Head and Neck Infections

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Abstract The head and neck have several compartments with very rich blood and nerve supply. Organisms from the oral cavity and skin can gain access to the vital structures of the head and neck causing severe infection. The infection can spread rapidly to vital locations causing life threathening complications. Prompt diagnosis and therapy are essential especially in neutropenic patients.

In this chapter we will review the most common infections of the head and neck seen in neutropenic patients.

Keywords Malignant otitis · Periorbital cellulitis · Necrotizing gingivitis · Vincent's angina · Herpetic gingivostomatitis · Submandibular space infections · Ludwing's angina · Lateral pharyngeal space infection · Retropharyngeal and prevertebral space infections

Malignant Otitis Externa

Malignant otitis externa is an infection of the external canal with the potential spread to soft tissues, cartilage and bone. The most common bacteria isolated include *pseudomonas, staphylococcus aureus, aspergillus* spp, *klebsiella oxytoca,*

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proteus mirabilis, burkholderia cepacia, and candida parapsilosis. The infection has been classically reported in elderly diabetic patients, AIDS patients, and patients with other types of immunosuppression [1–6].

The clinical manifestations include otorrhea, and otalgia mainly nocturnal with severe pain radiated to the temporomandibular joint.

In neutropenic patients, the infection can be secondary to molds and it is usually severe and potentially lethal causing osteomyelitis of the base of the skull, VII cranial nerve palsy, and brain abscess [7–9].

The diagnosis is usually clinical and microbiological. Radiological studies such as computed tomography (CT), and magnetic resonance imaging (MRI) can complement the diagnosis, but does not always correlate with the clinical course [10].

It is paramount to obtain gram stain and cultures from the ear discharge for microbiologic diagnosis and therapy. These cultures should include bacteria as well as fungus.

The treatment is debridement and antibiotics directed to the organisms isolated. Empiric antibiotics pending the culture results should include agents to cover *pseudomonas* and *staphylococcus aureus* (including methicillin resistant). Ideal choices include vancomycin plus cefepime, ceftazidime, piperacillin-tazobactam, or carbapenem such as imipenem, meropenem or doripenem. Quinolones such as ciprofloxacin and levofloxacin are widely used as prophylaxis in this population, therefore concerns for pseudomonas resistant malignant otitis remains a concern. Quinolones may still be an acceptable option provided that the pseudomonas isolated in the ear culture is still suceptible. If *aspergillus spp.* is isolated, the ideal choice is voriconazole, alternatively lipid amphotericin can be used [11].

Periorbital Cellulitis

Periorbital cellulitis is an infection of the tissues around the bony orbit. The most common cause of periorbital cellulitis in non-neutropenic patients include *H. influenza, staphylococcus aureus,* and *streptococcus spp.* [12]. In neutropenic patient molds such as *mucorales spp*, *aspergillus spp*, and *fusarium spp* are also very important pathogens. In such cases the infection usually spread from the sinuses to the periorbital tissues [13–15].

Periorbital cellulitis is further divided into preseptal or postseptal (orbital) depending on the area of infection. Preseptal cellulitis is an infection of the eyelid and the skin anterior to the orbital septum (Fig. 1). Postseptal (orbital cellulitis) is an infection posterior to the orbital septum. It involves the muscles and fat of the orbit. Postseptal cellulitis is a potential lethal infection. The infection may originate after local skin trauma (scratch, insect bite) with skin flora causing the infection or from direct spread from the sinuses to the orbit [16]. The latter is the most common cause of orbital cellulitis in neutropenic patients.

Clinical symptoms include edema, erythema and superficial pain. Pain with ocular movement, proptosis, diplopia and opthalmoplegia may be a sign of post septal cellulitis. If a mold infection is present, a nasal or palate necrotic eschar can be seen

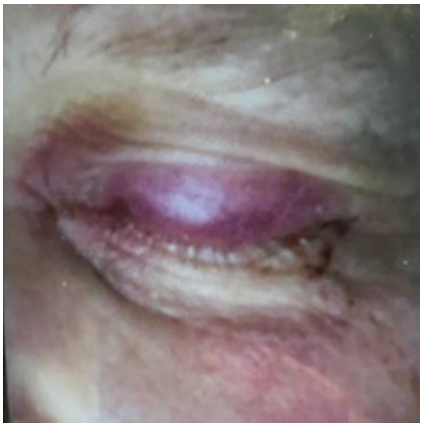

Fig. 1 Patient with preseptal cellulitis

on physical examination. Mold infections can rapidly cause angioinvasion spreading to the brain causing vascular thrombosis and tissue infarction [15].

The diagnosis of orbital cellulitis is based on clinical symptoms and physical examination. Radiological imaging such as CT of the orbit and sinuses are indicated in this population to rule out concomitant sinusitis.

If sinusitis is seen, an otorhinolaryngologist (ENT) specialist should be consulted for deeper evaluation and debridement of the sinuses. Mucosal samples should be sent to microbiology for gram stain, bacterial and fungal cultures. If deep tissue is obtained, the tissue should also be sent for special fungal stains.

Empiric therapy with vancomycin plus piperacillin tazobactam, cefepime, ceftazidime, or carbapenem such as imipenem, meropenem or doripenem, plus an antifungal such as lipid amphotericin should be started pending microbiological information. Combination of antifungal therapy with an azole or an echinocandin can be attempted in severe immunosuppressed patients but its use is still controversial [15]. Once the microbiological information is obtained, the antimicrobial therapy can be de-escalated to target the isolated pathogen.

Oral Mucosa Infections and Necrotizing Gingivitis

Mucotoxic chemotherapy can cause extensive inflammation to the oral mucosa leading to mucositis, which can be complicated by periodontal infections, gingivitis, and gum ulcers [17–19].

The oral flora of the immunocompromised patients change as a result of the chemotherapy and prophylactic antibiotics. Bacteria, other than the usual oral flora, such as pseudomonas can colonize the mucosa causing or complicating preexisting necrotic gum ulcer or gingivitis [17, 20] (Fig. 2). Other important pathogens that can spread from the mucosa to the blood stream in neutropenic patients with mucositis include *Streptococcus mitis*, *Fusobacterium spp*, *Klebsiella*, *E coli*, *Enterobacter spp* and *Stomatococcus spp*. [21, 22]

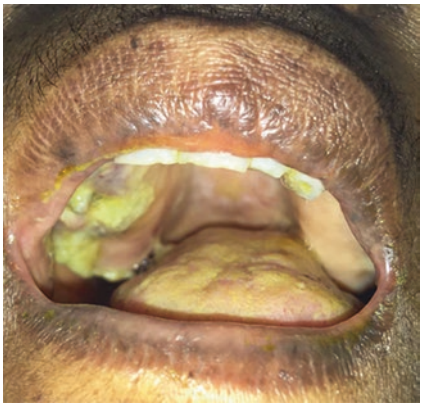

Fig. 2 Patient with pseudomonas necrotizing gingivitis

The latter can also be associated with gum or buccal mucosa ulcers that can be complicated by Vincent's Angina or trench mouth. This infection is a rapidly progressive necrotizing gingivostomatitis visualized as necrotic tissue with a grayish-white pseudomembrane [23]. *Fusobacterium spp* and other anaerobes can spread further causing deep neck infections discussed later in this chapter.

Candida spp can cause thrush in neutropenic patients, particularly in the absence of antifungal prophylaxis. Thrush is visualized as white creamy plaques in the tongue, palate and buccal mucosa. The plaques are usually associated with satellite lesions. Erythematous plaques without membranes and angular cheilosis can also be caused by candida infection. The differential diagnosis of thrush is hairy tongue. Hairy tongue is caused by abnormal desquamation of the filiform papillae resulting from several factors [24].

Herpetic gingivostomatitis is caused by herpes simplex virus (HSV) type 1 and rarely type 2. In the setting of hematological malignancy, reactivation may occur in up to 60% of the cases and in up to 80% in bone marrow transplant recipients that are not on prophylaxis. Given immunosuppression, the neutropenia and the thrombocytopenia, the clinical manifestations of HSV may not be classical. Ulcers with irregular or serpentiginous borders or extensive hemorrhagic lesions can be seen in place of the typical cluster vesicles (Fig. 3). Given the atypical presentation, HSV lesions may be confused with trauma. Alternatively, HSV reactivation may also occur from minor trauma caused by oral –gastric and endotracheal tubes. Occasionally, the lesions may progress despite of acyclovir, famciclovir, or valacyclovir. In such cases, the diagnosis of HSV acyclovir resistant virus needs to be considered and the therapy may have to be changed to foscarnet [25, 26].

It is important to perform a complete oral examination to detect any buccal or gingival ulcer. If an ulcer is detected, swab for gram stain, bacterial, fungal cultures and HSV PCR should also be obtained.

The empiric treatment of necrotizing gingivitis in neutropenic patients should be with piperacillin tazobactam or cefepime plus metronidazole or ceftazidime plus metronidazole, meropenem, imipenem, or doripenem pending cultures. Clindamycin can be an alternative to metronidazole. If HSV is isolated or suspected, famciclovir

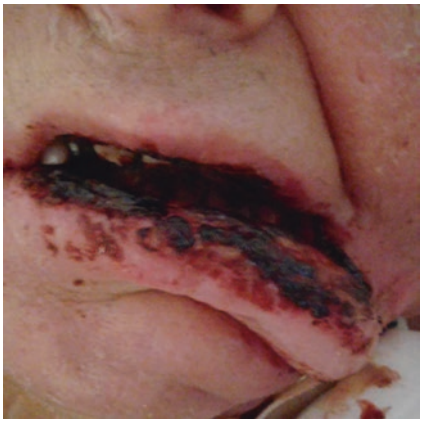

Fig. 3 Patient with hemorrhagic HSV

or valacyclovir should be added. Further therapy can be de-escalated to target the specific organism once the results of the cultures are available.

Cervicofacial Space Infections

Submandibular Space Infections

The submandibular space infections are also known as Ludwing's angina. This infection is caused by cellulitis of the bilateral sublingual, and submental space. The culprit is usually an infection of the second or third mandibular molar, but non odontogenic infections or unknown etiology can also cause it [27].

On physical exam, the patient has drooling, dysphagia, stridor, and fever. The mouth is usually open and the tongue is edematous displaced against the palate. An area of induration and with crepitus may be felt under the submandibular area. The patient usually lean forward to maximize the diameter of the airway [28]. If untreated, the infection can progress to lymphangitis, submandibular face cellulitis with progression to necrotizing fasciitis and mediastinitis.

The disease is commonly polymicrobial including *peptostreptococcus spp*, *fusobacterium spp*, *prevotella spp*, *Staphylococcus aureus*, and *Pseudomonas spp*. Other enteric gram negatives are also important pathogens in neutropenic patients [28].

The treatment is with systemic antibiotics discussed below. If rapid progression of the infection or worsening edema is seen, protection of the airway should be ensured. Intubation including tracheostomy before stridor or obvious airway compromise is seen must be preformed. Systemic antibiotics such as Vancomycin, plus piperacillin tazobactam, or cefepime plus metronidazole, or ceftazidime plus metronidazole, or metronidazole, meropenem, imipenem, or doripenem should be started as soon as possible. Clindamycin can be an alternative to metronidazole.

If fluctuance is appreciated or clinical deterioration is seen in 36–48 hours, needle aspiration or debridement should be done [28].

Infections of the Lateral Pharyngeal Space

This compartment is further divided into anterior and posterior compartments by the styloid process. The posterior compartment and the cranial nerves IX to XII are within the posterior compartmental space. Infections of the lateral pharyngeal space carry high morbidity and mortality because they can spread to the carotid sheath leading to hematogenous dissemination. Dental infections, tonsillar abscess (quinsy abscess or postanginal sepsis), otitis, mastoiditis or parotitis are usually the infections of the lateral pharyngeal space.

Clinical symptoms include trismus, edema below the angle of the mandibula, fever, and sepsis. Unfortunately, this infection can spread rapidly especially in neutropenic patients, and involve the retropharyngeal space and the mediastinum. In these cases, surgery is an emergency.

Complications of the lateral pharyngeal space include suppurative internal jugular thrombophlebitis or postanginal sepsis also known as Lemierre's syndrome (Fig. 4). Most cases are caused by *Fusobacterium necrophorum.* Other potential involved bacteria include Bacteriodes, *Eikenella*, Streptococcus, peptostreptococcus, Porphyromonas, Prevotella, Proteus, meticillin-sensitive *Staphylococcus aureus,* and meticillin-resistant *Staphylococcus aureus* [29].

Lemierre's syndrome develops from lymphatic spread of infection. Trismus is usually absent and the patient may present only with fever of unknown origin with systemic toxicity. Unilateral sore throat may be present but not universally. Dyspnea may develop as the infection involves the epiglottis and the larynx.

Suppurative jugular thrombophlebitis is a feared vascular complication. Trismus may be minimal or absent, vocal cord palsy or cranial nerve involvement may be

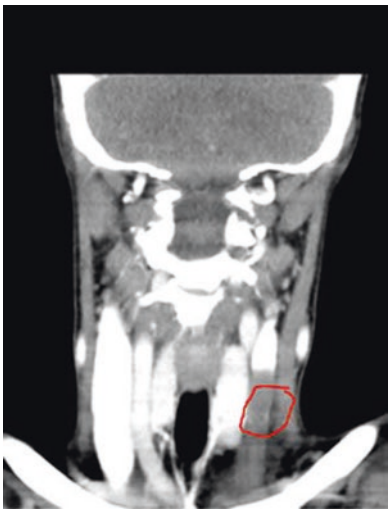

Fig. 4 CT of the neck demonstrates left jugular vein thrombosis (red circle) in a patient with Lemierre's syndrome

present. On physical examination, small area of edema may be palpated behind the sternocleidomastoid muscle [29]. Metastatic abscess to the lung, bones, and joints may develop. If retrograde dissemination occurs, meningitis or brain abscess may develop.

The treatment of the lateral pharyngeal space infections is with the same systemic antibiotics discussed for infections of the submandibular space. CT scan may be useful to localize the infection and determine the presence of local suppuration. If local suppuration is seen, needle aspiration may be considered or required [28].

In patients with acute leukemia tonsilar or oral sweet's syndrome may present similarly to the infections discussed above. Biopsy is crucial to make the diagnosis. Steroids are indispensable to prevent airway obstruction [30].

Infections of the Retropharyngeal and Prevertebral Space

Infections of this space are rare but life threatening (danger space) (Fig. 5) since the infection can spread directly into the anterior and posterior portion of the upper mediastinum. Necrotizing mediastinitis may develop with rupture into the pleural cavity causing empyema. Pericarditis with infected pericardial effusions and even tamponade may also complicate the picture.

Prompt diagnosis and debridement are the mainstays of treatment. Systemic antibiotics as discussed for submandibular infections are also indicated [28].

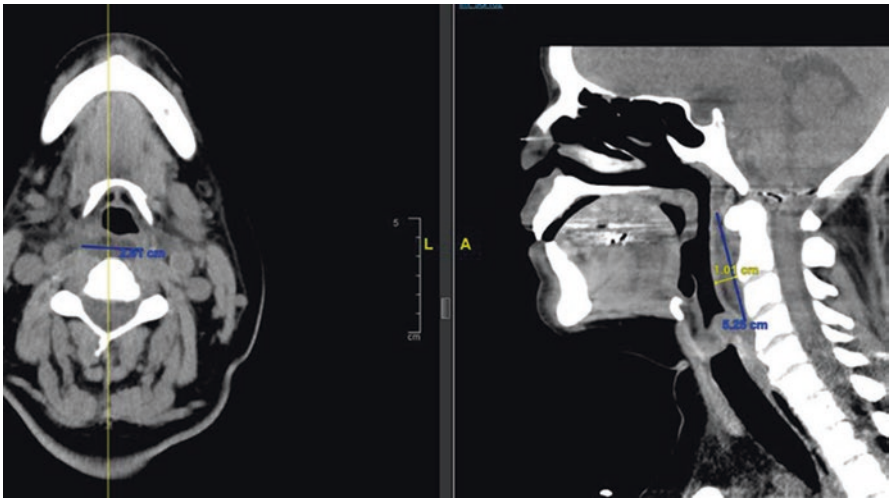

Fig. 5 CT of the neck of a patient with C3-C4 prevertebral abscess

Key Points

Disease	Organisms	Treatment
Malignant otitis externa	*Pseudomonas, Staphylococcus aureus, Aspergillus, Klebsiella oxytoca, Proteus mirabilis, Burkholderia cepacia*, and *Candida parapsilosis*	Vancomycin plus one of the following: cefepime, ceftazidime, piperacillin-tazobactam, or carbapenem. Vancomycin plus quinolone if the organism is proven to be sensitive.
Periorbital cellulitis	*H. influenza*, *staphylococcus aureus, streptococcus spp*, *mocorales, aspergillus spp*, and *fusarium spp*	Vancomycin plus one of the following: piperacillin tazobactam cefepime, ceftazidime, or carbapenem plus an antifungal such as lipid amphotericin pending microbiological information. ENT consult
Mucosal infections and necrotizing gingivitis	*Streptococcus mitis spp*, *stomatococcus spp*, *fusobacterium spp*, and other anaerobes, *candida spp* and HSV, *Pseudomonas*, MDR GNR	Piperacillin tazobactam, or cefepime plus metronidazole, or ceftazidime plus metronidazole, or carbapenem plus fluconazole. Clindamycin can be an alternative to metronidazole. If HSV is isolated or suspected, famciclovir or valacyclovir.
Neck space infections	*Peptostreptococcus spp.*, *fusobacterium spp*., *prevotella spp. Staphylococcus aureus, Psudomonas spp*. and other enteric gram negatives	Vancomycin, plus one of the following: piperacillin tazobactam, or cefepime plus metronidazole, or ceftazidime plus metronidazole, or meropenem, or imipenem, or doripenem. Clindamycin can be an alternative to metronidazole. Steroids to prevent airway obstruction. ENT evaluation

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