DOWNLOAD PDF 14 DEMATIACEOUS FUNGI

Chapter 1 : A Resident's Fungal Morphology

The dematiaceous fungi contain melanin in their cell wall which causes the dark, brown pigmentation of the hyphae. Melanin is resistant to factors the host cell uses to defend itself such as the oxidative burst by phagocytic cells, hydrolytic enzymes, and antifungal [7].

DISCUSSION Infections caused by dematiaceous fungi have a great variety of clinical manifestations, represented clinically on the skin as phaeohyphomycosis, chromoblastomycosis and eumycotic mycetoma. Allergic diseases may occur such as fungal sinusites apart from pneumonia and lung abscess. The genus Exophiala is composed of dimorphic fungi. The yeast colonies are of brown or black color and dry aspect4. Optical microscopy showed dark yest cells, septate and branched hyphae or hyphae formed by chains of spherical cells moniliform or muriform hyphae with abundant buds and annelid conidiogenesis, unicellular, rarely septate, hyaline or dark. They were farmers that presented risk factors for the traumatic inoculation of these fungi. The immunosuppression condition verified in one of them that develops fungal infection and its occurrence is increasing due to a increasing population of patients with secondary immune deficiency. The clinical presentation of the disease, in our patients, was classic and considered as: Sabbaga et al describe four patients who had had a renal transplantation and developed phaeohyphomycosis caused by Exophiala jeanselmei and who had had good results after surgical excision, as our patient. Bone invasion suggests an advanced disease, refractory to inadequate therapeutics that had been used for 20 years, progressing to limb amputation. This microorganism, usually of low virulence, presents itself clinically and of importance when the host is exposed to its risk factor, in the cases decribed, the inoculation and the immunosuppression. Three patients had results of culture with Exophiala jeanselmei, while the fourth had Exophiala sp, coinciding with the literature that cites Exophiala jeanselmei as the dominant species followed by E. As for phaehyphomycosis, surgical excision is the most frequent procedure and it was carried out with success, without evidence of recurrence. The patient with mycetoma underwent a left lower limb amputation due to the refractoriness of the case to the medications used, a common fact concerning mycetomas. The analysis of these cases shows us that the clinical aspect of the infections caused by dematiaceous, in special from the Exophiala genus, is broad and recquires different procedures. The members of this genus is present in vitro and has a high degree of phenotypic plasticity as the fragment of tissue from skin lesions is rarely cultivated. Early diagnosis is primordial despite the chronicity and long evolution of these diseases. Its infiltrative feature is capable of leading to sequelae and amputations. There is no consensus yet regarding the treatment of subcutaneous fungal diseases and there are few clinical trials comparing different drugs. On the other hand, research indicates practicality in the in vitro susceptibility test of each causal agent with certain drugs13 that would provide a more targeted and effective treatment. It is noteworthy that educational measures in health are important to minimize the damage and injuries of such infections. Silveira F, Nucci M. Emergence of Black moulds in fungal disease: Curr Opin Infect Dis. Spectrum of clinically relevant Exophiala species in the united states. The Black yeast as disease agents: Subcutaneous phaeohyphomycosis by Exophiala jeanselmei in a cardiac transplant recipient. Infect Dis Clin N Am.

Chapter 2 : Dematiaceous fungi - 5

Dematiaceous or darkly pigmented fungi comprise a large, heterogeneous group of organisms that have been associated with a variety of clinical syndromes. These are uncommon causes of human disease, but can be responsible for life-threatening infections in both immunocompromised and immunocompetent individuals.

Many fungi causing human or animal infections belonging to this group are pale brown, dark brown or black. Clinical specimens obtained from the patients having fungal infections are processed for culture as well as examined under the microscope after staining appropriately by fungal stains. The fungal elements present in the direct smear of the clinical specimen are also examined for the presence of dark pigment in the fungal cell wall. Dark pigmented cell wall classifies fungus in dematiaceous group. In the absence of dark pigment in the cell wall of fungal elements, the structure of the fungal elements may provide some clues that a dark fungus may be involved. In this case, the direct smear prepared from the clinical specimen is stained by a special stain called Fontana Masson FM to observe melanin pigment in the fungal cell walls. Many fungi from this group are responsible for causing opportunistic infections local or systemic in a variety of patients especially the immunocompromised hosts. There are unique terms Chromoblastomycosis and Phaeohyphomycosis used for the dark pigmented fungi, indicating the site specificity of certain fungi causing infections in patients infected by dark pigmented fungi. Click circular thumbnails for larger images and descriptions. Brain Biopsy Ramichloridium mackenziei Wound Swab Fungi producing olive-grey, brown or black melanin pigment in the cell wall of fungal hyphae or conidia are classified as dematiaceous dark fungi. Most fungi in dematiaceous group produce grey to dark color from the very beginning as they first appear on culture media. However, some dark fungi may start off as white and pale at first, turning darker upon further incubation. Fungi producing conidia enclosed within brown to dark colored round bodies such as pycnidia or producing sexual spores in ascocarp are not included among dematiaceous group. In clinical microbiology laboratory, simple tests such as Gram stain and wet preparation may be very useful to suspect dark fungi during direct microscopic examination of the clinical specimen. Many times the shape of the fungal elements showing pale to dark boundary of the cell wall may indicate the presence of a dark fungus in the clinical specimen. It is important to demonstrate melanin pigment in suspected fungi and must be confirmed by a specific melanin stain such as Fontana Masson FM. Early detection of phaeohyphomycotic agent present in the clinical specimen may provide relevant information to the clinician to select appropriate antifungal therapy for the patient. Figure 1 Fungal elements observed in abscess aspirate stained by Fungi Fluor FF x are septate in nature. Fluorescent stain is not suitable to show pigment in the fungal cell wall. The smear was observed under the bright field by switching off the UV filter and turning on white light. Figure 2 The structures observed in wet preparation x under the bright field showing fungal elements as pale and not hyaline in nature. Figure 3 Gram smear x of abscess aspirate showing oval cells in chains. Pseudohyphae looking structures often found in clinical specimens containing dark fungi personal experience. Cell wall of fungal elements is some what prominent and darker. However, not all dark fungi present in the specimen display dark cell wall. Figure 4 Dark fungi suspected by routine staining procedures must be confirmed by special melanin stain known as Fontana Masson FM. In the image FM x morphology of the fungal elements remains similar to Gram stain. The cell wall is darker, confirms dematiaceous fungus involved. Not all fungi showing pale darker cell wall in Wet Prep or Gram stain are true dematiaceous. This darkness does not confirm the presence of melanin pigment since the end point of GMS is to stain all fungi as dark. This fact is proven in this example that Fig. The fungus in question is not dark in nature. This fungus was identified as Aspergillus terreus that belongs to hyaline group. Figure 5 Figure 7 Figure 8 Some dark fungi do not display dark cell wall in Gram stained smear. Such fungi may be suspected as dark by morphology and confirmed by melanin stain. However, morphology of the filamentous form appears to be different and not fitting into pseudohyphae or hyaline septate hyphae categories.

Chapter 3 : Filamentous Fungi

Dematiaceous Fungi The term "dematiaceous" refers to the characteristic dark appearance of this group of fungi as it grows on agar. Colonies are dark gray, brown, or black and, importantly, have a black reverse when the bottom of the agar plate is examined.

There are no patents, products in development or marketed products to declare. Conceived and designed the experiments: Received Jan 12; Accepted Jul This article has been cited by other articles in PMC. Abstract Dematiaceous fungi black fungi are a heterogeneous group of fungi present in diverse environments worldwide. Many species in this group are known to cause allergic reactions and potentially fatal diseases in humans and animals, especially in tropical and subtropical climates. This study represents the first survey of dematiaceous fungi in Malaysia and provides observations on their diversity as well as in vitro response to antifungal drugs. Seventy-five strains isolated from various clinical specimens were identified by morphology as well as an internal transcribed spacer ITS -based phylogenetic analysis. The combined molecular and conventional approach enabled the identification of three classes of the Ascomycota phylum and 16 genera, the most common being Cladosporium, Cochliobolus and Neoscytalidium. Several of the species identified have not been associated before with human infections. Fluconazole appeared to be the least effective with only Overall, almost half Introduction Dematiaceous fungi are a heterogeneous group of fungi with dark colonies and pigmented fungal elements. They are typically soil saprophytes, plant pathogens, and laboratory contaminants with a worldwide distribution in humid environments. Until , more than species from 70 genera have been recorded to be associated with infections in humans and animals [1] , a vast increase from the 59 species belonging to 28 genera reported in by Rossmann et al. The genera most frequently involved in human infections include Bipolaris, Curvularia, Exserohilum, and Alternaria [3]. Many of the fungi are common allergens growing indoors. Besides causing hypersensitivity reactions in susceptible individuals that sometimes lead to acute exacerbation of asthma, they are also important opportunistic pathogens in immunocompromised patients [4] , [5]. Although many of the cutaneous, subcutaneous, and corneal infections associated with dematiaceous fungi have been reported to be common in tropical and subtropical countries [6] , to our knowledge, there has not been any extensive report on the diversity and in vitro antifungal susceptibility patterns of dematiaceous fungi isolated from clinical samples in a tropical country like Malaysia. The spectrum of diseases associated with dematiaceous fungi ranges from superficial skin and soft tissue infections to disseminated sepsis with high mortality. The most common infections are phaeohyphomycosis [7] , chromoblastomycosis [8] , and eumycetoma [9] , [10]. In a retrospective analysis of cases of central nervous system CNS phaeohyphomycosis, over half occurred in immunocompetent patients [11]. Chromoblastomycosis is mainly associated with Fonsecaea, Phialophora, Cladosporium, Exophiala and Rhinocladiella species [8]. Eumycetoma is caused primarily by Madurella mycetomatis, but the aetiological agents of this disease vary with geographical regions [9]. In the tropics, Curvularia species are significant causes of fungal keratitis associated with trauma from fungus-contaminated plant materials [12] , [13] while the Bipolaris, Curvularia, Exserohilum, Alternaria and Drechslera are frequently reported to be involved in invasive sinusitis [14] â€” [17]. Systemic dematiaceous fungal infections are rare compared to systemic candidiasis and aspergillosis. However, dematiaceous fungi are being increasingly recognized as invasive human pathogens [18] especially in organ transplant recipients [7]. The identification of dematiaceous fungi is traditionally based on the observation of differentiating morphological structures such as annellides or phialides, the presence or absence of collarettes on adelophialides, the differentiation of conidiophores, and septation of macroconidia. Molecular tests that are available today offer an alternative approach to the identification of dematiaceous fungi [19] , [20]. The molecular test strategy most often used is DNA amplification, followed by sequence analysis of variable regions within pan-fungal conserved genes 18S rRNA, 5. In the past decade, the ITS The aim of this study was to appraise the diversity of dematiaceous fungi isolated from patients with signs and symptoms of fungal infection and the antifungal drug susceptibility profiles of these isolates. The information from this survey could be useful for the formulation of appropriate

drug therapy for patients with suspected fungal infections in a tropical setting. Materials and Methods Ethics Statement This study involved only the phenotypic and phylogenetic analysis of dematiaceous fungi isolated from routine cultures in the mycology laboratory. Skin scrapings and nail clippings were collected from patients with suspected dermatomycosis. Respiratory specimens were routinely screened for fungal pathogens in patients presenting with respiratory tract infection. Other tissue fluids and tissues were processed for fungal isolation only on request by physicians when patients had clinical manifestations of fungal infection. Positive blood samples were sub-cultured onto SDA with chloramphenicol and sheep blood agar. Swabs and nasopharyngeal secretions were inoculated directly onto SDA with chloramphenicol and sheep blood agar. When mixed colonies were observed, each colony type was sub-cultured for purity. Each fungal culture was observed macroscopically for colonial characteristics such as colour, texture, and topology. Tease mounts and slide cultures were carried out to study the arrangement of conidia under the light microscope. The slides were examined periodically, with lactophenol cotton blue staining carried out when sufficient growth was attained. The suspension was then collected into a 15 mL centrifuge tube with PBS washed glass beads and vortex-mixed for 5 min. Cleaned sequences with complete ITS The sequences obtained in this study were deposited in GenBank under accession numbers shown in Table S1. To avoid false identification due to the errors deposited in NCBI GenBank database, we collected the top five hits from the blast results. ITS sequences of all species collected were then randomly mined from the NCBI GenBank for their complete ITS sequences with at least two sequences verified for each species, except when there was only one record in the database. Phylogenetic Analysis All ITS sequences from clinical isolates, together with those retrieved from the NCBI database and two out-group strains of Saccharomyces boulardii, were subjected to phylogenetic analysis. Multiple sequence alignment of all data mined ITS sequences was generated using M-Coffee [29] which adopted other packages to compute the alignments and used T-Coffee to combine all these alignments into one unique final alignment. Phylogenetic analysis was then performed using MrBayes [30]. A total of , generations were run with a sampling frequency of , and diagnostics were calculated every 1, generations. The antifungal drugs tested in this study were amphotericin B AMB , five azoles, viz. These isolates were mostly obtained from superficial skin, nail, subcutaneous and nasopharyngeal specimens 62 , blood 10 , and tissue biopsies 3 Table S1. All isolates formed typical dark brown, olivaceous or black colonies, appearing dark on the reverse side of the agar plate and displaying septate fungal elements under the microscope. Morphological Identification Identification based on morphological characteristics enabled the classification of most Generally, Bipolaris, Curvularia and Exserohilum were characterized by floccose and brown to black colonies. The macroconidia of Curvularia had thin cell walls and transverse septa. They often appeared as curved structures due to the swelling of the central cell, which was darker compared to the end cells. The macroconidia were thick-walled and fusiform, with three to four septations in Bipolaris, and cylindrical in shape with seven to eleven septa in Exserohilum. Alternaria colonies were greenish black with short, woolly hyphae. The conidia of this genus were longitudinally and transversely septate, brown and ovate arranged singly or in chains. Members of Neoscytalidium produced colonies that were densely fluffy with gray to dark gray aerial mycelia. These fungi were typified by arthroconidia arranged in chains in a zig-zag appearance. Cladosporium isolates were velvety with olivaceous green to black green colonies. Their characteristic features included conidiophores that were straight and branched at the apical region, conidia that were ovoid to globose, with dark scarring and arranged in chains, and ramoconidia.

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Chapter 4 : Black yeast - Wikipedia

Study 14 Dematiaceous fungi flashcards from Katie D. on StudyBlue. these sclerotic bodies are diagnostic of chromoblastomycosis (usually caused by fonsecaea pedrosoi, phialophora verrucosa, or cladosporium carrionii).

Received May 9; Accepted Oct Abstract Background Pleurostomophora richardsiae formerly Phialophora richardsiae is a dematiaceous fungus that is an uncommon cause of ocular infection. Herein, we present a case of endogenous endophthalmitis associated with disseminated P. Findings This is a descriptive case report with a brief review of literature. A year-old male admitted to the hospital following an acute cerebellar hemorrhage was found to have a swollen and tender wrist. The patient was afebrile with leukocytosis. Right eye examination noted anterior chamber cells and flare, vitreous haze and multiple large, and fluffy retinal infiltrates. Diagnostic vitrectomy revealed a mixed inflammatory cell infiltrate with numerous fungal elements. Blood cultures were negative, multiple transesophageal echocardiography studies revealed no vegetations, and synovial fluid aspiration of the wrist and biopsy of the radius were unremarkable. The patient was treated with intravitreal cefazolin, vancomycin, and amphotericin B, topical ciprofloxacin and natamycin, and intravenous amphotericin B and voriconazole. Visual acuity in the right eye declined to light perception, and examination revealed increasing anterior and posterior chamber inflammation. The patient died several weeks after presentation due to a massive intracranial hemorrhage. Fungal culture results from the vitrectomy were received post mortem and were positive for P. Infections typically occur following traumatic skin inoculation; however, a long refractory period may occur before symptoms develop. Early diagnosis and combination antimicrobial therapy are essential to optimize visual outcomes. Pleurostomophora richardsiae, Dematiaceous fungus, Phaeohyphomycosis, Endogenous endophthalmitis Findings Introduction Dematiaceous fungi are a heterogeneous group of organisms characterized by the presence of melanin or melanin-like pigment in their cell walls. These pervasive saprobes are commonly found in soil, decomposing plant material, and wood [1 , 2]. Phaeohyphomycosis is one of three clinical syndromes caused by these fungi and refers to a spectrum of diseases including superficial and deep local infections, pulmonary infection, and central nervous system infection as well as disseminated disease [1 , 2]. Infection typically results following traumatic skin inoculation although many patients do not recall the injury resulting in a long latency period before symptoms develop. Dematiaceous fungi are also an increasing cause of fungal keratitis worldwide [1]. Excluding keratitis, ocular infections with these organisms are uncommon. The dematiaceous fungus Pleurostomophora richardsiae formerly Phialophora richardsiae has rarely been implicated in human disease. One case of disseminated P. In this patient, endocarditis was also present as well as positive blood cultures; however, no detailed ophthalmic exam and no vitreous biopsy were described [3]. Herein, we present a case of P. Case report A year-old man was admitted to the hospital following an acute cerebellar hemorrhage. He complained of recent fever, chills, and left wrist pain. Past medical history included alcoholic cardiomyopathy, porcine mitral valve replacement, chronic atrial fibrillation, and multiple intracranial hemorrhages associated with warfarin toxicity. The chronic left wrist pain and swelling had been previously diagnosed as gout. Social history was notable for heavy ethanol abuse and intravenous drug abuse. Medications upon admission included warfarin, aspirin, metoprolol, and simvastatin. During the preceding four months, he was also treated with systemic corticosteroids following multiple intracerebral hemorrhages. On admission, the patient was afebrile, and the left wrist was moderately swollen and tender to palpation. His white blood cell count was Blood cultures were negative, and transesophageal echocardiography revealed no vegetations or perivalvular abscess. Ten days following admission, an arthrocentesis of the left wrist was performed after the patient developed increased swelling and marked worsening of pain. Gram stain revealed numerous white blood cells but no organisms or crystals, and cultures of the synovial fluid were negative. Intrarticular depomedrol was administered following the arthrocentesis. Two days following the arthrocentesis, the patient complained of right eye pain with redness and blurry vision. Fundus examination revealed multiple large, fluffy retinal and vitreous infiltrates in the right eye Fig. Examination of the left eye was unremarkable.

Chapter 5 : Mycology: Hyaline and Dematiaceous Fungi (by LabCE)

"Black yeasts", sometimes also black fungi, dematiaceous fungi, microcolonial fungi or meristematic fungi is a diverse group of slow-growing microfungi which reproduce mostly asexually (fungi imperfecti).

Dematiaceous Fungi The term "dematiaceous" refers to the characteristic dark appearance of this group of fungi as it grows on agar. Colonies are dark gray, brown, or black and, importantly, have a black reverse when the bottom of the agar plate is examined. This distinguishes the dematiaceous fungi from fungi with black conidia but an otherwise pale mycelium, such as A. Nomenclature and Disease Phaeohyphomycoses are clinical entities defined by the presence of pigmented hyphae, pseudohyphae, or yeast-like cells in tissue; this is in contrast with the hyalohyphomycoses, which lack pigmentation in tissue sections. Melanin stains can help to identify pigment in poorly-pigmented strains. Chromoblastomycoses, also known as chromomycoses, are chronic infections of the skin and subcutis developing after traumatic implantation of dematiaceous fungi; they are typically fungating, discolored, hemorrhagic lesions. Mycetomas eumycotic mycetomas are chronic, localized, progressive infections of the skin, subcutaneous tissue, muscle or bone that are caused by hyaline or dematiaceous fungi; their hallmark is the formation of granules of organized mycelial elements in tissue with the formation of abscesses and draining sinus tracts. Note that some authors consider chromomycosis and older term for phaeohyphomycosis. Note the color of the hyphae and the prominent, multicelled macroconidia. Longitudinal septae are difficult to appreciate at this power. Ulocladium Usually considered a contaminant Colonies mature rapidly and are typically wooly or cottony and dark brown to black; the reverse is black Conidia more spherical than Alternaria, do not form chains, and are borne on short, geniculate conidiophores FIG. Ulocladium in slide culture. Note muriform septation in the macroconidia indicated by the arrow. Again, note the color of the macroconidia and of the hyphae; while hyphae are stained with lactophenol cotton blue stain, macroconidia resist staining in this preparation and appear brown. Epicoccum Usually considered a contaminant Colonies grow fairly rapidly and progress from cottony yellow or orange to brown or black. The reverse may be red and diffusible yellow, red, brown, or orange pigment may be present Hyphae branch repeatedly in a focal pattern known as sporodochia Short conidiophores arise from sporodochia Muriform macroconidia are spherical to club shaped FIG. Epicoccum in slide culture. Sporodochia, conidiophores and small, muriform macroconidia are present. Dematiaceous Fungi with Transversely Septated Macroconidia Curvularia May cause fungal sinusitis and keratitis, endocarditis, pulmonary infections, and subcutaneous phaeohyphomycosis; may also be contaminants Colonies dark olive green to brown or black; surface pink-gray and wooly; the reverse is dark Macroconidia characteristically cells separated by transverse septae which arise sympodially from twisted conidiophores; macroconidia have a characteristic curved appearance secondary to disproportional enlargement of a central cell FIG. Curvularia in slide culture. Note the characteristic boomerang shaped macroconidia. Drechslera Not reported as a pathogen Produce cylindrical, multicelled macroconidia from geniculate conidiophores Resemble Bipolaris species; may be distinguished in saline mounts by germ tubes extending from the conidium between base and septum at right angle to the long axis of the macroconidium. In contrast, Bipolaris germ tubes arise from both ends of the base of the conidium and extend parallel to the long axis of the macroconidium FIG. Drechslera in slide culture. Macroconidia closely resemble those of Bipolaris Dematiaceous Fungi with Microconidia Cladosporium May cause cutaneous, subcutaneous, and eye infections, but are among the most common dematiaceous mold contaminants Nomenclature is changing, as with the rest of medical microbiology: Cladosporium carrionii may currently be better named Cladophialophora carrionii , but Koneman et al. Cladosporium in slide culture. Elliptic microconidia are found in long chains. Phialophora verrucosa Causes chromoblastomycosis, phaeohyphomycosis, or mycetoma Colonies are slow growing, dark gray or black, and hairlike Characteristic urn-shaped phialides bear tight clusters of spherical to elliptical, hyaline conidia FIG. Phialophora verrucosa in slide culture. Flask-shaped phialides with cup-shaped collarettes and conidia in balls at the apices of the phialides are characteristic. This high power photomicrograph shows a double-flask-shaped phialide; conidia spill from its apex. Fonsecaea pedrosoi Causes chromoblastomycosis, phaeohyphomycosis Colonies are

typically slow-growing, dark brown, olive or black, and may be covered with a velvet-like, silver mycelium; the reverse is black Conidiophores pale to brown, usually erect, apically swollen Isolates are notoriously pleomorphic, with cladosporium-type , rhinocladiella-type, phialophora-type , and fonsecaea-type conidiation FIG. Fonsecaea pedrosoi in slide culture. This figure illustrates so-called fonsecaea-type conidiation: Primary conidia may support secondary conidia, which in turn may support tertiary conidia, but long chains of conidia-denticle-conidia structures are not seen Wangiella dermatitidis Causes phaeohyphomycosis involving skin, subcutis, eye, brain, joints Colonies mature slowly. Immature colonies resemble black yeasts but eventually display delicate hair-like or velvety mycelium. Wangiella dermatitidis in slide culture. Note the absence of collarette on the very slender phialide. Dematiaceous Fungi that Defy the Above Grouping Phaeoannellomyces werneckii Colonies grow slowly and resemble pale yeast colonies before turning olive black; the reverse is black May cause tinea nigra, a superficial, asymptomatic fungal skin infection, especially of the palms A black yeast, formerly Exophiala werneckii; the genus Phaeoannellomyces was created in to accommodate black yeasts whose yeast cells function as annellides. Controversy still exists regarding this nomenclature. Forms yeasts with 2 cells Thick walled hyphae may form in aging colonies FIG. Phaeoannellomyces werneckii in slide culture. Note the 2 celled yeast forms. Note the thick walled hyphae seen in this aging culture. Chaetomium species An opportunistic moniliaceous mold; usually regarded a contaminant Young colonies are cottony white or pale and usually darken with maturity to tan-gray or gray-olive Single-celled ascospores are usually olive-brown pigmented ; Chaetomium is therefore considered here with dematiaceous fungi; it is, however, listed with other moniliaceous hyaline or brightly colored fungi in the ASM Manual of Clinical Microbiology 7th ed. Chaetomium in slide culture.

Chapter 6 : Dematiceous Fungi Index - Mycology Image Gallery - TML & MSH MicroWeb

Fungi producing olive-grey, brown or black (melanin) pigment in the cell wall of fungal hyphae or conidia are classified as dematiaceous (dark) fungi. Most fungi in dematiaceous group produce grey to dark color from the very beginning as they first appear on culture media.

The virulence factors in these fungi that are responsible for eliciting allergic reactions are unclear at present. Diagnosis These ubiquitous fungi can be contaminants in cultures, making the determination of clinical significance problematic. A high degree of clinical suspicion as well as correlation with appropriate clinical findings is required when interpreting culture results. Unfortunately, there are no simple serological or antigen tests available to detect these fungi in blood or tissue, unlike for other common mycoses that cause human disease. Polymerase chain reaction PCR is being studied as an aid to the diagnosis of fungal infections, but as yet is not widely available or reliable. However, studies have begun to examine the potential of identifying species within this diverse group of fungi using PCR of highly conserved regions of ribosomal DNA. In tissue, they will stain with the Fontanaâ€"Masson stain, which is specific for melanin,2 although sometimes only faintly, and longer than normal staining times may be required. This can be helpful in distinguishing these fungi from other species, particularly Aspergillus. I n addition, hyphae typically appear more fragmented in tissue than seen with Aspergillus, with irregular septate hyphae and beaded, yeast-like forms. An important issue is that much of the older literature is often inconsistent with regard to methodology, making reliable observations difficult. In addition, interpretive breakpoints are not available for most drugs relative to the filamentous fungi. Therefore, suggestions regarding susceptibility are guidelines only. The newer azoles itraconazole and voriconazole demonstrate the most consistent in vitro activity against dematiaceous fungi, except S. For itraconazole, the capsule form requires an acidic environment for absorption, while the suspension with cyclodextrin does not, being more consistently absorbed. Itraconazole demonstrates good activity against the vast majority of dematiaceous fungi tested. Voriconazole is the most recently licensed azole, and has become the treatment of choice for invasive aspergillosis, supplanting amphotericin B for this indication. Other azoles have a much more limited role in the therapy of these infections. Ketoconazole was the first oral azole, and has a relatively broad spectrum. However, a number of side-effects has significantly limited its current use with the availability of newer agents that are much better tolerated. Sparse in vitro data are available for dematiaceous fungi, but good activity is noted for the most common fungi causing chromoblastomycosis and mycetoma. Among investigational azoles, posaconazole has a broad spectrum similar to itraconazole, though with more activity, particularly against Aspergillus and other moulds. Use of lipid amphotericin B preparations allows for much higher doses than possible with standard amphotericin B, which may improve their efficacy against these fungi. Development of resistance during monotherapy has resulted in its use in combination therapy for systemic mycoses, most notably cryptococcal meningitis.

Chapter 7 : Dematiaceous fungal endophthalmitis: report of a case and review of the literature

Dematiaceous fungi (black fungi) are a heterogeneous group of fungi present in diverse environments worldwide. Many species in this group are known to cause allergic reactions and potentially fatal diseases in humans and animals, especially in tropical and subtropical climates.

Treatment is challenging and involves a highly individualized plan that often combines both surgical and long-term medical treatment. History A year-old man from Costa Rica with a history of a renal transplant, who was treated with chronic immunosuppressive therapy, was admitted for pneumonia to Tisch Hospital in December, The Dermatology Service was consulted for evaluation of an asymptomatic lesion on the right lower leg that began as a papule in and slowly evolved to become a nodule. One month prior to admission, the patient was started on voriconazole based on identification of fungal elements in a culture from the nodule. Tissues obtained from two punch biopsies were submitted for histopathologic examination and tissue culture analysis. During the course of hospitalization, pneumonia was diagnosed on the basis of clinical and radioimaging studies and cefepime, levofloxacin, vancomycin, and amphotericin B were initiated. Bacterial lavage, sputum, and blood cultures failed to identify bacterial, fungal, or atypical mycobacterial organisms. After two weeks of treatment, clinical and radiographic evidence indicated resolution of pneumonia and the patient was discharged. The hospital course was complicated by transient acute renal failure related to amphotericin B. Histopathologic evaluation of the nodule lead to a diagnosis of subcutaneous dematiaceous fungal infection chromoblastomycosis versus phaeohyphomycosis. Although tissue culture was negative for bacteria, fungus, or atypical bacteria, an additional excisional biopsy was deferred because of concern for poor wound healing, owing to the location of the lesion and the history of diabetes mellitus and peripheral vascular disease. After a multidisciplinary discussion, a treatment plan was developed that combined medical and surgical therapy in an effort to balance the risks of surgery with those of adverse drug reactions that could result from the long-term use of antifungal agents with tacrolimus. Itraconazole was initiated in an attempt to decrease the size of the lesion prior to surgical excision; after two months of therapy, the size of the cutaneous nodule had decreased. The current plan is to perform surgical excision in the future followed by several months of systemic antifungal therapy. Past medical history included diabetes mellitus, diabetic retinopathy, a renal transplant in , coronary-artery disease, hypertension, and peripheral vascular disease. Medications include amlodipine, isosorbide mononitrate ER, furosemide, insulin, aspirin, calcitriol, mycophenalate mofetil, tacrolimus, pantoprazole, prednisone, and sulfamethoxasole-trimethoprim. The patient has no drug allergies. Physical examination A hyperpigmented, indurated nodule is present on the distal, posteriolateral aspect of the right leg. Laboratory data Complete blood work and comprehensive metabolic profile were normal. Histopathology Figure 2 Within a predominantly fibrotic dermis are foci of granulomatous inflammation with pigmented fungal spores. Fungal elements also are visualized on a periodic acid-Schiff-diastase stain. Discussion Subcutaneous dematiaceous fungal infections, which include chromoblastomycosis and phaeohyphomycosis, are a heterogeneous group of clinical entities caused by dematiaceous or pigmented fungi that are found in soil. Chromoblastomycosis and phaeohyphomycosis are both caused by pigmented fungi and share a number of clinical features and causative organisms, yet are considered two distinct clinical entities. Chromoblastomycosis is a subcutaneous infection with highest prevalence in the tropics; it is typically seen in immunocompetent hosts and results from traumatic inoculation of skin by pigmented fungi. The principle causative agents are fungi of the genera Fonsecaea tropical forests , Cladophialophora dry climates , and Philalophora [1]. The disease is most commonly observed in agriculturists on the lower legs, which likely explains the observed propensity for men of lower socioeconomic status. Chromoblastomycosis typically presents with an asymptomatic papule or nodule that develops slowly over years into a localized verrucous plaque that expands and leaves behind a central sclerotic or keloidal scar. The disease most often remains localized, but satellite lesions from autoinoculation and lymphatic spread have been documented [2]. Secondary complications may result from bacterial superinfection, ulceration, secondary lymphedema, and, rarely, development of a squamous-cell carcinoma. In an immunocompromised state, there is a risk of

extension into underlying skeletal muscle and bone [3]. The diagnosis of chromoblastomycosis rests on identification of thick-walled, multiseptate, brown, sclerotic cells termed Medlar bodies, copper pennies, or muriform cells. These pathognomonic features can be observed in tissue biopsy specimens or by direct microscopic examination of a scraping of black dots from the surface of the nodule with 10 percent potassium hydroxide. Identification of the causative fungal species can be achieved by tissue culture but is not reliably positive. Phaeohyphomycosis describes a heterogeneous group of fungal infections that are caused by over species and 60 genera of dematiaceous that are fungi found in soil worldwide, with varied clinical presentations that are greatly influenced by the immune status of the host [4]. Common causative agents of phaeohyphomycosis include fungi of the genera Exophiala, Wangiella, Bipolaris, Alternaria, and Phialophora [5]. The most common clinical presentations in immunocompetent hosts include localized cutaneous infection superficial or subcutaneous , fungal sinusitis, allergic bronchopulmonary mycosis similar to the presentation of allergic bronchopulmonary aspergillosis , and, rarely, fatal brain abscess. The subcutaneous lesions of phaeohyphomycosis typically result from direct inoculation via trauma to exposed skin, and, in immunocompetent patients, most commonly present as a single, inflammatory, cystic or indurated plaque [6]. In immunocompromised patients, phaeohyphomycosis is increasingly being recognized as an opportunistic infection [7]. In these individuals, the clinical presentation is variable and ranges from an isolated nodule to disseminated, indurated plaques, nodules, escars, and ulcers. In addition, immunocompromised patients are at risk for locally invasive phaeohyphomycosis, and, rarely, but often fatal, pneumonia or disseminated disease. Treatment for both chromoblastomycosis and phaeohyphomycosis can be challenging and often requires a combination of medical, surgical, cryotherapy, or thermal therapy. With early or localized disease, the goal of treatment can be curative, but with extensive disease, treatment goals are to reduce disease burden, limit spread, and prevent complications. Medical therapy consists of long courses months to years of antifungal agents, specifically itraconazole to mg daily or pulse dosing of mg daily for one week every month and terbanifine to mg daily. Combination therapy with itraconazole and terbanifine has been shown to be synergistic [8]. Newer agents, such as voriconazole and posaconazole, have shown promise, but experience is limited [9]. Fluconazole, ketaconazole, amphotericin B, and flucytosine are not indicated either because of poor efficacy or a poor side effect profile [3]. Cryotherapy is effective, but generally requires multiple treatment cycles [10 , 11 , 12]. Irrespective of the treatment modality, drug therapy should be continued for several months after cure to prevent relapse. Reported overall cure rates for phaeohyphomycosis could not be found in the literature, but for chromoblastomycosis they range from 15 percent to 80 percent [13]. Standard-of-care treatment guidelines have not be been established because of a lack of studies and a lack of correlation between in vitro efficacy and clinical efficacy. Current understanding is based on individual case reports or small case series [14 , 15 , 16 , 17]. In addition to these limitations, the varied clinical presentation and comorbidities dictate that the treatment for chromoblastomycosis and phaeohyphomycosis be individualized. Lupi O, et al. J Am Acad Dermatol ; Bonifaz A, et al. Queiroz-Telles F, et al. Med Mycol ; Infect Dis Clin North Am ; Pang KR, et al. Derm Ther ; Ben-Ami R, et al. Phaeohyphomycosis in a tertiary care cancer center. Clin Infect Dis ; Vermeire SE, et al. Cutaneous phaeohyphomycosis in renal allograft recipients: Diagn Microbiol Infect Dis ; Zhang JM, et al. Synergistic effects of terbinafine and itraconazole on clinical isolates of Fonsecaea monophora. Eur J Dermatol ; Negroni R, et al. Posaconazole treatment of refractory eumycetoma and chromoblastomycosis. Hiruma M, et al. Hyperthermic treatment of chromomycosis with disposable chemical pocket warmers: Summerbell RC, et al. Subcutaneous phaeohyphomycosis caused by Lasiodiplodia theobromae and successfully treated surgically. Castro LG, et al. Treatment of chromomycosis by cryosurgery with liquid nitrogen: Int J Dermatol ; Trop Doct ; Treating chromoblastomycosis with systemic antifungals. Expert Opin Pharmacother ; 5: Esterre P, et al. Treatment of chromomycosis with terbinafine: Br J Dermatol ; Ungpakorn R, Reangchainam S. Pulse itraconazole mg daily in the treatment of chromoblastomycosis. Clin Exp Dermatol ; Gupta AK, et al. Alternate week and combination itraconazole and terbinafine therapy for chromoblastomycosis caused by Fonsecaea pedrosoi in Brazil.

Chapter 8 : Dematiaceous (Melanized) Molds | Clinical Gate

Objectives. 1. Describe the dematiaceous fungi, including natural habitat, transmission, and diseases with signs and symptoms. 2. Identify the site where mycetomas are frequently located and the population or populations at risk of infection.

This slide culture of the fungus Fonsecaea pedrosoi, revealed the presence of a phialide with accompanying phialospores. Fonsecaea pedrosoi is one of the etiologic pathogens responsible for the infection known as chromoblastomycosis, especially in the more humid regions of the world. Normally it is found amongst rotting woods and soil debris. The 3 most common agents are: Fonsecaea pedrosoi figure 1 Cladosporium carrionii figure 2 and 4 Phialophora verrucosa figure 3 These fungi, recognized by a variety of names, are saprobes located in soil and decaying vegetation. The route of entry is usually by trauma. The lesions are sub-cutaneous and the surface can be flat or verrucous figure 4A. The lesions take several years to develop. These organisms are called dematiaceous fungi, because they have a black color in the mycelium cell wall in culture and in tissue. In tissue these fungi form sclerotic bodies which are the reproductive forms dividing by fission figure 4B. These organisms induce a granulomatous reaction. The etiologic agents of chromoblastomycosis are septate, mold-like, branching, darkly pigmented which produce asexual fruits called conidia. We identify these fungi in culture by the shape and formation of the conidia. The fungi have a world-wide distribution especially in warmer climates like the tropics or the southern U. The melanin in the pigment may be a virulence factor. These organisms are distributed world-wide. There is no really successful therapy. Excision and local heat have been used with some success. Flucytosine 5-FC and itraconazole have also been used to treat or control this disease. Posaconazole is showing some promise as a therapeutic agent. There are no serological tests to aid in the diagnosis. Figure 2 Cladosporium Cladophialophora carrionii, magnified X. Georg Figure 3 Conidia-laden conidiophores of a Phialophora verrucosa fungal organism from a slide culture. Note the flask-shaped phialides, each lipped by a collarette. Each phialide terminates in a bundle of round, to ovoid conidia. Libero Ajello Figure 4 Plate culture of Cladosporium carrionii, at four weeks growth. In tissue these fungi form sclerotic bodies which are the reproductive forms dividing by fission Dr Arthur DiSalvo Figure 5. Used with permission Figure 6. These are called eumycotic mycetoma tumors caused by the TRUE fungi as opposed to those caused by actinomycetes figure 6. These tumors frequently invade contiguous tissue, particularly the bone. A diagnosis of the etiologic agent is essential for patient management because the prognosis and therapy differs. Madurella mycetomatis figure 7 and 8 2. These organisms are associated with the soil, thus you see many infections in the feet and legs. Clinical specimens for diagnosis: The agents of mycetoma are all filamentous fungi which require days for visible growth on the culture media and then another several days for specific identification. These fungi are identified by the colonial morphology, conidia formation and biochemical reactions. The species of fungi cannot be distinguished in histopathological tissue sections. Treatment is very difficult, but terbinafine and itraconazole have been used with some success. Posaconazole seems to be efficacious. Libero Ajello Figure 8. The fungus enters the human body via trauma, which usually affects the foot. This disease process may take several years. Conidiophores of the fungus Exophiala jeanselmei. Exophiala jeanselmei, is a well documented human pathogen. Clinical manifestations include mycetoma, localized cutaneous infections, subcutaneous cysts, endocarditis, cerebral involvement, and systemically disseminated infections. Conidiophores with conidia of the fungus Pseudallescheria boydii from a slide culture. Libero Ajello Figure Eumycotic mycetoma due to the fungus Pseudallescheria boydii. Pseudallescheria boydii is the most common etiologic agent associated with eumycetoma in the United States. The disease is a chronic cutaneous and subcutaneous infection with the foot being the most common site for lesions. Histopathologic changes seen in zygomycosis due to Rhizopus arrhizus using FA stain technique. Rhizopus arrhizus, the most common Rhizopus spp. William Kaplan Figure Histopathologic changes seen in a heart valve due to zygomycosis caused by Mucor pusillus. Using methenamine silver stain, one can detect the presence of fungal elements associated with zygomycosis, including sparsely septate hyphae, amongst a mostly acute inflammatory process with some island of chronic granulomatous inflammation. Libero Ajello

Figure 14 Mucor sp. Mucormycosis is an acute inflammation of soft tissue, usually with fungal invasion of the blood vessels. This rapidly fatal disease is caused by several different species in this class. The zygomycetes, like the Candida species, are ubiquitous and rarely cause disease in an immunocompetent host. Some characteristic underlying conditions which cause susceptibility are: The three most common genera causing this clinical entity are: Rhizopus species figure 12 Absidia species Characteristics These fungi are found world-wide, commonly in soil, food, organic debris etc. They are seen on decaying vegetables in the refrigerator and on moldy bread. Rhinocerebral infections are common. This disease is frequently seen in the uncontrolled diabetic patients. Typical case An uncontrolled diabetic patient comes to ER may be comatose depending on the state of diabetes and a cotton-like growth is observed on the roof of the mouth or in the nose. These are the hyphae of the organism. If untreated, the patient will die within a few hours or days. What do you do to help this patient first? Controlling the diabetic state is most important before administering amphotericin. These fungi have a tendency to invade blood vessels particularly arteries and enter the brain via the blood vessels and by direct extension through the cribiform plate figure This is why they cause death so quickly. With age, and the formation of sporangia, the colony becomes dark gray. The sporangia contain the dark spores figure The mycelium is wide microns , ribbon-like and non-septate coenocytic. This same appearance is clear in tissue sections. The species are identified by the morphology in culture. Treatment Treatment consists of debridement and amphotericin Identification There is an immunodiffusion test available, but the physician cannot wait for these results before instituting rapid, vigorous intervention. The diagnosis and treatment must be immediate and based primarily on clinical observations. Figure 15 This patient presented with a case of a periorbital fungal infection known as mucormycosis, or phycomycosis. Mucormycosis is a dangerous fungal infection usually occurring in the immunocompromised patient, affecting the regions of the eye, nose, and through its growth and destruction of the periorbital tissues, it will eventually invade the brain cavity. Mucor is a common indoor mold, and is among the fungi that cause the group of infections known as zygomycosis. The infection typically involves the rhino-facial-cranial area, lungs, GI tract, skin, or less commonly other organ systems. Georg Figure 16 Conidia: Conidial heads of Aspergillus niger are large, globose, and dark brown, and contain the fungal spores, facilitating propagation of the organism. Georg Figure 18 This photomicrograph depicts the appearance of a conidiophore of the fungus Aspergillus flavus. Like the zygomycetes, they are ubiquitous in nature and play a significant role in the degradation of plant material as in composting. Similar to Candida and the Zygomycetes, they rarely infect a normal host. The organism is distributed world-wide and is commonly found in soil, food, paint, air vents. They can even grow in disinfectant. There are more than one hundred species of aspergilli The most common etiologic agents of aspergillosis in the United States: Aspergillus fumigatus figure

Chapter 9 : Infections caused by dematiaceous fungi and their anatomoclinical correlations

Subcutaneous dematiaceous fungal infections, which include chromoblastomycosis and phaeohyphomycosis, are a heterogeneous group of clinical entities that are caused by dematiaceous or pigmented fungi found in soil. These infections have a wide spectrum of clinical presentations that depend largely.