the adult group (>18 years of age), elderly patients with DNIs had more multiple space involvement, complications, surgical interventions, and longer hospital stays. However, outcome in the 2 groups were the same. Therefore, aggressive management for DNI should not be withheld simply because of old age.[19]

Antibiotic use

Empiric antibiotic therapy with a combination of penicillin plus a beta-lactamase inhibitor, eg, amoxicillin/clavulanate, is recommended among other options, providing sufficient coverage for both anaerobic and aerobic bacteria.[1]

Clindamycin may no longer be considered a first-line antibiotic in DNIs, as current resistance rates among *Bacteroides fragilis* strains reach 20% to 50% or more, worldwide.[1]

In our study, a significant amount of patients displayed more than 1 bacterium and these often included gram negatives found in our study population; hence, clindamycin would not be an appropriate first choice in our setting.

Surgical exploration and drainage of DNIs may be considered in selected cases at presentation or in cases that fail to respond to parenteral antibiotics within the first 24 to 48 hours. Cultures should be performed intraoperatively to establish the pathogen(s) involved and to obtain an antibiogram to tailor the antibiotic treatment.[12]

In this study, when all microorganisms were considered, only 7% (n = 4) were isolated and identified anaerobes; there was no routine reporting on antibiotic susceptibility of identified anaerobes, although metronidazole was suggested for the treatment of prevotella. *Staphylococcus epidermidis* (STAEP) resistance to clindamycin was reported in 1% of cases. *S pyogenes* and group F streptococcus sensitivity to clindamycin was reported in 1% of cases, respectively. Routine surveillance of endemic microorganisms and antibiotic susceptibility trends is emphasized.

Conclusions

The epidemiology of DNIs needs to be monitored for changing trends and the impact of underlying host immunity and developing microbial multidrug resistance is established.

Surveillance at laboratory level should include mandatory susceptibility testing of all microbes commonly identified in adult DNI MC&S specimens, to the then current locoregional empiric antibiotics in use. The role of susceptibility testing of microbes not commonly identified in adult DNI MC&S specimens, to the then current locoregional empiric antibiotics in use, needs further review, in selected patients on a clinical case-by-case basis.

A key factor in ensuring adequate empiric antibiotic coverage would be to elucidate the clinical significance and impact on morbidity and mortality rates, of idiopathic sources of DNIs among other sources, unidentified microbes, isolated on microscopy only but not cultured, with particular emphasis on unidentified gram-negative bacilli (GNB), that of "no growth" and polymicrobial growth patterns, including the relevance and cost versus benefit of intraoperative DNI specimen collection in guiding directed antibiotic usage.

Further research must also provide a superior quality of evidence in routinely monitoring and analyzing trends of common microorganisms implicated in adults with DNIs including those isolated in patients with DNIs who demised and empiric antibiotic usage patterns in adults with DNIs, with the intent to periodically update practice guidelines at a regional and even national health level, thereby deterring multidrug resistance, in part contributing to the management of patients with DNIs.

The recommendation for continued empiric usage of amoxicillin-clavulanic acid as well as that of appropriate alternative empiric antibiotic usage requires further periodic surveillance of commonly identified microbes and antimicrobial sensitivity results, using standardized protocols.

The increase in the reported resistance to amoxicillin-clavulanic acid, particularly in uncommonly identified GNB, as well as polymicrobial growth patterns and its influence on antimicrobial sensitivity, also requires further elucidation.

Author Contributions

SM: Write up, data anaylsis and editing.
SA: Concept, Write-up, data collection.
PP: Editing and write up.

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