

Histopathological Spectrum of Fungal Infections in a Tertiary Care Hospital

Abilash Sasidharannair Chandrakumari^{1,5}, Pammy Sinha², Shree Lakshmi Devi Singaravelu^{3,5}, Jaikumar S⁴

Abstract

Context: Infections caused by fungi are increasing at a steady rate worldwide. Elderly individuals and who are at an immunocompromised state are at risk of developing this disease. Though fungal infections which either manifest as cutaneous or invasive type, Cutaneous lesions are very common. Fungal diseases are diagnosed usually by correlating the clinical findings with histopathology and confirmation is done based on culture. **Aim:** The current study was aimed at categorizing the spectrum of fungal infections diagnosed in the histopathology specimens and their distribution according to age, sex and site of involvement. **Settings and Design:** This was a cross sectional analysis, conducted over a period of one year from September 2016 to August 2017. **Methods and Material:** A total of 60 cases were enrolled in the study. Clinical findings inclusive of age and sex parameters were noted from hospital registrars. Specimens were fixed in formalin and processed under standard procedure protocols. Slides were prepared and stained with routine H & E stain; special stains like PAS and GMS stains were used wherever necessary. **Statistical analysis used:** Data analysis was using IBM Statistical Package for the Social Sciences Software version 21. Significance of the statistical tests at P value less than 0.05 was based on 95% confidence interval. **Results:** Out of 60 cases, 18 cases turned out to be positive for fungal infection. The mean age of the studied population was 49.11 years (SD 11.02). The male female ratio was found to be 0.8:1. The mean age of male population was found to be 53.375 years (SD 7.44), mean age of female population was 45.7 years (SD 12.54). The commonest fungal infection encountered in our study was Rhinosporidiosis. **Conclusions:** Histopathological examination provides reliable diagnosis in individuals with uncertain clinical findings of fungal infection.

Keywords: Immunocompromised; Cutaneous; Rhinosporidiosis; Histopathology; periodic acid- Schiff.

How to cite this article:

Abilash Sasidharannair Chandrakumari, Pammy Sinha, Shree Lakshmi Devi Singaravelu. Histopathological Spectrum of Fungal Infections in a Tertiary Care Hospital. Indian J Forensic Med Pathol. 2019;12(2):73-77.

Authors Affiliation: ¹Associate Professor, Dept of Pathology, ³Associate Professor, Dept of Pharmacology, Shri Sathya Sai Medical College & Research Institute Chennai, Tamil Nadu 603108, India. ²Professor & Head, Dept of Pathology, ⁴Professor, Dept of Pharmacology, Sri Lakshmi Narayana Institute of Medical Science Medical College & Hospital, Puducherry 605502, India. ⁵Research Scholar, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu 600126, India.

Corresponding Author: Abilash Sasidharannair Chandrakumari, Associate Professor Pathology, Shri Sathya Sai Medical College & Research Institute, Ammapettai, Nellikuppam, Thiruporur-Guduvancherry Road, Tamil Nadu 603108, India.

E-mail: abey4aris@gmail.com

Received on 07.04.2019, **Accepted on** 04.05.2019

Introduction

Infections caused by fungi are increasing at a steady rate due to increased exposure and also because of the advanced treatment modalities that allows longer survival of at risk population, these at-risk populations include patients who underwent transplant surgeries, those who are on chemotherapeutic and immunosuppressive drugs, AIDS patients, diabetic and elderly individuals, etc [1, 2]. Some of the fungal infections are associated with changes in the climatic conditions and human habitats, frequent travel and population relocations [3, 4].

Fungus can cause infections which can be either cutaneous or invasive lesions. Cutaneous infections are very common when compared to deep or invasive mycosis which are rare and usually occur in immunocompromised individuals. Majority of the cutaneous mycosis is caused by dermatophytes and candida. Aspergillosis, chromoblastomycosis, pheohyphomycosis and eumycosis causes deep cutaneous mycosis [5,6].

Diagnosis of fungal infections is usually based on correlating clinical findings with histopathology and confirmation is done by culture in selective media. Histopathological examination of specimens is required in all cases in which deep and cutaneous fungal infection. Dermatophytes are not easily identified with histopathological analysis, since the hyphae of dermatophytes are stained pale blue by routine Hematoxylin & eosin (H&E) stains. For invasive fungal infections histopathological analysis remains cost-effective, rapid and gold standard diagnostic modality for a presumptive definitive diagnosis [7,8].

Histopathological diagnosis of fungal elements is definite challenge even in the hands of experienced histopathologists, to facilitate the process of visualization; the fungal elements are stained by using special stains such as periodic acid- Schiff (PAS) which gives hyphae red colour and Grocott's methenamine silver (GMS) which stains the hyphae black. The current study was proposed to categorize, the spectrum of fungal infections diagnosed in the histopathology specimens and their distribution according to age, sex and site of involvement.

Materials and Methods

The current study was a cross sectional analysis, conducted in the department of pathology for a period of one year from September 2016 to August 2017. All clinically suspected patients and incidentally detected fungal infections were sampled. Institutional ethics committee approval was obtained and a total of 60 cases were enrolled in the study.

Relevant clinical data was obtained from hospital registry; the specimens received were fixed in formalin and processed under standard procedure protocols. Slides were prepared and stained with routine H&E stain; special stains like PAS and GMS stains were used wherever necessary..

Statistical analysis

Data analysis was performed by using IBM Statistical Package for the Social Sciences (SPSS)

software version 21.0. Univariate analysis was carried out to find out frequency, mean and standard deviation (SD). Multivariate analysis was performed for sex and age. Significance of the statistical tests at p value less than 0.05 was based on 95% confidence interval.

Results

Out of 60 cases, 18 cases turned out to be positive for fungal infection. The mean age of the studied population was 49.11 years (SD 11.02). The male female ratio was found to be 0.8:1. The mean age of male population was found to be 53.375 years (SD 7.44), mean age of female population was 45.7 years (SD 12.54). Difference in the mean age was found to be statistically significant ($p < 0.001$). Increased proportion of the disease was seen among sixth decade followed by fifth decade of life. Age clustering with sex distribution of individuals positive for fungal infection was shown in table 1.

The commonest fungal infection encountered in our study was Rhinosporidiosis (5 cases), followed by Aspergillosis and Dermatophytosis (3 cases each). Distribution of fungal lesions was shown in table 2.

Table 1: Distribution of fungal lesions

Fungal Lesions	No of cases (%)
Maduro mycosis	2 (11.11%)
Pheohyphomycosis	3 (16.67%)
Dermatophytosis	2 (11.11%)
Aspergillosis	3 (16.67%)
Chromoblastomycosis	2 (11.11%)
Cryptococcosis	1 (5.55%)
Rhinosporidiosis	5 (27.78%)
Total	18 (100%)

Table 2: Age and sex distribution of fungal infections

Age	Male	Female	Total
21 - 30	0	1	1
31 - 40	1	1	2
41 - 50	2	3	5
51 - 60	3	4	7
61 - 70	2	1	3
Total	8	10	18

In the study, most common site involved were extremities, followed by nasal cavity and lung. All cases of Rhinosporidiosis presented with nasal obstruction with polypoid mass. Microscopic examination revealed mixed inflammatory inflammation with numerous thick walled sporangia.

Both the cases diagnosed with maduramycosis presented with discharging sinuses in the foot. Histologically both these cases showed brown fungal filaments surrounded by granulomatous inflammation with abscess formation.

Three cases of pigmented fungi (phaeohyphomycosis) were diagnosed in the study and all the three cases presented with a cystic swelling in the extremities. Histopathological examination showed granulomatous inflammatory response composed of lymphocytes, histiocytes, giant cells and one case showed microabscesses formation. The organism was found in the cyst wall in the form of pale brown pigmented budding yeasts and dematiaceous hyphae. Special stain with PAS highlighted the fungal elements in magenta colour [Fig. 1]. Two cases of superficial dermatophytosis diagnosed in the study showed histologically neutrophilic infiltrate with thin fungal elements in stratum corneum.

Cases with aspergillus presented with otomycosis and nasal obstruction. Histopathological examination showed thin filamentous, septate hyphae with acute angle branching and spores surrounded by lymphoplasmacytic infiltrate, eosinophils and foreign body giant cells [Fig. 2]. Single case of Cryptococcus presented with lung mass and histopathology of bronchial brush specimen showed numerous round encapsulated fungal organisms surrounded by chronic inflammatory cell infiltrate.

Two cases of chromoblastomycosis presented with nodular lesions in the foot with a history of trauma. Microscopically there is epithelial hyperplasia and lymphohistiocytic infiltrate, fungal elements were seen as sclerotic bodies and as pigmented hyphae.

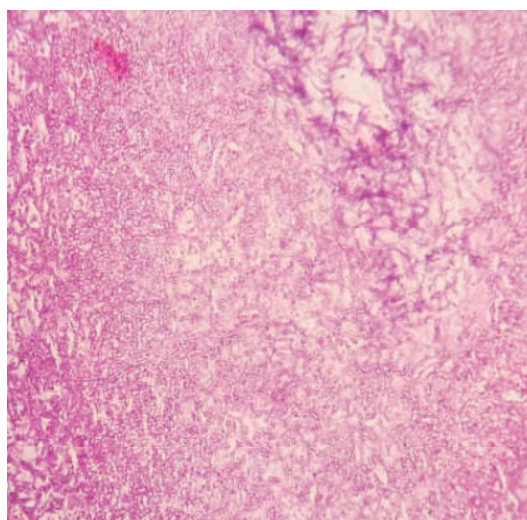


Fig. 1: H & E showing thin acute angled septate hyphae

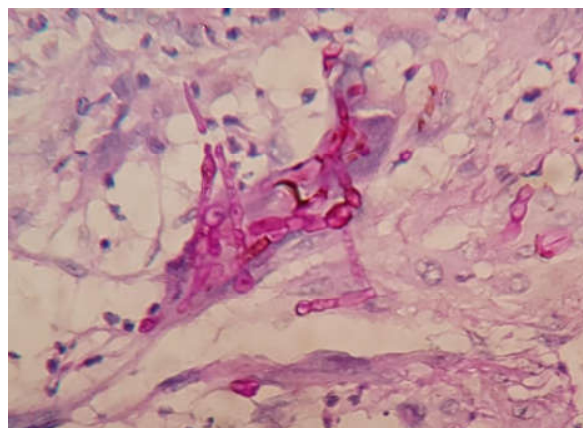


Fig. 2: PAS staining showing pigmented hyphae and yeast forms

Discussion

Infections due to fungi are in the rise in developing countries like India, because of multiple demographic factors like low socioeconomic status, overcrowding, poor hygiene and other cultural practices. There are very minimal studies available about the clinical pathological aspects and incidence of various fungal lesions in south India. In the current study we made an effort to categorize various fungal diseases in clinically suspected cases from the histopathological specimens received in the department. In two cases the fungal elements were incidentally made out. All the fungal lesions identified in this study were localized without any evidence of immunosuppression [9,10].

In the study Rhinosporidiosis is the commonest fungal lesion diagnosed. This finding is in accord with the other similar studies carried out in various regions of south India and Srilanka [11,12] but contradictory to the other studies done in other parts of the world [12,13]. This is might be because of the fact that people belonging to this geographic regions use stagnant water bodies like pond and well for bathing and swimming.

Aspergillosis was the second commonest lesion encountered in the study. Among the three cases of aspergillus two cases presented with otomycosis and the organism was seen as fungus ball. Aspergillus was diagnosed based on presence of septate, thin acute-angled branching hyphae. The hyphae were usually deeply basophilic, and it will be eosinophilic in appearance when the hyphae are degenerated or necrotic. Similar studies done by authors Muniyappa Usha, et al. and Jeannette Guarner et al. showed chronic pulmonary aspergillosis or aspergilloma, bronchopulmonary aspergillosis and invasive aspergillosis are the most

common lesions, our study findings are in contrast with these studies [8,14].

Among the fungal infections reported in our study, Phaeohyphomycosis comprise a remarkable fraction. Phaeohyphomycosis is a group of heterogeneous fungal infections caused by dematiaceous fungi. These fungi cause progressive superficial, subcutaneous and deep visceral infections and it is diagnosed by the presence of pigmented dark brown yeast/hyphae forms. When left untreated this often leads to life-threatening disease especially in immunocompromised individuals. Similar studies done by Ponnuswamy et al. and Kaliyamoorthy S et al demonstrated all cases of phaeohyphomycosis presented with cystic swelling, our study results were in concurrence with these findings.

In our study two cases of Maduramycosis were reported and both the cases had discharging sinuses in the extremities. Maduramycosis can present as actinomycotic or eumycotic mycetoma. Morphologically it is characterized by draining sinus tracts with brown to black pigmented grains comprising of fungal elements. Our study findings were similar to the study done by Sidhalingreddy et al. and Kaliyamoorthy S et al. [15,16]. There were two cases of Dermatophytosis demonstrated in the study and both these cases on histopathology revealed spores and branched, septate hyphae invading the stratum corneum. This is in concurrence with the other similar study done by sridevi et al. [17].

A single case of Cryptococcus demonstrated in the study was a male patient presented with chronic cough, dyspnoea and chest pain. Bronchial brushing and biopsy confirmed the diagnosis. Study done by Kanjanapradit et al. also showed similar findings [18].

Conclusion

Histopathological examination provides valid diagnosis in individuals with uncertain clinical findings of fungal infection. Diagnosis of fungal infections on histopathology is based on the appearance of fungal elements on H & E stain and Special stains and also by the presence of host response like granulomatous reactions, foreign body giant cells and eosinophilic infiltrates.

Key Messages:

The diagnosis of fungal infections on histopathology is based on the appearance of fungal elements on H & E stain and Special stains

and also by the presence of host response like granulomatous reactions, foreign body giant cells and eosinophilic infiltrates.

Conflict of Interest: No

References

1. Naggie S, Perfect J R. Molds: hyalohyphomycosis, phaeohyphomycosis, and zygomycosis. *Clin. Chest Med.* 2009;30(2):337-53.
2. Das A, Bal A, Chakrabarti A, Panda N, Joshi K. Spectrum of fungal rhinosinusitis; histopathologist's perspective. *Histopathology.* 2009;54(7):854-9.
3. Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. *Mycoses.* 2008;51(Suppl 4):2-15.
4. Ginter-Hanselmayer G, Weger W, Ilkit M, Smolle J. Epidemiology of tinea capitis in Europe: current state and changing patterns. *Mycoses.* 2007;50 (Suppl 2):6-13.
5. Damjanov I, Linder J. *Andersons pathology*, tenth edition. 1996:951-62.
6. Elder DR. *Levers Histopathology of the skin.* 10th ed. Philadelphia; Wolter Klnwer/ Lippincott Williams & Willams, 2008.
7. Bancroft D, Gamble M. *Theory and practice of histological techniques.* 5th ed. 2002.
8. Muniyappa Usha, HB Rakshitha, Jasuja Avnika, Asok Aneesha, Reginald Sharon. Morphological spectrum of fungal infections: a retrospective study. *International Journal of Medical Science and Public Health.* 2016;5(8):1673.
9. Richardson MD. Changing patterns and trends in systemic fungal infections. *J Antimicrob Chemother* 2005;56:5-11.
10. M. Richardson and C. Lass-Flo'rl. Changing epidemiology of systemic fungal infections, *Clin Microbiol Infect.* 2008;14(Suppl. 4):5-24.
11. Sarath N.A. and leonel Mendoza. Rhinosporidiosis. In: *Topley and Wilsons Medical mycology* 10th ed. Hodder Arnold. pp436-72.
12. Lulu Ahmad Al-Bhlal, fungal infection of the nasal cavity and paranasal sinuses: review of 26 cases. *Ann Saudi Med.* 1996;16(6):615-21.
13. Goldstain MF. Allergic fungal sinusitis-an underdiagnosed problem. *Hosp prac.* 1992;27-73.
14. Jeannette Guarner and Mary E. Brandt. *Histopathologic Diagnosis of Fungal Infections in the 21st Century.* *Clinical Microbiology Reviews.* 2011 April;24(2):247-80.
15. Karkuzhali P, Yogambal M, Karthik S. Two Cases of Multiple Subcutaneous Cystic Phaeohyphomycosis in Immunocompromised Patients with a Rare Causative Organism. *Indian J Dermatol.* 2014;59(4):421.

16. Kaliyamoorthy S, Srinivasan S. Histopathological study of cutaneous and soft tissue fungal infections. *Int J Res Med Sci.* 2016;4:1933-7.
17. Sridevi M, Vimala C, Chitra S. Clinicopathological spectrum of fungal infections in a Tertiary Care Centre. *Indian Journal of Pathology and Oncology* 2018;5(1):130-5.
18. Kanjanapradit K, Kosjerina Z, Tanomkiat W, Keeratichananont W, Panthuwong S. Pulmonary Cryptococcosis Presenting With Lung Mass: Report of 7 Cases and Review of Literature. *Clinical Medicine Insights: Pathology.* 2017;10:1-5.

