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Fungal And Protozoal Infections In Oral Cavity

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ABSTRACT:

The increasing prevalence of invasive fungal infections in nosocomial settings is attributed to a rise in immunocompromised individuals, including patients with HIV, cancer, and those undergoing transplant procedures. This review categorizes various oral fungal and protozoal infections, outlining their clinical features and management strategies. Oral candidiasis, including hyperplastic, erythematous, and pseudomembranous types, often presents as white, scrapable plaques, particularly in immunocompromised individuals. Aspergillosis, primarily caused by Aspergillus species, arises from spore inhalation, leading to serious respiratory tract infections and potentially necessitating surgical intervention alongside antifungal therapy. Cryptococcosis, stemming from Cryptococcus gattii and C. neoformans, can lead to severe CNS symptoms and requires ongoing monitoring post-treatment. Histoplasmosis, driven by Histoplasma capsulatum, and blastomycosis, caused by Blastomyces dermatitidis, commonly manifest in respiratory symptoms and involve intricate treatment regimens. Mucormycosis, often linked to COVID-19 complications, is an aggressive infection requiring swift identification and surgical intervention. Geotrichosis presents with oral mucosal lesions and necessitates antifungal treatment for severe cases. Rhinosporidiosis, a chronic granulomatous disease, primarily affects the nose, and effective management usually involves surgical excision. Other infections like toxoplasmosis and leishmaniasis exhibit diverse symptoms, necessitating tailored therapeutic approaches. Fungal infections show rising trends in healthcare settings, emphasizing the importance of recognition and management to improve patient outcomes in increasingly susceptible populations.

KEYWORDS : Fungal disease, protozoal disease, oral cavity.

INTRODUCTION

The prevalence of invasive fungal infections in nosocomial settings is rising. Furthermore, the incidence of nosocomial fungal infections is expected to rise over the next few decades due to the increasing frequency of risk factors for these infections. This growth is predicated on a rise in the number of immunocompromised individuals, such as those with HIV, cancer patients experiencing neutropenia from chemotherapy, and transplant recipients undergoing immunosuppressive treatment. Improved antimicrobial treatments and better management of underlying illnesses lead to longer survival times, which increases the risk of opportunistic fungal and protozoal infections in these individuals. This review aims to provide oral fungal and protozoal infections into categories, introduction, clinical features, and management.[1]

CANDIDIASIS

INTRODUCTION

The condition known as oral candidiasis (OC), or "thrush," is characterized by fungal overgrowth and penetration of superficial tissues. It includes infections of the tongue and other oral mucosal locations [2,3,4] Since Candida albicans is a highly adaptable commensal organism, it can invade almost any location when the host microenvironment alters in a way that promotes its growth. This can include invasive disseminated illness that affects several organs or superficial mucosal infections [5,6,7].

CLINICAL FEATURES

The three types of oral candidiasis are hyperplastic, erythematous, and pseudomembranous. Denture stomatitis, central papillary atrophy, and angular cheilitis are oral lesions linked to Candida.[8]

The clinical presentation of various types of oral candidiasis can differ. The most common kind of oral candidiasis is pseudomembranous candidiasis, which occurs when the oral mucosa develops white or yellow scrapable plaques.[9]

ACUTE PSEUDOMEMBRANOUS CANDIDIASIS

The type of candidiasis typically found in immunocompromised people and newborns is acute pseudomembranous candidiasis. Steroid inhalers, rinses, gels, and ointments may be linked to this infection. [10]

Fungal hyphae, fibrin, and desquamated epithelial cells combine to produce the pseudomembrane. The tongue, labial and buccal mucosa, gingival tissues, hard and soft palate, and oropharynx are among the areas where the lesions typically show up without any symptoms. Patients who experience symptoms include alterations in taste perception, oral bleeding, and a burning feeling in their tongue.[11,12]

ACUTE ATROPHIC CANDIDIASIS

Since it usually manifests acutely, this type of candidiasis is most likely attributable to the use of antibiotics or other iatrogenic therapeutic agents. Erythematous mucosa is seen upon examination; however, there is no sign of pseudomembranous overgrowth, which may be localized or widespread. The symptoms of an acute form of burning mouth/tongue type include increased sensitivity to different foods and flavourings, as well as mucosal discomfort.[10]

CHRONIC ATROPHIC CANDIDIASIS

Usually asymptomatic, this is the most prevalent kind of candidiasis in denture patients. Although the majority of patients wear their dentures around the clock, this type may occasionally be connected to orthodontic retainers.

The dentist is frequently the first to notice the issue because persistent atrophic candidiasis is

asymptomatic.[13] Inflammatory papillary hyperplasia (IPH) may potentially be linked to or occur concurrently with chronic atrophic candidiasis. Perhaps brought on by the ongoing bacterial and fungal overgrowth, inflammatory papillary hyperplasia provides the perfect conditions for the fungal elements to thrive. [14]

CHRONIC HYPERPLASTIC CANDIDIASIS

The whitish lesion that is persistent is known as chronic hyperplastic candidiasis (CHC). Although the prevalence of CHC is higher in tobacco users, there is also an overall rise in white lesions in this population. [10] Whitish plaques that are well-defined and slightly elevated; they are typically found on the buccal mucosa but can also spread to the labial commissures. Additionally, the lesions could be spotted or nodular.[12]

TREATMENT

The elimination of the biofilm layer formed on the prosthetic surface will be aided by the use of conservative measures prior to beginning medication treatment, encouraging proper oral hygiene, and taking out the dentures at night.[15] In addition to treating underlying conditions and risk factors, dentists should encourage the use of oral antiseptics and antibacterial rinses such Chlorhexidine or Hexetidine. [16] For many years, nystatin at doses of 100,000 IU/ml [5 ml four times a day] and amphotericin B at doses of 50 mg [5 ml three times a day] have been the main choice for local treatment. [17]

ASPERGILLOSIS

INTRODUCTION

Aspergillosis is the second most common opportunistic fungal infection, according to reports.[18] Generally speaking, Aspergillus species can be found in moist soil, grain, cereal, mouldy flour, and organic waste that is decomposing or composting.[19] The most common cause of aspergillosis is spore inhalation, which can lead to bronchopulmonary aspergillosis, an infection of the upper and lower respiratory tracts. [20]

CLINICAL FEATURES

The paranasal sinuses, larynx, eyes, ears, or oral cavity can all be sites of primary aspergillosis. Black or yellow necrotic tissue on an ulcer base over the palate or in the posterior tongue is the classic symptom of oral aspergillosis. Aspergillosis hyphae toxins aid in piercing the blood vessel wall and causing thrombosis, which results in necrosis and infarction. The organisms that cause aspergillosis grow centrifugally linearly before becoming ball-shaped aggregates. On radiographic examination, the mass's center, which includes calcium phosphate, is recognized as a foreign body. [21,22]

TREATMENT

When it comes to treating invasive sinus aspergillosis, surgery is crucial. Treating invasive aspergillosis also requires systemic pharmaceutical control of the disease. Itraconazole, caspofungin, voriconazole, and amphotericin B (AMB) all produced positive results in published cases. After surgery, local debridement with amphotericin B is used as an adjuvant therapy method. Reports in local debridement using amphotericin B, however, are scarce.[23]

CRYPTOCOCCOSIS

INTRODUCTION

The two main species that cause cryptococcal meningitis, which can be fatal, are Cryptoccocus gattii and C. neoformans. Although immunocompromised people are particularly susceptible, cryptococcal infections in immunocompetent hosts have also been documented.[24] Other special risk groups, including children, expectant mothers, people living in resource-constrained situations, and people infected with Cryptococcus gattii, have particular advice.[25]

CLINICAL FEATURES

For Cryptococcus, the respiratory system is the primary point of entrance. Life-threatening pneumonia with acute respiratory distress syndrome is one of the clinical symptoms of pulmonary cryptococcosis, as is asymptomatic colonization of the airways or a simple pulmonary nodule on a chest radiograph. Numerous symptoms, including headache, fever, cranial neuropathies, altered mental status, lethargy, memory loss, and indications of meningeal irritation, are clinical manifestations of CNS cryptococcosis. Patients may have a range of skin lesions as clinical symptoms of cryptococcosis. A skin sample with culture and histology is crucial for a conclusive diagnosis because lesions are frequently indistinguishable from those caused by other illnesses. The occurrence of cutaneous lesions typically signals the existence of a disseminated infection because primary cutaneous cryptococcosis is extremely uncommon and typically linked to skin damage and direct yeast inoculation.[26]

TREATMENT

AmBd dosages for treating paediatric cryptococcosis have been reported to range from 0.5 to 1 mg/kg daily.[27] Fluconazole is frequently the only therapeutic choice in situations where AmBd is not accessible or economical, where admission and IV therapy facilities are lacking, or when renal and potassium monitoring are not quick enough or dependable enough to permit the safe use of AmBd. It is essentially a fungistatic medication at doses up to 400 mg daily, and results are subpar, with a 10-week mortality rate of about 50%.[28,29] A successful response to HAART (defined as a CD4 T cell count ≥100 cells/uL and an undetectable or low viral load) should be followed by clinical monitoring for infection recurrence and serial monitoring of serum cryptococcal antigen and CD4 T cell counts if fluconazole maintenance therapy is stopped.[30]

HISTOPLASMOSIS

INTRODUCTION

Histoplasmosis, a profound systemic mycosis that is found all over the world and can afflict both immunocompetent and immunocompromised people, is caused by Histoplasma capsulatum. The primary mode of transmission for histoplasmosis is airborne. When H. capsulatum-contaminated soils are disturbed, microconidia are aerosolized and finally inhaled by the host.[31]

CLINICAL FEATURES

The tongue, palate, and/or buccal mucosa may develop ulcerative, erosive lesions as a result of the mucocutaneous type of histoplasmosis. In many cases of disseminated histoplasmosis, oral lesions are found. Acute pulmonary histoplasmosis might potentially present with oral symptoms. Rarely are isolated cases of oral histoplasmosis reported. When oral lesions are present, they manifest as isolated ulcerations of the oral mucosa that can be painful or painless and last for several weeks. Usually, oral ulcerations have hard, rolled edges that resemble cancerous growths.[9,31]

TREATMENT

Itraconazole (200 mg three times a day for three days and then 200 mg twice a day for a total of twelve weeks) is advised after lipid formulation of amphotericin B (3.0–5.0 mg/kg daily intravenously for one–two weeks) (A-III). For patients with a low risk of nephrotoxicity (A-III), the deoxycholate formulation of amphotericin B (0.7–1.0 mg/kg daily intravenously) is an option to a lipid formulation. During the first 1-2 weeks of antifungal medication, patients who experience respiratory problems, such as hypoxemia or severe respiratory distress, should receive 0.5-1.0 mg/kg intravenously of methylprednisolone (B-III).[32]

BLASTOMYCOSIS

INTRODUCTION

Blastomyces dermatitidis is a dimorphic fungus that causes pyogranulomatous infections like blastomycosis. Inhaled Blastomyces conidia cause a primary lung infection. Nonetheless, lymphohematogenous spread to the genitourinary system, skin, and bones and joints might result in dispersion. Osteomyelitis and arthritis are two clinical signs of bone infection.[33]

CLINICAL FEATURES

In the oral cavity, ulcerated lesions with a raised border and induration are the hallmark of disseminated blastomycosis. Because of its raised margins and induration, the lesion is mistaken for a carcinomatous region.[34]

TREATMENT

Depending on the severity of the condition, amphotericin B or itraconazole are two possible treatments for blastomycosis. Because itraconazole has fewer side effects, it is recommended for mild to moderate disease that does not impact the central nervous system. Systemic antifungal medication for a minimum of 12 months is advised for individuals with bone and joint blastomycosis.[35]

MUCORMYCOSIS

INTRODUCTION

A secondary opportunistic infection like mucormycosis, or black fungus, has been acquired by patients during COVID-19 due in large part to the sporadic use of steroids, supportive oxygen from cylinders, and ventilators (in critically ill patients). Angioinvasive mucormycosis is a serious fungal illness that quickly spreads to other body areas. Mucormycosis can have fatal consequences for those who are afflicted if it is not identified and treated in a timely manner.[36]

CLINICAL FEATURES

Mucormycosis manifests as facial puffiness, fever, headache, sinus or nasal congestion, and a black scratch on the nose or upper part of the mouth. Many physiological areas, including the brain, lungs, and sinuses, are impacted by mucormycosis.[37] The fungus has the capacity to physically and toxically harm the interior lamina of blood vessels, especially the veins, lymphatics, and arteries. Spores penetrate the sinuses, where they begin to germinate into many hyphae in immunocompromised people. Fungal hyphae are thought to be most abundant in the pterygopalatine fossa.[38]

TREATMENT

A starting dose of 5 mg/kg per day of liposomal AmB or L-AmB complex is advised. To manage the co-infection, the dosage may be increased to 10 mg/kg each day. Both oral and parenteral versions of the broad-spectrum azoles posaconazole and isavuconazole are very effective against mucormycosis. When a patient exhibits intolerance to AmB, posaconazole is used as a salvage treatment. In surgical treatment, sinuses are drained, and the orbital contents of the afflicted brain region may need to be removed. Excision of pulmonary lesions is carried out if they are limited to a single lobe in order to fully control pulmonary mucormycosis. While the GI undergoes the essential resection of GI tumors, cutaneous mucormycosis involves the excision of whole cutaneous lesions.[39]

GEOTRICHOSIS

INTRODUCTION

A common filamentous yeast-like fungus, Geotrichum candidum is found in human and other mammal digestive tracts, soil, air, water, milk, silage, and plant tissues. Cheese is frequently matured using this species as an auxiliary culture. In the genus Geotrichum, there are eighteen species.[40]

CLINICAL FEATURES

Palatal ulcerations, villous hyperplastic regions, or a white, velvety, patch-like pseudomembranous look are the hallmarks of oral mucosal geotrichosis. There have been twelve documented cases of oral geotrichosis linked to acute lymphocytic leukemia, Hodgkin's lymphoma, HIV infection, or non-insulin-dependent diabetic mellitus. When making a differential diagnosis for ulcerative presentations in immunocompromised patients, oral ulceration should be taken into account because it is a common sign of geotrichosis. However, a culture should be examined under a microscope to determine the presence of a geotrichosis infection.[34]

TREATMENT

Patients with disseminated disease, severe lung infection, CNS involvement, and underlying immunosuppression should be treated with polyene AmB formulations. Oral itraconazole can be prescribed as a capsule or a solution, however the way these formulations are administered is not the same. Itraconazole solution does not require stomach acidity to be absorbed, and it can be taken without regard to food. Voriconazole, posaconazole, and isavuconazole are among the most recent triazoles that exhibit efficacy against B. dermatitidis.[41]

RHINOSPORIDIOSIS

INTRODUCTION

The fungus Rhinosporidium seeberi is the cause of the chronic granulomatous infectious disease known as rhinosporidiosis. The most frequently affected areas are the nose and nasopharynx. The second most frequent location is ocular lesions, specifically those of the conjunctiva and lacrimal sac. Lips, mouth, uvula, maxillary antrum, epiglottis, larynx, trachea, bronchus, ear, scalp, vulva, penis, rectum, and skin are uncommon sites of involvement. In rare cases, spread infections that affect the limbs, trunk, viscera, and brain have also documented.[42]

CLINICAL FEATURES

15% of cases feature ocular lesions, especially those of the conjunctiva and lachrymal sac; 70% of cases involve the nose and nasopharynx, frequently in a unilateral form.
The disease's primary feature is the presence of a polypoidal, reddish, friable, painless, pedunculated, hyperplastic soft tissue mass in the nasal region; this mass usually develops slowly and chronically. The remaining cases that have been recorded relate to various locations and uncommon localizations, including the uvula, maxillary antrum, lips, palate, epiglottis, larynx, pharynx, and trachea/bronchi ear. It is uncommon for people without underlying immunocompromised conditions to have a disseminated sickness that simultaneously affects the limbs, trunk, internal organs, and even the brain. [43]

TREATMENT

In at least 90% of cases, surgically excising the lesion and cauterizing the attachment base is nearly curative. Due to the frequency of refractory patients, multiple methods are now being examined for the management of disseminated illness. Combinations of cycloserine, dapsone, and ketoconazole, among others, have shown promising clinical outcomes.[44,45]

TOXOPLASMOSIS

INTRODUCTION

The majority of toxoplasmosis infections occur orally, and the disease causes a variety of clinical symptoms, from retinochoroiditis and inflammatory bowel disease to meningoencephalitis. Direct food contact, such as eating raw or undercooked meat that contains parasite cysts, contracting the infection congenitally through the placenta, or contaminating soil or water with oocysts, can result in infection with Toxoplasma gondii.[46]

CLINICAL FEATURES

Acute illness symptoms include chills, fever, headaches, myalgia, lymphadenitis, and exhaustion; sometimes, these symptoms mimic those of infectious mononucleosis. Signs and symptoms of chronic disease include myocarditis, encephalomyelitis, hepatitis, lymphadenitis, and sometimes a rash. As is frequently observed in reactive hyperplasia, microscopic analysis shows persistent lymphadenitis with noticeable lymphoid hyperplasia. The lymph node is dotted with histiocytes that stain palely. [47]

TREATMENT

For at least six weeks and four to six weeks after the resolution of clinical signs and symptoms, pyrimethamine 200 mg is administered orally as a loading dose on the first day, followed by 50 mg once daily for patients under 60 kg and 75 mg once daily for those over 60 kg. Additionally, sulfadiazine 1,000 mg is administered orally four times a day for patients under 60 kg and 1,500 mg is administered orally four times a day for patients over 60 kg.[48]

LEISHMANIASIS

INTRODUCTION

Leishmania species are the cause of leishmaniasis, a neglected tropical illness that can present with a wide range of clinical symptoms, including cutaneous, visceral, and mucocutaneous presentations.[49]

CLINICAL FEATURES

Most frequently, mucosal diseases manifest as inflammatory nasal cavity enlargement or destructive ulceration. Typical "pizza lesion" on a patient's skin when they have cutaneous leishmaniasis. Giemsa-stained impression smear of a skin biopsy sample displaying many released amastigotes. Observe that the majority of amastigotes have a tiny rod-shaped kinetoplast and a big oval nucleus.[50]

TREATMENT

The antibiotic aminoglycoside paromomycin (formerly known as aminosidine) is effective against Leishmania and is available in parenteral and 15% topical forms. The combination of 15% paromomycin and 12% methylbenzethonium chloride has been utilized in topical formulations; after 20 days of application, it demonstrated 77% efficacy compared to 27% for a placebo; nevertheless, methylbenzethonium has been linked to significant irritability and intolerance.[51]

PARACOCCIDIOMYCOSIS

INTRODUCTION

Its exact natural history is unknown, but Paracoccidioides brasiliensis, a fungus found in the soil of some parts of Latin America, primarily between latitudes 23° and 34°, from Mexico in the north to Argentina in the south, is the cause of Paracoccidioidomycosis (Pmycosis, formerly known as Lutz' disease). Although P. brasiliensis is a dimorphic fungus, it only manifests in humans as yeast, which typically has a diameter of 2 to 10 mm, though cells as large as 30 mm are also sometimes seen. In its parasitic state, the main feature is the helm-like evagination of the mother cell wall, which creates young yeast. The image is likened to a "grenade" in scanning electron microscopy.

For mycelial (25°C) or yeast (37°C) expressions, temperature is crucial. The fungus has one or more nuclei and nucleoli, making it a eukaryote. Golgi and lysosomes are absent from the cytoplasm, but vacuoles, endoplasmic reticulum, and ribosomes are present. Young cells have many mitochondria, mostly in the periphery, and as cells age, the number of vacuoles rises. The double refractile wall of the cells is between 0.2 and 1 mm thick. Two layers are visible in the cell wall. The a-1-3-glucan in the yeast phase and the b-1-3-glucan in the mycelium create the electron-dense outer layer. In contrast to the cytoplasmic membrane, the thick, electron-lucent inner layer of the cell wall is made of chitin. [52]

CLINICAL FEATURES

The most common clinical signs of a lung infection include fever, lethargy, cough, and dyspnea. lung sequelae, including lung fibrosis, bullae, and pulmonary hypertension, are found in one-third of the patients. As previously stated, this reactivation might happen months or years after the initial infection. The most common symptom is pulmonary involvement. Except in youngsters, enlarged lymph nodes are uncommon. A hematogenous spread with mucous membrane involvement occurs in more than half of the cases; this typically involves laryngeal and pharyngeal lesions that cause stridor, dysphagia, dysphonia, and perioral granulomatous plaques. Loss of teeth can result from gingival involvement, which is common. Pharyngeal and nasal ulcers may be linked to distinctive erosions of the mouth that resemble mulberries (Aguiar-Pupo stomatitis). [53]

TREATMENT

Itraconazole's strong response rate makes it the preferred treatment for mild to moderate cases. 100–400 mg once daily is the suggested dosage range. Itraconazole is administered once daily to children at a dose of 5–10 mg/kg, with a maximum dosage of 200 mg.[54]

CONCLUSION

Oral fungal and protozoal infections may not occur frequently, but when they do occur, it is necessary to determine the underlying probable systemic illness and do an examination. To ascertain the disease burden of fungal infections, public and healthcare provider education and surveillance are required. Improved diagnostic procedures and therapies result in early diagnosis, which lowers morbidity and death.

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