Research Article

Subcutaneous phaeohyphomycosis: a clinicopathological study

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Received: 02 September 2014

Accepted: 22 September 2014

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ABSTRACT

Background: Phaeohyphomycosis is a subcutaneous or systemic infection characterized histologically by dark-colored fungal hyphae. With the increasing number of immunocompromised patients, the incidence of the disease has increased recently. The objective of the study is to emphasize the role of histopathology in the diagnosis of phaeohyphomycosis.

Methods: The biopsy specimens of seven cases of subcutaneous phaeohyphomycosis were examined using routine and special stains. The clinical presentation in these cases was also evaluated.

Results and Conclusions: Diagnosis was made in all cases by demonstration of fungal structures. Histopathology is an important tool in the diagnosis of phaeohyphomycosis. Phaeohyphomycosis should be considered in the differential diagnosis of suppurative granulomatous inflammation presenting as subcutaneous nodules. Fine needle aspiration cytology can also be used as a diagnostic method.

Keywords: Phaeohyphomycosis, Dematiaceous fungi, Subcutaneous

INTRODUCTION

Phaeohyphomycosis is a mycotic infection of humans and lower animals caused by a number of dematiaceous (brown-pigmented) fungi, characterized by the development of dark colored hyphae. Clinical forms of phaeohyphomycosis range from localized infections involving the skin and subcutis to invasive lesions involving paranasal sinuses, eyes, bones or central nervous system. Subcutaneous phaeohyphomycosis can clinically present as papulonodules, cysts or abscesses. 109 species classified in 60 genera are known to cause phaeohyphomycosis. In India, commonly associated genera are *Exophiala*, *Phialophora*, *Cladosporium*, *Curvularia*, *Fonsecaea* and *Alternaria*.^{1,2} Subcutaneous infections usually occur following the traumatic implantation of fungal elements from contaminated soil, thorns or wood splinters.

Histopathological examination of surgical specimens is necessary to differentiate between chromoblastomycosis and phaeohyphomycosis. Chromoblastomycosis is

another type of dematiaceous fungal infection which is characterized by the presence in tissue of brown pigmented, planate-dividing, rounded sclerotic bodies. In phaeohyphomycosis, the tissue morphology of the causative organism is mycelial.^{3,4}

Here we present clinical, cytological and histopathological features of seven cases of phaeohyphomycosis that presented as subcutaneous nodules mostly overexposed areas. To the best of our knowledge, this is the first series of subcutaneous phaeohyphomycosis from India.

METHODS

This study was conducted during the period of August 2006-December 2013. The clinical details were obtained from the case files of patients. Fine needle aspiration cytology (FNAC) was done only in one case and was diagnostic. Excision biopsy was done in all the cases. The surgical specimens were processed using routine technique and sections were examined using hematoxylin

and eosin stain. Multiple deeper sections were studied in those cases where the organisms could not be identified in the initial sections. Special stains like periodic acid Schiff reagent (PAS) and Gomori's methenamine silver were also done.

RESULTS

The clinical details are given in Table 1.

The majority of the patients were in the seventh and eighth decades of life. There was a male predominance. All the patients presented with slow growing masses in the extremities. The duration of the disease ranged from 1 year to 5 years. Three patients were diabetic. History of trauma could not be elicited in any case.

FNAC done in one case showed necrotizing granulomatous inflammation with a few pigmented hyphae. The gross specimens ranged in size from 1 cm to 3 cm (Figure 1). The sections studied from all cases showed cystic areas with suppurating granulomas surrounded by a thick fibrous capsule (Figure 2). The center of the lesion showed necrotic debris mixed with neutrophils. The granulomas were composed of epithelioid cells, histiocytes, giant cells of foreign body and langhan types and neutrophils. The organisms were found within the cyst cavity usually inside the histiocytes (Figure 3). The hyphae often had

irregularly placed branches and showed constrictions around their septae. Pigment was not always obvious. Special stains like PAS highlighted the hyphae (Figure 4).

Figure 2: Microscopy showing cystic area with suppurating granulomatous reaction (H and E, ×40).

Figure 3: High power showing the hyphal structures (H and E, ×400).

Figure 1: Gross specimen.

Figure 4: Hyphae highlighted by periodic acid schiff (PAS) stain (PAS, ×400).

DISCUSSION

Dematiaceous fungi are characterized by their dark pigmentation derived from the deposition of melanin in their cellular wall. The major infection patterns, typically based on histological findings, are grouped into three broad classes: Chromoblastomycosis, phaeohyphomycosis and eumycotic mycetoma. The three entities are distinguished by their morphology in tissue sections. Eumycotic mycetoma is characterized by grains and chromoblastomycosis by the presence of sclerotic bodies or muriform cells. Phaeohyphomycosis is characterized histopathologically by the presence of septate hyphae, pseudohyphae and yeasts.⁴⁻⁶ Some fungi can cause mycetoma or chromoblastomycosis in one patient while in another patient it can cause phaeohyphomycosis. This depends on the response of the inciting agent within the host.⁷⁻¹⁰

The term phaeohyphomycosis was introduced by Ajello in 1974.¹¹ It can be caused by many different organisms and clinical presentations vary.¹² The classification proposed by McGinnis in 1983 was later modified by Rippon.^{4,9,13} Phaeohyphomycosis can be divided into five types according to this classification - superficial: Black piedra and tinea nigra; cutaneous: Dermatophytosis and onychomycosis; mycotic keratitis; subcutaneous or phaeohyphomycotic cyst; invasive, systemic and cerebral.

The commonest type of lesions is subcutaneous cysts or abscesses. Patients are usually adults. The clinical manifestation is typically a discrete, asymptomatic, well-encapsulated subcutaneous mass that rarely involve muscle or bone. It can be a solid mass, cyst or abscess. If left undetected, the lesion grows so slowly and becomes chronic. The overlying epidermis is usually unaffected, and formation of a sinus tract or ulceration is rare. Uninvolvement of epidermis is helpful in the differential diagnosis from mycetoma that is characterized by draining sinus tracts with granules. Lymph node involvement and systemic spread are also very rare.

Other clinical differential diagnoses include ganglion cyst, epidermal inclusion cyst, baker cyst, foreign body granuloma, erythema nodosum and benign neoplasms like lipoma and neurofibroma. These entities can be differentiated from phaeohyphomycosis by histopathologic examination.

All the cases in this series presented with cystic swellings in the extremities of long duration mimicking benign neoplasms or cysts. One case presented with multiple lesions. The patients were in the sixth, seventh and eighth decades. Zieher and Connor¹⁴ reviewed the clinicopathologic features of 25 cases of phaeomycotic cysts. Almost three-fourths of their cases were located on or near the hands or feet. There was a history of preceding trauma in four patients. It usually occurs in people who are not overtly immunosuppressed, but immunosuppression does increase the risk of infection.¹⁵ Out of our seven cases, three were diabetic. Three of the seven patients reported by Kempson and Sternberg¹⁶ also had diabetes.

The diagnosis of subcutaneous phaeohyphomycosis depends on histologic examination and culture.¹⁷ A positive culture will show a non-specific black morphology which makes the identification of an organism difficult. Histopathology plays a paramount important role in the diagnosis of phaeohyphomycosis. A positive histologic examination reveals the fungal structures in the wall of the abscess. The presence of hyphae separates it from other clinical types of disease involving dematiaceous fungi where the tissue morphology of the organism is a grain as in mycotic mycetoma or sclerotic body as in the chromoblastomycosis. FNAC can also be used in the diagnosis in certain cases if the fungal structures with typical morphology can be demonstrated in the smears.

CONCLUSION

Phaeohyphomycosis should be considered in the differential diagnosis of suppurating granulomatous lesions presenting as cutaneous or subcutaneous cysts or abscesses. As the pigment may not always be evident, it has to be differentiated from other fungal organisms like aspergillosis that is also based on morphology of the hyphae. Fungal stains are useful in highlighting the morphology. Hence, histopathology is an important diagnostic tool in the differential diagnosis of subcutaneous nodules. FNAC can also be useful in some cases.

ACKNOWLEDGMENTS

We would like to acknowledge all surgeons who contributed the specimens for this study. We are also grateful to the dean and the CEO of the institution for the support given.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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DOI: 10.5455/2349-2902.isj20141106

Cite this article as: Abraham LK, Joseph E, Thomas S, Matthai A. Subcutaneous phaeohyphomycosis: a clinicopathological study. Int Surg J. 2014;1:140-3.