

Original Research Article

Histomorphological spectrum of fungal infections

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ABSTRACT

Background: Fungal infections have become very common resulting in a wide range of diseases from superficial infections to invasive fungal lesions. These organisms are now capable of affecting not only the immunocompromised patients but also healthy immune-competent individuals. All other non-culture methods except histologic method cannot detect all the types of fungi and are not available widely especially in developing countries like India.

Methods: This retrospective study conducted in the department of Pathology for a period of 5 years. A total of 29 cases were studied. The aim of this study was to detect the type of fungal infections and their distribution according to age, sex, and organ involvement in histopathologic specimens received in our department.

Results: Twenty-nine cases with fungal infections were studied. Of these (22; 75.8%) were males, (7; 24.1%) were females with male dominance. The cases displayed extensive range of age prevalence between 12 and 77 years. The most common type of fungal infection encountered in this study was mucormycosis. The most common site involved in infection was maxillary sinus. Maxillary sinus was the most common site for mucormycosis.

Conclusions: The histopathologic examination can provide a swift provisional identification of infectious fungal organisms and remains the only existing reliable means to identify certain pathogens.

Keywords: Fungal, Infection, Maxillary, Mucor mycosis

INTRODUCTION

Recognition of fungi have been made much earlier than bacteria as the causative agent of human disease. Michele (1729) described aspergillosis and it was named because of its likeness to "rougher head".¹ Fungal infections have become very common resulting in a wide range of diseases from superficial infections involving the stratum corneum of the skin to systemic infection involving the brain, heart, lungs, liver, spleen and kidneys. Invasive fungal lesions are likely to be more common in patients like transplant recipients, cancer patients on chemotherapy and immunosuppressive treatment, HIV patients, premature infants, old aged patients and those undergoing major surgeries. These patients are at high risk for acquiring invasive fungal infections.^{2,3} These organisms are now capable of affecting not only the

immunocompromised patients but also healthy immune-competent individual.⁴

Hence, this retrospective study was undertaken to find the prevalence of fungal infections and characterize the common fungal species isolated in this tertiary referral center. Although culture is considered as gold standard for etiologic diagnosis fungal infections, it is a slow method compared to other methods. All other non-culture methods except histologic method cannot detect all the types of fungi and are not available widely especially in developing countries like India. Although histopathological method may not detect fungal infections in all the instances due to sparse organisms, morphologic overlapping, observer inexperience, it helps in etiologic diagnosis in a very good number of cases.⁵ Not to be forgotten is that histopathology is the only method for etiologic diagnosis of some organisms like

Rhinosporidiosis, Lobomycosis and Pneumocystis.^{5,6} The aim of this study was to detect the type of fungal infections and their distribution according to age, sex, and organ involvement in histopathologic specimens received in our department.

METHODS

This was a retrospective study conducted in the Department of Pathology, Government Medical College, Jammu over a period of 5 years from January 2014 to December 2018. A total of 29 cases were studied.

All the histopathological reports maintained in the histopathological section were reviewed and hematoxylin and eosin stained slides of every case were re-examined. Further sections were cut from paraffin blocks wherever required and new slides were prepared and stained. The sections were stained with routine hematoxylin and eosin (H and E) and special stains such as periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) wherever required. Commonly in the histological tissue section, fungi can present in either form i.e.; hyphae or budding yeast or spherules or a combination of these forms. Hematoxylin and Eosin stain enables to evaluate the host response, in addition to detect other micro-organisms. Whenever the fungi are sparsely distributed, or under-stained, there are chance for missing them in H and E stained sections.

Also, some fungal lesions have confusing morphological features like Histoplasmosis and Blastomycosis and may not be obvious as they may show retraction artifact in the cytoplasm, or variation in the sizes making their evaluation more difficult. Some fungi with pseudo hyphae, or patient undergone therapy may show altered fungal morphology in tissue sections. There comes the role of special stains like periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS), also known as “broad spectrum” fungal stains. Even in case where fungi are degenerated and non-viable, GMS gives better contrast thus extremely preferred for screening.⁷⁻⁹ All cases diagnosed to have fungal infections either clinically suspected or incidentally detected during this study period were included in this study. Specimens obtained from autopsy cases, also requisition form without proper clinical information or particulars of the patient were excluded. All medical records were reviewed and clinical details including age, sex, and predisposing conditions were obtained from the requisition forms of the patients available in the department. For data analysis, authors used Statistical Package for the Social Sciences (SPSS) version 16.0. Age and morphological patterns were expressed as frequency and percentage.

RESULTS

Twenty-nine cases with fungal infections were studied. Of these (22; 75.8%) were males, (7; 24.1%) were females with male dominance. The cases displayed

extensive range of age prevalence between 12 and 77 years. So, there was no age predilection for prevalence of fungal infections noticed in this study. A graphic presentation depicting sex distribution in fungal infections Figure 1.

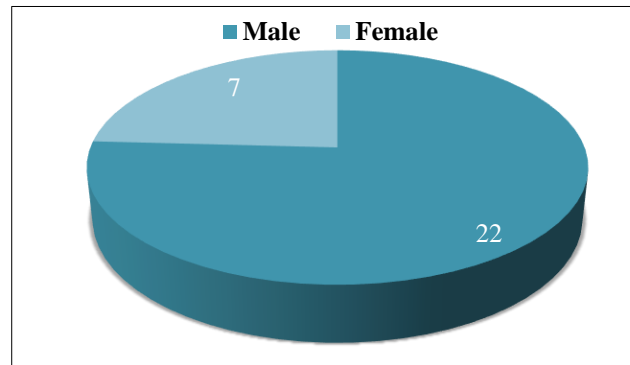


Figure 1: Depicting sex distribution.

The most common type of fungal infection encountered in this study was Mucor-mycosis (14) followed by candidiasis (6), others were three cases each of Rhinosporidiosis, cryptococcosis, and aspergillosis. Tabulated presentation of distribution of different type of fungal infections in the present study Table 1.

Table 1: Distribution of different type of fungus.

Type of fungus	No. of cases	Percentage (%)
Mucor mycosis	14	48.3
Candidiasis	6	20.8
Rhinosporidiosis	3	10.3
Cryptococcosis	3	10.3
Aspergillosis	3	10.3
Total	29	100

The most common site involved in infection was maxillary sinus (10) followed by nasal cavity (9) and esophagus (5). Single case was found in each of the following sites: skin, foot, hand and soft tissue around bone and bronchus. Tabulated presentation of involvement of different sites Table 2.

Table 2: Involvement of different sites.

Site	No. of cases	Percentage (%)
Maxillary sinus	10	34.6
Nasal cavity	9	31.1
Esophagus	5	17.3
Skin	1	3.4
Foot	1	3.4
Hand	1	3.4
Soft tissue around bone	1	3.4
Bronchus	1	3.4
Total	29	100

Maxillary sinus was the most common site for Mucor mycosis in this study. In nasal cavity, two cases of Mucor mycosis and three cases of rhinosporidiosis were noticed. All five cases of fungal infection in the esophagus were of candidiasis. In two cases, candidiasis was associated with adenocarcinoma, one case it was associated with squamous-cell carcinoma and two were associated with AIDS. In the bronchus, one case of aspergillosis was found.

A histological section from a specimen sent as nasal mass biopsy shows Rhinosporidiosis having large sporangia with multiple internal endospores Figure 2 (H and E; 10X).

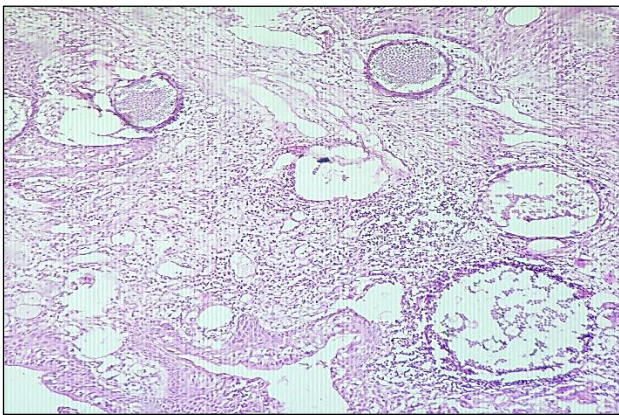


Figure 2: Rhinosporidiosis having large sporangia with multiple internal endospores (H and E; 10x).

A histological section from a specimen sent as nasal mass biopsy showing a large sporangium with multiple internal endospores Figure 3 (H and E; 40X).

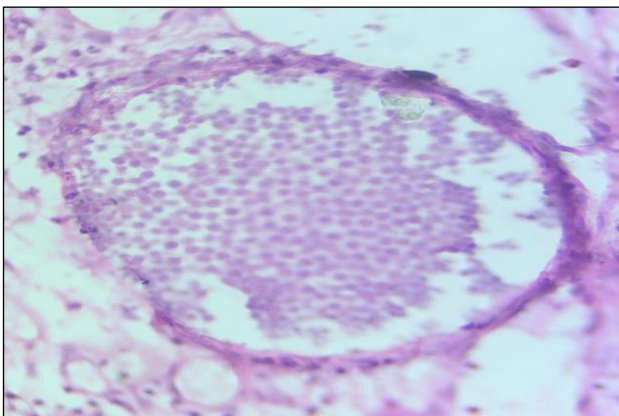


Figure 3: A large sporangium with multiple internal endospores (H and E; 40X).

A histological section from a specimen sent as mass maxillary sinus shows irregularly branching non-septate fungal hyphae Figure 4 (H and E; 40X).

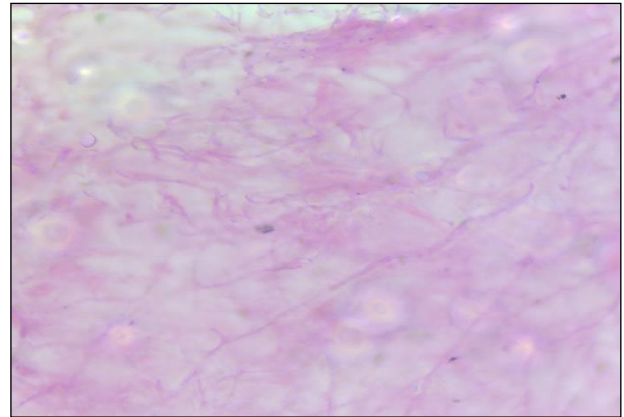


Figure 4: An irregularly branching non-septate fungal hyphae (H and E; 40x).

DISCUSSION

Fungal infections based on the site of infection can be superficial limited to stratum corneum, cutaneous involving the skin appendages, subcutaneous or deep involving the abdominal viscera, lungs, bones and the central nervous system. Deep mycoses are either caused by primary pathogenic or opportunistic fungal pathogens. The primary pathogenic fungi can infect a normal host as well, enter through the respiratory system, whereas, opportunistic pathogens infect immunocompromised patients and invade through the respiratory tract, alimentary tract, or intravascular devices.^{2,7}

Tissue culture is the gold standard for diagnosing fungal organisms. But few exceptions, they can only be diagnosed by histopathological examination and not by culture are Pneumocystis and Rhinosporidiosis, for providing a definitive diagnosis of an invasive fungal infection histopathology continues to be a cost-effective and rapid diagnostic technique. Similarly, for evaluating tissue invasion and host reaction to the organism's histopathology is mandatory.^{8,10} Hence histologic evaluation of tissue sections is a quick and easy way for identifying fungal organisms, and also a strong adjunct to microbiologic culture in diagnosing fungal infections.^{2,6}

Some fungi cannot be cultured. Some fungi are so adherent and tightly bound that they are rarely visible in body fluids and exudates. In this scenario, histopathologic examination remains one of the major diagnostic tools in mycology, because it permits rapid, presumptive identification of fungal infections.^{11,12}

In this 5-year retrospective study, all histopathologic slides were reviewed, which were diagnosed with fungal infections and studied according to age, sex and organ-wise involvement. An attempt was made in our study on limiting the diagnostic difficulties as per morphology that are encountered while reporting fungal infections, as the result of overlapping morphology.

The most common infection in our study was Mucor mycosis in maxillary sinus, which was identified based on morphology, irregularly branching non-septate hyphae and the angle of branching usually advances 90°. The most common differential diagnosis of Mucor mycosis is with Aspergillus species, as they have thin, septate, with regular branching, and they branch at 45° angle as opposed to 90° of mucormycosis.¹²

Candidiasis was the next common infection that was noticed commonly in esophagus in this study and organisms appeared as sheets of yeasts measuring 3-5µm in diameter intermingled with pseudo hyphae or filaments. Histopathologic examination of specimens is very important to define invasion of tissues and vessels, because growth from skin, lung, gastrointestinal or genitourinary tract is only indicative of colonization. Candida species can also be confused with Aspergillus species, but elongated pseudo hyphae appeared to be branching in Candida are slender and do not have septations. Germinating Candida blastopores can also appear to be branching but can be distinguished by the absence of a constriction between the base of the blastopore and the germ tube. While classically extracellularly or intracellular Candida species can mimic Histoplasma species pointers for the discrepancy of Candida include the variably sized yeast cells, lack of a pseudo capsule and a typical suppurative tissue reaction, whereas in case of Histoplasma species tend to provoke a more granulomatous reaction. Luna M has shown drawbacks of morphological identification of Candida species.^{12,13}

Three cases of R. seeberi, Cryptococcus, and Aspergillus were also noted. R. seeberi, a mesomycetozoon parasite causes palate and nasopharyngeal polyps, produces large sporangia with multiple internal endospores. The most common differential diagnosis R. seeberi is coccidioidomycosis spherules, but R. seeberi sporangia and endospores are larger than Coccidioides spherules, and its inner sporangial wall stains with mucicarmine stain.¹⁴

Although culture studies are considered as the gold standard for the identification of etiologic agents, they may not always be available or positive.¹⁵⁻¹⁷ Moreover, differentiating colonization and contamination from pathogens may be difficult. Also, the studies by Sundaram et al, and Guarner and Brandt have shown the difficulties in differentiating colonization and contamination of fungi.^{7,15} Accurate diagnosis of the etiologic agent is important as the in vitro susceptibility to antifungal agents of different species and the emerging pathogens are variable.^{7,18} Histopathology provides rapid and cost-effective means of providing diagnosis.

Histopathology usually cannot provide the fungal genus and species, which are very important for treatment. Infections with more than one fungus, the morphological diversity may be subtle and not appreciated. Thus, other

tests should be used to determine if more than one organism is present. Several studies have demonstrated the usefulness of special stains in the identification and classification of fungal organisms in tissue sections.¹⁹⁻²²

CONCLUSION

Sometimes even microbiological examination fails to diagnose fungal infections, at the same time contamination by other fungi can lead to misdiagnosis. The histopathologic examination can provide a swift provisional identification of infectious fungal organisms and remains the only existing reliable means to identify certain pathogens. The evidence of tissue invasion or an inflammatory reaction can help to determine whether an organism represents contamination, colonization, or true infection. Its plays a major role.

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