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Dematiaceous Fungi Causing Human Mycoses. General Considerations

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Abstract:

Mycoses caused by dematiaceous fungi originate from contact of the fungus through the skin in a traumatic way. Dematiaceous fungi belong to a varied group of microorganisms characterized by the presence of melanin in their wall, which gives rise to macroscopically observing dark colonies on the reverse and obverse and microscopically observing fumaroid cells or Medlar cells. The objective of this research is to analyze the updated scientific information on dematiaceous fungi that cause mycoses in humans. To acquire bibliography, a search was carried out in SciELO, PubMed, Google Scholar and repositories of doctoral theses, for articles in English and Spanish, published in the last 5 years (2019-2024). Priority was given to high-impact journal articles, review and research articles. Search terms included "mycoses," "dematiaceous fungi," "*fungemias*," "oportunistic infections", "infectious diseases".

Keywords: *Dematiaceous Fungi; Mycoses; Infectious Diseases*

Introduction

Dematiaceous fungi belong to a heterogeneous group of microorganisms, characterized by septate hyphae or yeast-like elements with a dark wall. They are fungi widely distributed in nature, located in soil, wood and decomposing plant matter. They are characterized by the production of spores resistant to environmental changes in temperature, humidity, heat and desiccation. They are transmitted through splinters or thorns of contaminated plant material, although inhalation is also possible. Due to the presence of melanin, macroscopically they generate dark colonies, both on the front and back, and microscopically, the fungal elements are observed with a dark wall. It is believed that melanin may be an important virulence factor in the pathogenesis of the infection caused by these fungi since it confers on the fungal cell: protection against the attack of free radicals produced by phagocytic cells (host defense mechanism); has the ability to bind to hydrolytic enzymes, providing protection to the plasma membrane and reducing the action of some antifungals. Micosis hongos dematiáceos [1, 2].

Dematiaceous fungi produce a wide spectrum of infections, including: cutaneous and subcutaneous infections, allergic diseases, pneumonia, brain abscesses or disseminated infections [3].

These fungi can cause disease in immunocompetent people; however, serious infections occur in immunosuppressed patients and are not included in defined clinical conditions. There are more than 57 genera and 104 species that cause infections in humans [4].

In 1988, Fader et al. classified infections caused by dematiaceous fungi into three categories: *chromoblastomycosis*, *pheohyphomycosis* and mycetoma. Currently there is no consensus, but a simple and practical way is recommended by Bonifaz, which classifies it into four categories: superficial, subcutaneous, cerebral and disseminated or systemic [5, 6].

Development

Phaeohyphomycets

Phaeohyphomycetes come from the order Chaetothyriales, as well as from different divisions or Phyla such as Ascomycetes and Basidiomycetes. They are ubiquitous and pollutants of soil, air, water and wood pulp. Pheohyphomycosis are infections caused by black dematiaceous or pheohyphomycete fungi. Pheohyphomycosis has a worldwide distribution; however, cutaneous cases are more frequently found in tropical and subtropical climates.

Etiological agents

Bipolaris spp, Curvularia spp, Exserohilum spp, Hortaea werneckii, Piedraia hortae, Neoscytalidium dimidiatum, Scytalidium hyalinum, Cladophialophora bantiana, Exophiala spinifera, Exophiala jeanselmei, Alternaria alternata, Bipolaris spicifera, Veronaea botryosa, Exophiala dermatitidis, Cladosporium cladosporioides, Rhinocladiella mackenziei, Alternaria spp, Exophiala spp, Scedosporium prolifians, Bipolaris spicifera [7].

Cladophialophora Bantiana

It is a filamentous fungus (mold) belonging to the species *Ascomycota*, order *Chaetothyriales*, of the family *Herpotrichiellaceae*. This fungus has been known by several scientific names since its discovery, which are now considered synonyms: *Cladosporium bantianum, Cladosporium trichoides* and *Xylohypha bantiana*. Its habitat is limited to soil and organic matter in a state of decomposition, and it is saprophytic and thermotolerant (43°C), with asexual reproduction by unicellular conidia. Its distribution is cosmopolitan, especially in subtropical, tropical and neotropical climates. *C. bantiana* has clinical importance and is neurotropic, causing cerebral *pheohyphomycosis*. Agricultural work can cause greater susceptibility tocontracting fungal infection through interaction with plants, soil or other surfaces where *C. bantiana* spores are present. Fungal infection with *C. bantiana* can infect both immunocompromised and immunocompetent patients, and in both cases it can cause death [8].

Exophiala dermatitidis

Exophiala belongs to the *Ascomycotina* order *Chaetothyriales*. The taxonomic classification of E. dermatitidis has undergone revisions over time, and it is currently classifed under the genera Exophiala, formerly known as *Wangiella*.

E. dermatitidis exhibits distinct characteristics, among others, the melanized and thick cell walls, being responsible for high resistances to environmental stress, including temperature and

salt concentrations, and the capability to switch between conidial and hyphal forms. The presence of melanin in the cell wall contributes to the fungus's virulence and enhances its resistance to host defense mechanisms and antifungal treatments. In nature, E. dermatitidis is ubiquitously distributed in various environments, including extreme natural habitats, hydrocarbon-rich artificial settings like steam baths and bathrooms, decaying organic matter, and even dishwashers. It is suggested that the natural habitat of E. dermatitidis is the warm and wet tropics, as E. dermatitidis is regularly found in environments with high temperatures, high humidity and pH changes. One potential transmission route for E. dermatitidis is through aerosol inhalation from household dishwashers, although household-acquired colonization seems to be rare and predominantly observed in individuals with conditions such as Cystic Fibrosis (CF) or immunosuppression. E. dermatitidis rarely acts as the primary causative agent of fungal infections affecting immunocompromised individuals. E. dermatitidis has been described to cause invasive infections of the central nervous system, cutaneous and superficial infections in humans [9].

Neoscytalidium dimidiatum (Scytalidium dimidiatum, Nattrassia mangiferae, Hendersonula toruloidea).

N. dimidiatum is a dematiaceous fungus, soil saprotrophic and a potential phytopathogen, causing diseases in woody plants. It is located in tropical and semitropical areas, such as South America, Southeast Asia, India, the Caribbean and West Africa. In temperate zones it appears in immigrants from endemic areas. Due to its thermotolerance (420C maximum temp.) it can cause opportunistic and superficial lesions in humans, whether in nails, palmoplantar areas and interdigital regions [10, 11].

Invasive infections due to *Neoscytalidium dimidiatum* appear in immunocompromised individuals, and subcutaneous infections, abscesses, *mycetomas,* invasive sinusitis and fungemia and disseminated infections have been described in neutropenic patients [12, 13].

Morphology

The hyphae of *N. dimidiatum* are sinuous, with variable and non-uniform width. Occasionally, pigmented hyphae and even accumulations of brown arthroconidia can be found in the nail material. Superficial and deep infections caused by *N. dimidiatum* require culture in non-inhibitory media for diagnosis; such as Sabouraud agar with chloramphenicol [14, 15].

Chromomycosis

Chromoblastomycosis, also known as *chromomycosis*, is a rare, chronic subcutaneous infection of fungal origin, caused by trauma and inoculation of dematiaceous fungi (*Fonsecaea pedrosoi, Phialophora-verrucosa, Cladophialophora carrionii,* among others). Taxonomically, these groups of fungi is classified in the class *Ascomycetes*, order *Chaetothyriales*, family *Herpotrichiellaceae* and it's characterized by presenting thick, colored multicellular microscopic structures, called muriform or fumaroid bodies. It affects the skin and subcutaneous cellular tissue in the lower extremities, especially the feet, and it's characterized by verrucous, nodular or atrophic lesions that are difficult to treat. It frequently remains located in one of the lower extremities; have been described in rare cases of central nervous system infections, whether or not associated with skin lesions [16].

F. pedrosoi predominates in tropical and humid areas; while *C. carrionii* is reported more frequently in dry and semi-arid areas. On the other hand, the less common species are *P. verrucosa*, R. aquaspersa, E. dermatitidis and *F. monophora*. The 70% of registered cases come from tropical and subtropical areas [17].

Fungal Morphology

The colonies are velvety on the surface, taking on a dark brown or black color. The samples taken from the lesions present conidia, the cells are spherical that measure 4 to 12 µm in diameter, and are called muriform or sclerotic bodies. Its division occurs by transverse partitioning; while, in samples of exudate or scabs, their cells usually germinate, giving rise to branched and septate hyphae. The colonies of Fonsecaea pedrosoi are black-olive velvety with a flattened surface, developing brown, oval-shaped conidia. They measure around 1.5–3 x 3–6µm, their chains are short, with thin and smooth walls. *Cladophialophora carrionii* develops small colonies, olive to black in color with a hairy surface, its microscopic characteristics are long conidiophores, of an olive green hue, and may present branches, its endings are composed of conidia that measure around 1.5-3 x 2 -7µm in size. Exophiala dermatitidis has a similarity to yeasts until it forms ovoid hyphae of olive-gray color, they have branches and at their ends they form round conidia, 2-4 x 2.5-6µm. Phialophora verrucosa has dark gray colonies with a chamois appearance, while its hyphae are elliptical brown, bent like necklaces and its conidia adopt the shape of a cup. Rhinocladiella aquaspersa its strains are velvety dark green. The conidiophores are straight with thick walls, do not have branches and the conidia are ellipsoidal to claviform, brown in color [18].

Mycetoma

It is a chronic, infectious disease of the skin and underlying tissues caused by fungi (eumycetoma) or bacteria (actinomycetoma). It mainly affects men between the third and fourth decade of life, being common in farmers and individuals who carry out outdoor activities. The route of entry of the organism into the host usually occurs through penetrating trauma. It affects any part of the body, mainly the lower extremities. The clinical picture presents a triad consisting of increased volume, deformity of the anatomical area and fistulas that drain a thready exudate with the presence of "pimples". The diagnosis and determination of the etiological agent is carried out with direct analysis and culture of the secretion [19, 20].

The characteristic habitat of the causal microorganisms is found in areas with a subtropical or dry tropical climate, with well-defined rainy seasons, whose rainfall ranges from 500 to 1,000 mm and temperatures between 20 and 40°C, a climatic situation that is parallel between India, Africa and Mexico. This disease has been reported in 102 countries, and its distribution depends on the geographic and climatological conditions of the region. It predominates in a transverse band known as the Mycetoma Belt, which includes Sudan, Somalia, Senegal, Mexico, Venezuela, India, Mauritania, Chad, Ethiopia, Yemen and part of Colombia. In 2013, during its 69th Assembly, the World Health Organization (WHO) included this condition among the 17 most neglected tropical diseases, with low cure rates and priority attention [21, 22].

Etiology

Actinomycotic mycetoma: caused by aerobic bacteria of the actinomycetales group, such as:

Nocardia brasiliensis, Nocardia caviae, Nocardia asteroides, Streptomyces pelletieri, Stretomyces somaliensis, Actinomaduraadurae. These microorganisms in culture can resemble true fungi, both microscopically and macroscopically, but have bacterial cellular characteristics. Among them, the prokaryocyticcellular organization and the lack of a nuclear membrane stand out; their cell walls lack the chitin and glucans found in those of fungal cells.The reproduction is carried out by fission, neverthrough spores or budding, and its growth is inhibited by antibacterials. Nocardia brasiliensis is the most common causal agent in most endemic regions.

Eumycotic or Maduromycotic mycetoma: Eumycetomas are in turn produced by two types of septated filamentous fungi: black fungi (pheohyphomycetes of the type Madurella spp) and white hyaline fungi (*hyalohyphomycetes of the type Pseudallescheria spp, Acremonium spp, Fusarium spp*. or even *Aspergillus spp. or dermatophytes*). Although at least 41 species of fungi are included in these processes, worldwide more than 90% of them are associated with fo1.ur etiological agents: Madurella mycetomatis, Madurella (Trematosphaeria) grisea, Pseudallescheria (Scedosporium) boydii a2n. d Leptophaeria (Falciformispora). senegalensis.

Multiple other species, among which those of the genera Phialemonium spp, Fusarium sp3.p, Pyrenchaeta romeroi, Neotestundia rosatti, Cephalosporium corda and Phialophora jeanselmei, have been described as causes of this entity, although much less frequently [23] importance; they affect certain risk groups, which can progress to severity, with great impact on immunocompromised patients. It is common that difficulties arise when it comes to early diagnosis, due to the influence of certain factors in relation to the host. These fungi are widely distributed in nature and in some cases infected people may be far from medical care or use natural treatments that possibly relieve symptoms but do not affect the progression of the disease. It is advisable to establish a multidisciplinary consultation for diagnosis and treatment. The management of this infection must begin from the perspective of the general practitioner in Primary Care, who mostly detects these cases, their corresponding management by the Dermatology service which includes consultation with the Radiology services, Pathological Anatomy, laboratories of Microbiology and Clinical Laboratory to know the patient's condition, the degree of depth of the lesion and its ramifications and the surgery specialty valoration to effectively complement the treatment of these infections.

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