

Clinicopathological profile of uncommon tropical infections -A single centre experience with review of literature.

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Abstract

Introduction: Cutaneous, deep mycosis and bacterial infections are predominantly seen in hot tropical countries. They have become more common in the last decade due to immunosuppression and globalization. **Aim:** To study clinical behaviours, anatomical locations, histological findings of the fungal and bacterial infections seen in daily practice. **Materials and methods:** This is a prospective study conducted in a tertiary care hospital for 1 year. We studied the cases according to their age and sex, the clinical presentations and site, the treatment provided and the histopathological findings. **Results:** This study comprises of six cases of fungal, bacterial infections- cutaneous aspergillosis, histoplasmosis, chromoblastomycosis, actinomycosis arising from skin, aspergillosis of lungs, subcutaneous rhinosporidiosis with varied presentations. The patients have undergone treatment and were referred to dermatology, plastic surgery and surgery department for further management. **Conclusion:** Cutaneous fungal, bacterial infections and deep mycoses frequently have a variety of clinical presentation, leading to a broad range of differential diagnosis. So the study of their clinical profile and histopathological findings paves way for early diagnosis and better management.

Keywords : Cutaneous, fungal, pulmonary, subcutaneous

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Introduction

The 21st century completely changed the approach of the pathologist to cutaneous, deep mycosis and bacterial infections as immunosuppression has become a common condition because of generalized use of immunosuppressors in the treatment of many diseases. The *Aspergillus* species is present in soil, decaying vegetation, and stored grains. [1–6] There are more than 300 species of *Aspergillus* of which *Aspergillus fumigatus* causes around 90% of systemic cases in humans. However primary cutaneous cases are usually caused by *Aspergillus flavus*, *Aspergillus terreus*, *Aspergillus niger*, and *Aspergillus ustus*. [2–4,7] Chronic Pulmonary Aspergillosis has only recently been recognised as a significant global health burden and its incidence appreciated. [8] Infection by *H. capsulatum* var. *capsulatum* has worldwide distribution and the fungus can be isolated from vegetal detritus. Traumatic inoculation is the alleged mechanism for primary cutaneous lesions. [9] The initial lesions can take the form of a black-crusted plaque, erythematous papules, or hemorrhagic bullae, all of which can ultimately ulcerate. [5,7] However in secondary cutaneous involvement the fungus is usually inhaled leading to a systemic spread from the lungs which has a poor prognosis. [10,11] Secondary dissemination to the skin commonly presents as multiple necrotic, sometimes ulcerated, septic embolic papules, and plaques [12]. Primary cutaneous

histoplasmosis is rare and it is thought to be caused by direct inoculation of the microorganism. [13-18] Patients with Primary cutaneous histoplasmosis presents with nonspecific skin lesions including papules, plaques, ulcers, purpura, abscesses, impetigo, or dermatitis. [4] Chromoblastomycosis, is an extremely rare superficial mycoses, caused by pigmented fungus and has an indolent course. The infection is commonly due to minor trauma. [19] Actinomycosis is a rare subacute or chronic bacterial infection caused by Gram-positive anaerobic, higher prokaryotic bacteria belonging to the family Actinomyceataceae. [20] Primary cutaneous actinomycosis is a rare entity and is generally associated with trauma. [21]

Materials and methods

This is a prospective study conducted in a tertiary care hospital for 1 year from March 2020 to March 2021 of six cases. All patients presented with wide- ranging clinical features in relation to the causative organism and location of lesion. In all cases routine blood investigations and required radiological investigations were done. Informed consent was taken. All the surgically biopsied specimens were sent to the Department of Pathology. Gross examination of the specimens were done. H&E staining and PAS stain were done as on required basis. Using light microscopy, histopathological diagnosis were confirmed along with ancillary microbiological assay.

Results

Case-1 (Aspergillosis of skin)

A 27-year-old male presented with skin lesion for last 4 months. Skin biopsy was done. Grossly a flap like tissue piece measuring 1x0.5x0.5 cm was received. On light microscopy, section showed fibrocollagenous tissue infiltrated with dense mixed inflammatory

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infiltrate mainly neutrophils, lymphocytes, plenty number of histiocytes and giant cells (Figure 1A & 1B). PAS stained positive, showed septate branching filamentous hyphae with acute angle branching. The diagnosis of cutaneous aspergillosis was considered. The patient was put on antifungal therapy with Itraconazole.

Case-2 (Histoplasmosis of skin)

A 45-year-old male patient presented with a 2 cm large eroded, nodule below the left nostril, which had developed over 10 weeks. The patient was HIV negative and not immunocompromised. There was no other systemic manifestation. Punch Biopsy of the lesion was done. Grossly, a skin covered tissue piece measuring 0.2cc was received. On light microscopy section showed structure of epidermis underlying dermis and dermal appendages. Dense chronic inflammatory infiltrate containing neutrophils, lymphocytes, histiocytes present throughout the dermis. Histiocytes contain variable organisms with round budding and halo. The diagnosis of cutaneous histoplasmosis was considered (FIG 2A, 2B & 2C). The patient was put on antifungal therapy with Itraconazole and there was healing of the ulcer.

Case:3 (Chromoblastomycosis of skin)

A sixty-five-year-old diabetic female patient presented with a non-healing ulcer in the medial aspect of left leg near the medial malleolus for last six months. The ulcer is reddish-white gradually increasing in extent with development of granulation tissue and scar around the ulcer. A punch biopsy was done from the lesion. Grossly a skin covered tissue piece measuring (2 cm x 1 cm) received. On light microscopy the section showed pseudoepitheliomatous type of hyperplasia with extent of infiltration reaching till the dermal layer with infiltration of chronic inflammatory cells, consisting of lymphocytes, macrophages, eosinophils. Few foreign body giant cells were also noted. Round to oval shaped brownish thick-walled suspicious of fungal infection were found in focal areas. Fungal stain (PAS) was done, which showed positivity for the staining. Brownish structures resembling copper-penny bodies were found and a diagnosis of chromoblastomycosis was considered (FIG 3A, 3B & 3C). The patient was put on antifungal therapy with Itraconazole and there was healing of the ulcer.

Case-4 (Actinomycosis of skin)

A 53 years old male patient presented with multiple hard, pitted swellings involving the left leg with discharging sinuses for last 3-4 months. Punch biopsy from the swellings were done. Grossly a skin covered tissue piece measuring (1x1x0.5cm) received. On light microscopy, the sections revealed hyper-keratosis and mild-acanthosis of the epidermis. Inflammatory infiltrates comprising of plasma cell, macrophages and neutrophils were observed in the upper and mid dermis. Bacterial colonies (sulphur granules) found at the center of the inflammatory reaction, composed of basophilic radiating filaments. The features were suggestive of diagnosis of actinomycosis of skin. (FIG 4A & 4B) The patient was hence put on itraconazole, chlorphenamine therapy.

CASE:5 (Aspergillosis of lungs)

A 58 year old, male patient presented with constitutional symptoms, chronic productive cough, breathlessness, chest discomfort and occasionally haemoptysis for about 6 months. Radiological investigation was done that revealed single or multiple lung cavities, usually with thick walls and with or without a fungus ball (aspergilloma) and with concomitant pleural fibrosis. Lobectomy was done and the specimen was sent for histopathological examination. Grossly four tissue pieces received, one blackish tissue piece resembling upper lobe of lung measuring 6x2x2cm identified other three whitish tissue pieces largest one measuring 4x4x3cm received. On light microscopy the sections revealed plenty filamentous hyphae with acute angle branching and frequent septations. Background lung alveolar wall shows vascular congestion with plenty chronic inflammatory infiltrate. The features are suggestive of aspergillosis lung (FIG 5A, 5B & 5C).

CASE: 6 (Subcutaneous Rhinosporidiosis)

A 39-year-old female patient with no history of immunosuppression presented with multiple swellings involving the anteromedial aspect of thigh which was gradually increasing in size. There is past history of polypoidal mass involving the nose, nasopharynx and vocal cords. Clinical examination revealed lobular, non-tender swelling of different sizes with a normal colored overlying skin. Radiological investigation suggested cystic swellings involving the anteromedial aspect of thigh. Surgical removal of the swellings was done. Grossly irregular skin covered tissue pieces were identified, on cut sections yellowish friable areas were identified. On light microscopy numerous globular cysts at different stages of development were identified each of these cysts represents a thick-walled sporangium containing numerous spores, there was inflammatory infiltrate in the stroma. (FIG 6A -F)

Discussion

Non invasive and invasive rare fungal, bacterial and other infections in non-immunocompromised individuals is a less explored area specially in a tropical and developing country like India. Fungal infections are becoming more frequent because of expansion of at-risk populations and use of treatment modalities that permit longer survival of these patients. [22] Some of the changes in endemic fungal infections can be attributed to climate changes extension of human habitats, ease of travel, and shifting populations. It is very important to suspect fungal, bacterial and other infection from clinical features and perform skin biopsy and isolation of the organism for diagnosis of cutaneous infections. In our study we have seen a cutaneous aspergillosis, histoplasmosis, actinomycosis, chromoblastomycosis, pulmonary aspergillosis and a case of disseminated subcutaneous rhinosporidiosis mostly affecting non immunocompromised patients with no history of ICU stay. Histopathologic examination of tissues to detect fungi, bacteria and other organisms will remain an important tool to define the diagnostic significance of positive culture isolates, including invasion of tissues and vessels as well as the host reaction to the organism. Histopathology can also provide rapid presumptive diagnosis while waiting for culture results, or it may provide the only available material when no culture growth occurs or cultures were not ordered. Histopathologic examination of biopsy specimens, surgical resection specimens should always start with H&E staining of the tissue. GMS and PAS staining should be performed if a fungus is suspected after review of tissue sections because of presence of an inflammatory tissue response or when there is high clinical suspicion even if the H&E stain is unrevealing. Retrospective studies that correlate culture results with histopathology and cytology showed that the overall accuracy for microscopic morphological techniques can vary from 20 to 80% [23, 24, 25] The lowest correlation has been reported for invasive septate molds [25]. Descriptive diagnoses of the fungal elements together with a comment listing the fungi with consistent morphology are important to guide treatment [23]. Meersseman et al. conducted a multi-center retrospective study in Belgium and reported a frequency of invasive aspergillosis in critically ill patients without malignancy to be 6.9% [26]. Most common species isolated from the mini-BAL of patients with invasive aspergillosis was *Aspergillus fumigatus* (70%) followed by *Aspergillus flavus* (30%) and *Aspergillus terreus* (20%). Most studies from Europe revealed *Aspergillus fumigatus* (82-92%) as the commonest fungus causing invasive Aspergillosis [27,28]. Actinomycosis has been called the most misdiagnosed disease and listed as a rare disease by the Office of Rare Diseases of the National Institutes of Health. [29] The masquerading clinical presentations as cutaneous tuberculosis, fungal infections, malignancies and other systemic infections, difficult in vitro cultivation of the pathogen, and non-specific radiological picture are commonly associated outfits leading to misdiagnosis [30]. It is an unusual sub-acute or chronic suppurative and granulomatous bacterial infection characterized by multiple abscesses, tissue fibrosis, and the formation of sinuses and fistulae. [31]. Actinomyces spp are higher prokaryotic bacteria

belonging to the family Actinomyceataceae.[32].Highest incidence of Rhinosporidiosis cases is reported among river-sand workers in India and in Sri Lanka; this is particularly relevant to the mode of infection as it invades through abrasions caused by sand particles with the pathogen in the putative such as ground water. [33] While the Indian subcontinent accounts for the majority of the cases in literature sporadic cases from Europe and North America also have been reported.The spores are usually present in dust, clothes, and stagnant waters and the infection is transmitted to humans by direct contact.[34] Commonly starting as a pruritic papule that grows into an erythematous painless, friable, polypoid mass, blocking the nose and the nasopharynx.[35] The disease can also involve the maxillary antrum, paranasal sinuses, conjunctiva, lacrimal sacs, lips, palate, uvula, epiglottis, larynx, trachea, bronchus, ear, scalp, vulva, vagina, penis, urethra, rectum, and skin.[35-37].Subcutaneous dissemination is a very rare event and usually seen in immunocompromised patients.The most common organisms causing chromoblastomycosis is *Phialophora verrucosa*, *Fonseceaea pedrosoi* and *Cladophialophora*

carrion. [38] It progresses slowly with a long term course. It often gets overdiagnosed, as the course simulates that of a carcinoma.[19,39] There are only a few case reports found on this superficial dermatophytic infestation. The most common location is the lower extremity, although some species have a predilection to infect the trunk or the upper extremities.[40] Even without treatment the lesions persist in the skin and cases of spontaneous regression have even been described.[41] A single lesion is the most common, although multiple lesions are also possible.[42] The fungus spreads through lymphatic vessels and new cutaneous lesions can seem in the vicinity of the primary one.[43,44] Patients with primary cutaneous histoplasmosis present with nonspecific skin lesions including papules, plaques, ulcers, purpura, abscesses, impetigo, or dermatitis. In general clinical presentation is so variable that histoplasmosis has been called “fungal syphilis.”[13] The most involved areas are the face, extremities, and trunk.[45,46] In addition, oral, perianal, and genital involvement is common.[47,48] Diagnosis hinges on evidence of fungus in the wound and absence of systemic disease.

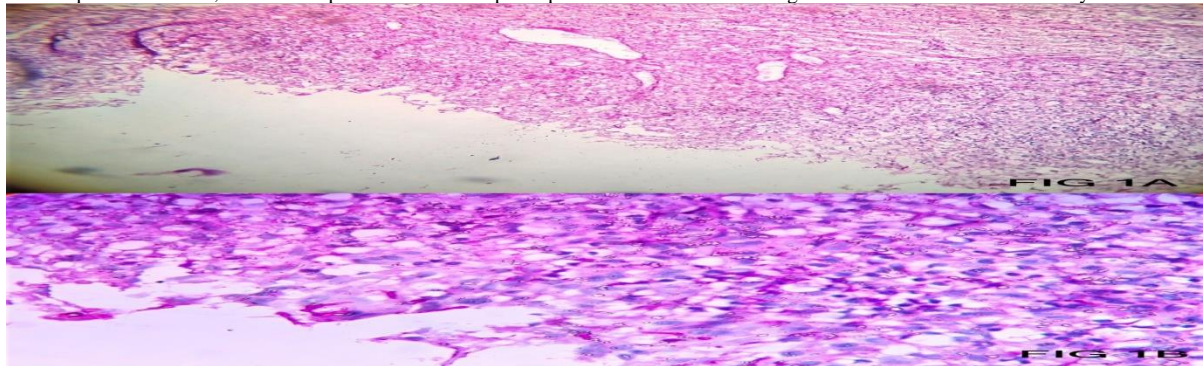


Fig 1 A :Photomicrograph showing cutaneous aspergillosis (x100 H&E)

Fig 1 B :Photomicrograph showing cutaneous aspergillosis (X 400 PAS)

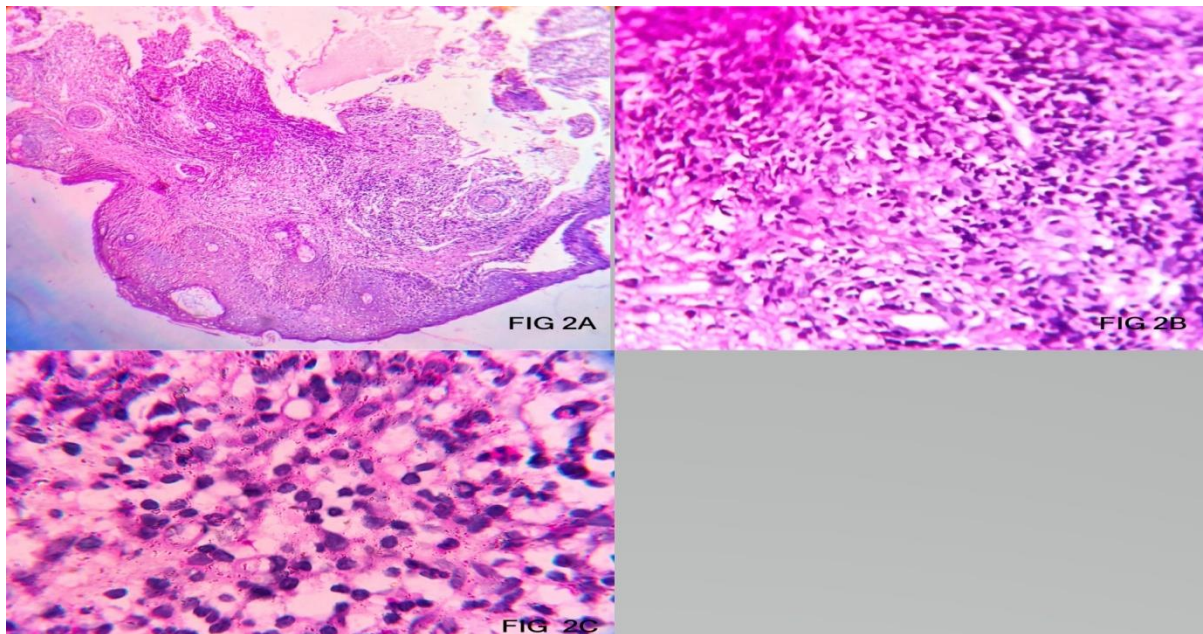


Fig 2 A : Photomicrograph showing cutaneous histoplasmosis (x 100 H&E)

Fig 2B: Photomicrograph showing cutaneous histoplasmosis (X 400 H&E)

Fig 2 C :Photomicrograph showing cutaneous histoplasmosis (X 400 PAS)

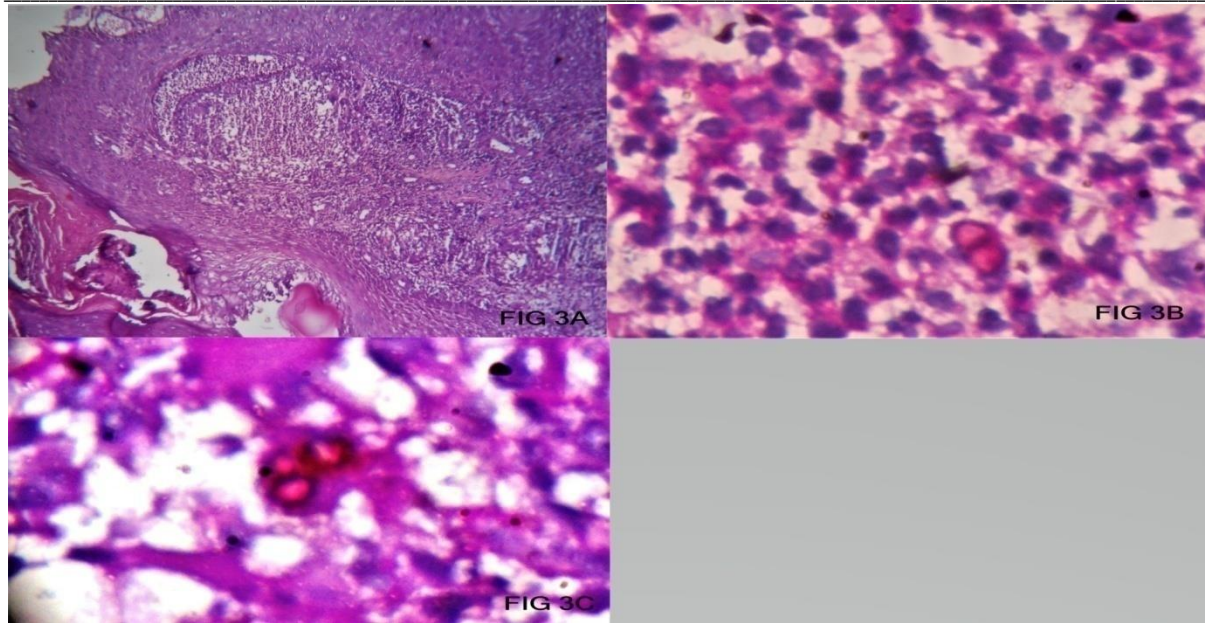


Fig 3A : Photomicrograph showing cutaneous chromoblastomycosis (x 100 H&E)

Fig 3B: Photomicrograph showing cutaneous chromoblastomycosis(X 400 PAS)

Fig 3C: Photomicrograph showing cutaneous chromoblastomycosis (X 400 PAS)

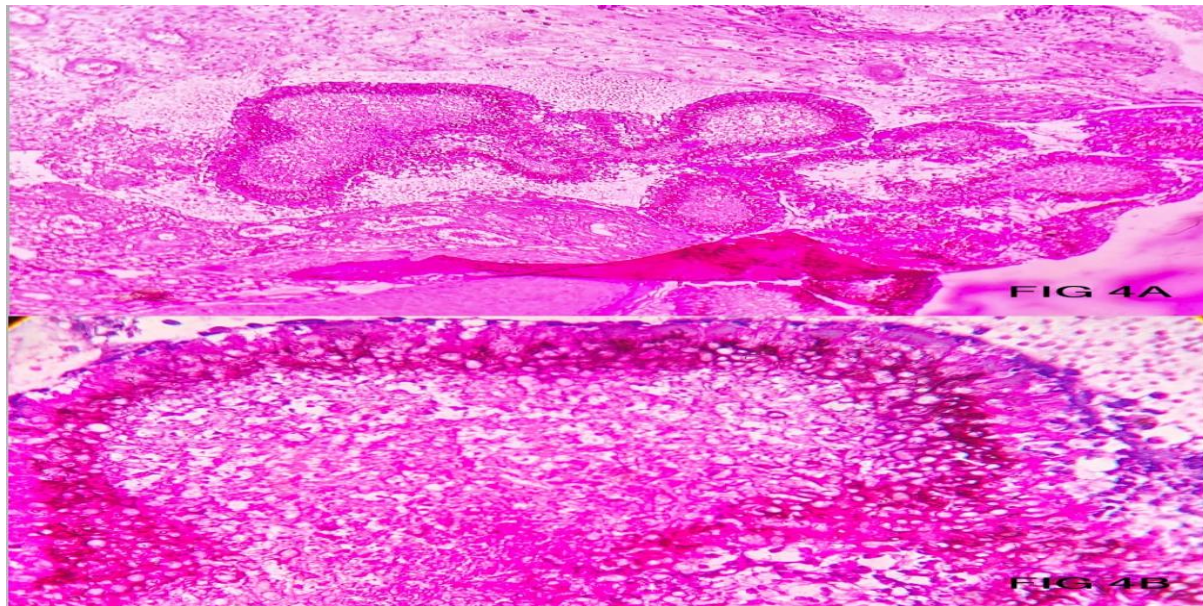


Fig 4 A : Photomicrograph showing cutaneous actinomycosis (x 100 H&E)

Fig 4B: Photomicrograph showing cutaneous actinomycosis (x 400 PAS)

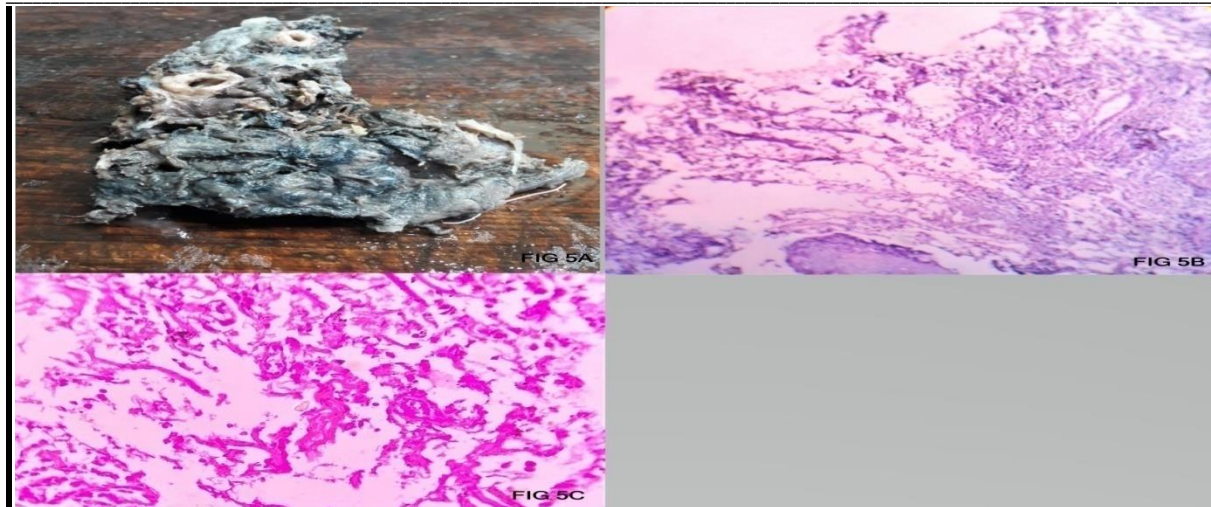


Fig 5 A: Photomicrograph showing gross picture of pulmonary aspergillosis
Fig 5 B: Photomicrograph showing pulmonary aspergillosis (X 100 PAS)
Fig 5 C : Photomicrograph showing pulmonary aspergillosis (X 400 PAS)

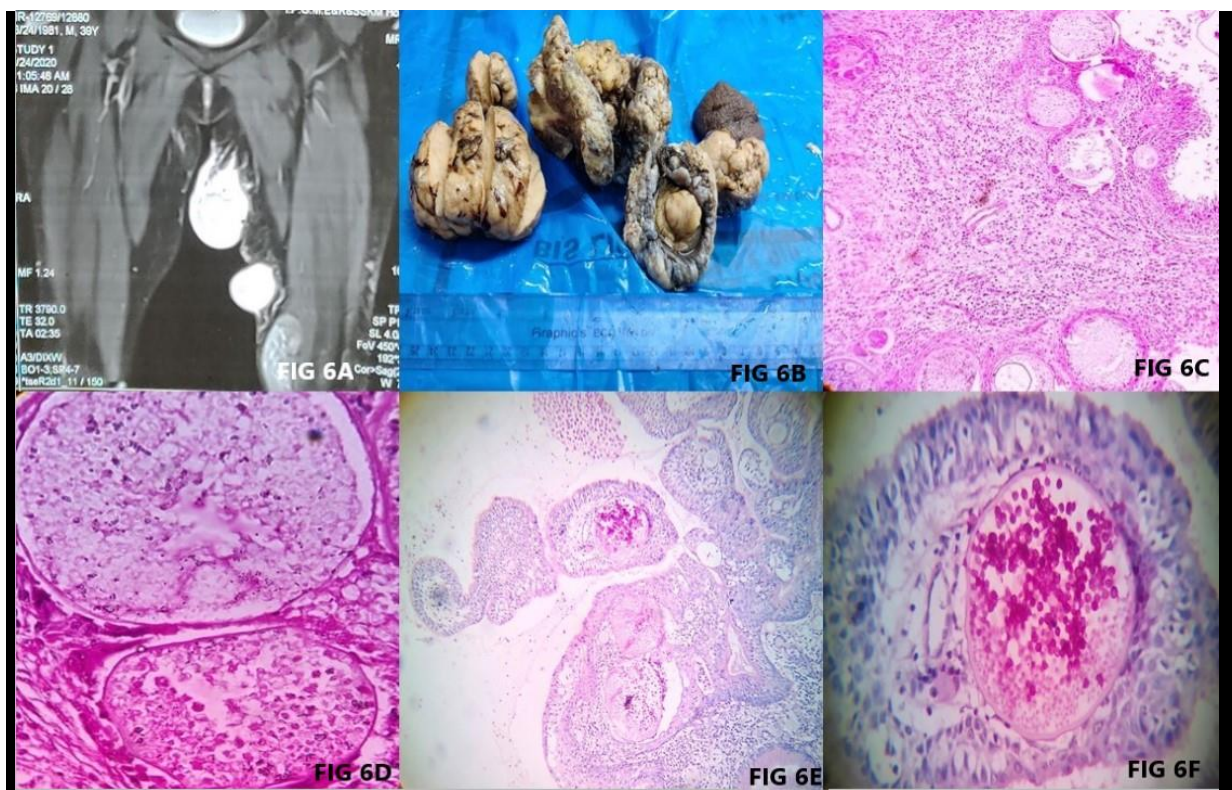


Fig 6 A: Photomicrograph showing radiology picture of soft tissue swelling of rhinosporidiosis
Fig 6 B: Photomicrograph showing gross picture of soft tissue swelling of rhinosporidiosis
Fig 6 C: Photomicrograph showing picture of rhinosporidiosis (x100 H&E)
Fig 6 D: Photomicrograph showing picture of rhinosporidiosis (x400 H&E)
Fig 6E :Photomicrograph showing picture of rhinosporidiosis (x100 PAS)
Fig 6 F:Photomicrograph showing picture of rhinosporidiosis (x400 PAS)

Conclusion

The aim of this study was to summarize the histopathologic findings of the main cutaneous and deep fungal infections that are commonly seen in daily practice. We also included actinomycosis (despite the fact that the infectious agent of this disease is bacterial and not fungal) and rhinosporidiosis (despite being caused by mesomycetozoa, which are not fungi). A shift in the trend has been observed as the propensity of these infections in non immunocompromised patients with no history of hospital stay has been observed which is a quite rare finding in a tropical country like India.

References

- Ajith C, Dogra S, Radotra BD, et al. Primary cutaneous aspergillosis in an immunocompetent individual. *J Eur Acad Dermatol Venereol.* 2006; 20:738–739.
- Ozer B, Kalaci A, Duran N, et al. Cutaneous infection caused by *Aspergillus terreus*. *J Med Microbiol.* 2009;58:968–970.
- Granstein RD, First LR, Sober AJ. Primary cutaneous aspergillosis in a premature neonate. *Br J Dermatol.* 1980;103:681–684.
- Romano C, Miracco C. Primary cutaneous aspergillosis in an immunocompetent patient. *Mycoses.* 2003;46:56–59.
- Woodruff CA, Hebert AA. Neonatal primary cutaneous aspergillosis: case report and review of the literature. *Pediatr Dermatol.* 2002;19: 439–444.
- Prasad PV, Babu A, Kaviarasan PK, et al. Primary cutaneous aspergillosis. *Indian J Dermatol Venereol Leprol.* 2005;71
- Paterson DL. New clinical presentations of invasive aspergillosis in non-conventional hosts. *Clin Microbiol Infect.* 2004;10(suppl 1):24–30.
- Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull World Health Organ* 2011;89:864–72.
- Tahir C, Garbati M, Nggada HA, et al. Primary cutaneous aspergillosis in an immunocompetent patient. *J Surg Tech Case Rep.* 2011;3:94–96.
- Umbert JJ, Su WP. Cutaneous mucormycosis. *J Am Acad Dermatol.* 1989;21:1232–1234.
- Chander J, Kaur J, Attri A, et al. Primary cutaneous zygomycosis from a tertiary care centre in north-west India. *Indian J Med Res.* 2010;131: 765–770.
- D'Antonio D, Pagano L, Girmenia C, et al. Cutaneous aspergillosis in patients with haematological malignancies. *Eur J Clin Microbiol Infect Dis.* 2000;19:362–365.
- Chang MR, Taira CL, Paniago AM, et al. Study of 30 cases of histoplasmosis observed in the Mato Grosso do Sul State, Brazil. *Rev Inst Med Trop Sao Paulo.* 2007;49:37–39.
- Buitrago MJ, Gonzalo-Jimenez N, Navarro M, et al. A case of primary cutaneous histoplasmosis acquired in the laboratory. *Mycoses.* 2011;54: e859–e861.
- Tesh RB, Schneidau JD Jr. Primary cutaneous histoplasmosis. *N Engl J Med.* 1966;275:597–599.
- Tosh FE, Balhuizen J, Yates JL, et al. Primary cutaneous histoplasmosis. Report of a case. *Arch Intern Med.* 1964 ; 114:118–119.
- Weinberg GA, Kleiman MB, Grosfeld JL, et al. Unusual manifestations of histoplasmosis in childhood. *Pediatrics.* 1983;72:99–105.
- Butler JC, Heller R, Wright PF. Histoplasmosis during childhood. *South Med J.* 1994;87:476–480.
- Bonifaz A, Carrasco-Gerard E, Saul A. Chromoblastomycosis: clinical and mycologic experience of 51 cases. *Mycoses.* 2001;44:1–7.
- Mabeza GF, Macfarlane J. Pulmonary actinomycosis. *Eur Respir J* 2003;21: 545–51.
- Bose M, Ghosh R, Mukherjee K, Ghoshal L. Primary cutaneous actinomycosis: a case report. *J Clin Diagnost Res* 2014;8: YD03.
- Naggie S., Perfect J. R. Molds: hyalohyphomycosis, phaeohyphomycosis, and zygomycosis. *Clin. Chest Med.* 2009;30:337–353.
- Sangoi A. R., et al. 2009. Challenges and pitfalls of morphologic identification of fungal infections in histologic and cytologic specimens: a ten-year retrospective review at a single institution. *Am. J. Clin. Pathol.* 131:364–375.
- Schofield C. M., et al. 2007. Correlation of culture with histopathology in fungal burn wound colonization and infection. *Burns* 33:341–3346.
- Tarrand J. J., et al. Diagnosis of invasive septate mold infections: a correlation of microbiological culture and histologic or cytologic examination. *Am. J. Clin. Pathol.* 2003; 119: 854–858.
- Meersseman W, Vandecasteele SJ, Wilmer A, Verbeken E, Peetermans WE, Van Wijngaerden E. Invasive aspergillosis in critically ill patients without malignancy. *Am J Respir Crit Care Med.* 2004; 170:621–625.
- Tortorano AM, Dho G, Prigitano A, et al. Invasive fungal infections in the intensive care unit: A multicentre, prospective, observational study in Italy (2006–2008). *Mycoses.* 2012; 55:73–79.
- Taccone FS, Van den Abeele AM, Bulpa P, Misset B, Meersseman W, Cardoso T, Paiva JA, Blasco-Navalpotro M, De Laere E, Dimopoulos G, Rello J, Vogelaers D, Blot SI; AspICU Study Investigators. Epidemiology of invasive aspergillosis in critically ill patients: Clinical presentation, underlying conditions, and outcomes. *Crit Care.* 2015; 19:7.
- Schall KP. Actinomycosis, actinobacillosis and related diseases. In: Borriello SP, Murray PR, Funke G. Topley and Wilson's microbiology and microbial infections. 9th ed. Vol. 3. Bacterial Infections. Great Britain: Arnold; 1998. pp 777–798.
- Chaudhry SI, Greenspan JS. Actinomycosis in HIV infection: a review of a rare complication. *Int J STD AIDS.* 2000; 11(6):349–55.
- Lustig S. Actinomycosis: etiology, clinical features, diagnosis, treatment, and management. *Infect Drug Resist.* 2014;7:183–97
- Mabeza GF, Macfarlane J. Pulmonary actinomycosis. *Eur Respir J* 2003;21: 545–51.
- Arseculeratne SN. Recent advances in rhinosporidiosis and *Rhinosporidium seeberi*. *Indian J Med Microbiol* 2002;20:119–31.
- Kumari R, Nath AK, Rajalakshmi R, et al. Disseminated cutaneous rhinosporidiosis: varied morphological appearances on the skin. *Indian J Dermatol Venereol Leprol.* 2009;75:68–71.
- Thappa DM, Venkatesan S, Sirka CS, et al. Disseminated cutaneous rhinosporidiosis. *J Dermatol.* 1998;25:527–532.
- Abud L, Pereira JC. Rhinosporidiose nasal—relato de quarto caso e revisão de literatura. *Arq Interm Otorinol.* 2007;11:428–435.
- . Deshpande AH, Agarwal S, Kelkar AA. Primary cutaneous rhinosporidiosis diagnosed on FNAC: a case report with review of literature. *Diagn Cytopathol.* 2009;37:125–127.
- Padmanaban KG et al. *Int J Res Dermatol.* 2016;2(40):135–138.
- Minotto R, Bernardi CD, Edelweiss MI, Scroferneker ML: Chromoblastomycosis: a review of 100 cases in the state of Rio Grande do Sul, Brazil. *J Am Acad Dermatol* 2001; 44:585–592.
- McGinnis MR. Chromoblastomycosis and phaeohyphomycosis: new concepts, diagnosis, and mycology. *J Am Acad Dermatol.* 1983;8:1–16.
- Nishimoto K, Yoshimura S, Honma K. Chromomycosis spontaneously healed. *Int J Dermatol.* 1984;23:408–410.
- Elgart GW. Chromoblastomycosis. *Dermatol Clin.* 1996;14:77–83.
- Al-Doory Y, Pairon R. A bibliography of chromomycosis. *Mycopathol Mycol Appl.* 1974;54:91–109.

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44. Rubin HA, Bruce S, Rosen T, et al. Evidence for percutaneous inoculation as the mode of transmission for chromoblastomycosis. *J Am Acad Dermatol.* 1991;25:951–954.
 45. Eidbo J, Sanchez RL, Tschen JA, et al. Cutaneous manifestations of histoplasmosis in the acquired immune deficiency syndrome. *Am J Surg Pathol.* 1993;17:110–116.
 46. Bellman B, Berman B, Saska H, et al. Cutaneous disseminated histoplasmosis in AIDS patients in south Florida. *Int J Dermatol.* 1997;36.
 47. Bonifaz A, Cansela R, Novales J, et al. Cutaneous histoplasmosis associated with acquired immunodeficiency syndrome (AIDS). *Int J Dermatol.* 2000;39:35–38.
 48. Cunha VS, Zampese MS, Aquino VR, et al. Mucocutaneous manifestations of disseminated histoplasmosis in patients with acquired immunodeficiency syndrome: particular aspects in a Latin-American population. *Clin Exp Dermatol.* 2007;32:250–255.

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