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Review Article

ORAL FUNGAL INFECTIONS: A REVIEW

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ABSTRACT

With the change in the lifestyle of the humans, there is increase in the opportunistic infections, because increase in the immunocompromised diseases. Thus the importance of the oral fungal infections has increased during the last decades. The fungi are also components of the normal oral flora. Both yeasts and the filamentous types can cause infection of the different parts of the oral cavity such as palate, buccal mucosa, tongue and gingiva. It is important to study these fungal infections because dental practitioners can come across these fungal infections in their routine practice and if not treated, it can lead to fatal complications. This review discusses various fungal infections affecting the oral cavity.

Keywords: Fungi, Immunocompromised host, Oral cavity, Opportunistic infection.

INTRODUCTION

Fungi are eukaryotic unicellular or multicellular organisms, which causes various infections in man[1]. Human beings are usually exposed to many hundreds of the fungal spores daily. There are more than 100,000 known fungi, but only can cause the disease in human tissues[2]. Elevated temperature and the cellular immunity or the various pulmonary defense mechanism are the main barriers to grow fungi in humans. These fungi are common saprophytes decaying vegetation and soil, and person to person transmission is rare, but *Candida* is an exception[2,3]. In recent years, the common use of corticosteroids and antibacterial chemotherapeutics agents has contributed to the increased incidence of the fungal infections. It seems likely that almost every human being is infected by a fungus at least once in his life[4].

Fungi are eukaryotic Prostita; which differs from bacteria and other prokaryotes in having rigid cell walls containing chitin and other polysaccharides. The cytoplasmic membrane contains sterols, possesses true nuclei with nuclear membrane and paired chromosomes. They divide asexually, sexually or by both processes and they may be unicellular or multicellular. Fungi had been recognized as affecting humans since long ago. Fungal infections can be superficial infection to deep burrowing type of infection, which can be fatal[5].

There is less studies or the reviews to focus on the oral fungal infections, thus the present article has been planned to summarize the fungal infections of the oral cavity.

Classifications of fungi:

A. Depending on cell morphology[5]:

I. Yeasts: These are unicellular fungi which occur as spherical or ellipsoidal cells and reproduce by simple budding. On culture, they form smooth, creamy colonies and the only pathogenic yeast is *Cryptococcus neoformans.*

II. Yeast like fungi: They grow partly as yeast and partly as elongated cells resembling hyphae. The latter form a pseudomycelium. Example is *Candida albicans.*

III. Moulds or filamentous fungi: They forms true mycelia and reproduce by the formation of different types of spores.

IV. Dimorphic fungi: These can occur as filaments or as yeasts, depending on the condition of growth. In host tissue or culture at 37°C they occur as yeasts, while in the soil and in culture at 22°C they appear as moulds. Most fungi causing systemic infections belong to dimorphic fungi.

B. Depending on their sexual spore formation[2]:

I. *Phycomycetes:* These are lower fungi which have nonseptate hyphae. They form endogenous asexual

spores, called *sporangiospores*, contained within swollen sac like structure called sporangia.

II. *Ascomycetes:* They form sexual spores (ascospores) within a sac or ascus. Ascomycetes include both yeast and filamentous fungi.

III. *Basidiomycetes:* These forms sexual spores (*basidiospores*) on a basidium or base.

IV. *Fungi imperfecti* (deuteromycetes or hyphomycetes): It consisting of fungi whose sexual phases have not been identified. Most fungi of medical importance belong to this group.

The last three classes of higher fungi have septate hyphae and form exogenous asexual spores called 'conidia'[2].

Fungal diseases:

- Fungal diseases usually caused by specific organism (Table 1) and various predisposing factors are responsible to increase its severity[1,2,7](Table 2).
- Can be divided into 3 groups; cutaneous, subcutaneous and the deep or systemic fungal diseases[8,9].
- Fungi causing superficial mycoses are normally parasite of humans and animals[1,8,9].
- Fungi causing subcutaneous and deep mycoses are believed to live normally as saprophytes in nature and are less well adapted for a parasitic role[1,9].
- The superficial mycoses have incubation period relatively short, the onset of disease is sudden and the symptoms are initially severe but decrease in severity with time, so that spontaneous healing may occur[4,8].
- Deep mycoses, on the other hand, have a protracted incubation period, the symptoms are insidious in their onset, and the course of disease becomes increasingly severe[4].

Table 1: Fungal infections of the oral cavity and etiological agent

Fungal infection	Etiological agent
Candidiasis	*C. albicans, C. tropicalis, C. glabrata, C. parapsilosis, C. krusei, C. kyfer, C. dubliniensis*
Aspergillosis	*Aspergillus fumigatus*
Zygomycosis	*Orders Mucorales and Entomophthorales*
Paracoccidiomycosis	*Paracoccidioides brasiliensis*
Coccidioidomycosis	*Coccidioides immitis*
Cryptococcosis	*Cryptococcus neoformans*
Histoplasmosis	*Histoplasma capsulatum*
Blastomycosis	*Blastomyces dermatitidis*
Penicilliosis	*Penicillium marneffei*
Sporotrichosis	*Sporothrix schenckii*
Geotrichosis	*Geotrichum candidum*

Table 2: Various predisposing factors[1,6,7]:

Predisposing factors
Nutritional deficiency
Use of steroids
Broad spectrum antibiotics
Extremes of age
Wearing of denture
Dry mouth
Patients with HIV infection
Systemic diseases like diabetes mellitus, hypothyroidism, hypoparathyroidism, addison's disease, sjogren's syndrome, etc.
Malignancy and cancer therapy
Other factors like cigarette smoking.

Fungal infections of the oral cavity:

Candidiasis:

These are the inhabitants of the normal flora of the oral and the gastrointestinal tract and they can be recovered from one third of the oral cavities of normal humans[6].

C. albicans is the predominant species associated with human oral mycoses and is the most virulent among pathogenic Candida species. The possible factors in the pathogenesis of candidiasis are the abilities of *C. albicans* to transform from blastospore to the hyphal phase and to form germ tubes, which mark the onset of hyphal growth of *C. albicans*[7].

The other species of Candida besides C. albicans encountered in human infections are *C. tropicalis, C. glabrata, C. parapsilosis, C. guillermondii, C. krusei* and *C. kyfer* and more recently *C. dubliniensis*[7].

Aspergillosis:

It is a ubiquitous organism and can be found in soil and in decaying vegetation. Mostly, it do not grow at normal human

body temperature, but only the pathogenic species have the ability to do so and it does not usually cause disease in the immunocompromised individuals. In 1994, Rowe Jones classified aspergillosis into three chief variants: Invasive, non-invasive and non-invasive destructive type[3,7,10].

Aspergillosis is the second most common opportunistic fungal infection after candidiasis. Aspergillosis fungus invades blood vessels, causing thrombosis and infarction of surrounding tissue or it invades the sinuses[7].

Mucosal soft tissue swellings and painful gingival ulcerations with gray or violaceous are the oral lesions. It can present clinically as a yellow or black ulcer with facial swelling. under the microscope, numerous small round to oval bodies which surrounded by a space, are seen within macrophages. Special staining with PAS or Gomori's methenamine can be performed to enhance the visulization[2,7].

Zygomycosis:

Two orders are of clinical concern: *Mucorales* and *Entomophthorales*. Zygomycoses are caused by saprophytic filamentous fungi, which grow rapidly and are widely distributed in nature. They are commonly considered to be opportunistic pathogens. Their incidence shows increase in diabetic subjects and in those receiving immunosuppressive therapies[11].

Disease onset occurs after inhaling a high infective dose of spores, which is initially localized in the paranasal sinuses, but can lead to a fatal outcome after spreading to the brain. Microscopically, it shows the large hyphae (5-50 *u*m), irregular in width and branching at right angles but not septate. They look like hollow tubes[2,11-13].

Paracoccidiodomycosis

It is caused by *Paracoccidioides brasiliensis*, which is found in soils of certain areas of South and Central America. It is a dimorphic fungi, and in human tissues presents only in the yeast form, usually 2-10 *u*m in diameter. Most accepted mechanism of contamination is inhalation of the conidium form of the fungus and transformation in yeast in the tissues, with a primary infection of the lungs and dissemination via lymphatic and blood vessels. There are no evidences of human to human transmission[2,14].

Erythematous finely granular hyperplasia is seen in oral lesions. Speckled with pinpoint hemorrhages, and a mulberry like surface ("moriforme" stomatitis) are frequently seen. Areas of ulcerations are common and usually the oral lesions are multiple, involving the lip, gingiva, buccal mucosa, palate, tongue and floor of the mouth[2,14].

Coccidioidomycosis:

Coccidioidomycosis is caused by Coccidioides immitis. It was once confined to the Western hemisphere but is now virtually seen anywhere in the world. Oral lesions are uncommon and have been described as ulcerated granulomatous nodules. Clinically the ulcers appear nonspecific and usually heal by hyalinization and scar. Diagnosis is by history and examination supported by histology[7].

Cryptococcosis:

Cryptococcosis is acquired by inhalation of spores mainly of *Cryptococcus neoformans* found in soil, especially excreta of birds like pigeons, canaries, parrots, and rotting fruit and vegetables. The most important lesions are in the lungs and meninges[2].

Microscopically it shows cystic areas and yeasts surrounded by a prominent halo of a gelatinous material from polysaccharide of the capsule. Absence of inflammation is typical. In H&E staining, *C. neoformans* appears as bubbles and PAS and Gomori stains the fungus, but not the capsule, and a halo is seen. The 4 to 6 um fungus with 3-5 um mucinous capsule, can be identified by mucicarmin and confirmed by immunostaining[2,15].

Sporotrichosis:

It is caused by fungus *Sporothrix schenckii,* which is found in soil, moss and rotting wood. Its incidence is higher among agricultural workers, florists and miners than the general population. Erythematous, ulcerative, suppurative, granulomatous, vegetative or papillomatous oral lesions can be seen. The oral lesions are usually painful and heal without scarring[7]. Histology and cultures are valuable in confirming the diagnosis. Since the parasitic yeast form of this fungus is difficult to observe under microscope, isolation in mycological media still remains the gold standard diagnostic method[7].

Histoplasmosis:

Histoplasmosis occurs in all parts of the world and is seen as small, 1-5um yeast cells. It is found as mold in nature, and the conidia can be inhaled from soil or dust contaminated with bird or bat faeces.[2,16] Histoplasmosis resembles tuberculosis in many aspects and it can spread via blood, with involvement of the mononuclear phagocytic system[2,16].

Geotrichosis:

It is caused by *Geotrichum candidium,* which is a component of the normal microflora of the skin and the mucosa of the respiratory and digestive tracts. It can also be isolated from vegetables, fruits, soil and plants. Oral lesions are usually caused by *G. candidum* and *G. capitatum*[3].

Saccharomyces infection:

It is a commensal inhabiting the gastrointestinal tract of humans, which has an important role in maintaining the normal homeostasis of the lower gastrointestinal tract. Intra-oral manifestations include ulcers with associated painful swallowing, dry mouth and burning sensation. Direct Gram stain from the swab will show majority of Gram-positive budding yeast cells and the culture will give creamy white yeast like growth[3].

Fusariosis

It presents as a necrotic ulceration of the gingiva, extending to the alveolar bone[3].

Penicilliosis:

It is caused by *Penicillium marneffei* which can cause fatal infection in HIV infected individuals.[3] Oral lesions include papules, erosions or shallow ulcers covered by yellow necrotic slough which are mainly seen on the palate, gingiva, labial mucosa, tongue and oropharynx[3].

CONCLUSION

Most of the fungi are the opportunistic infections and they show increased tendency for diseased condition in case of immunocompromised individuals. The outcome of fungal infection depends on various etiological and predisposing

factors, which can sometimes be fatal. Therefore prevention of the transmission of fungal infections is very important. Thus it is the responsibility of the dental practitioner to identify the disease in its early state, so that it can be very beneficial to the patient.

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