

Diagnosis and Treatment of Conidiobolomycosis: A Review of 75 Cases from the Indian Subcontinent

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ABSTRACT

Introduction: Conidiobolomycosis is a subcutaneous rhinofacial-zygomycosis caused by *Conidiobolus* spp. Its epidemiology in the Indian subcontinent is not well understood.

Aim: The aim of this study was epidemiological characterisation of conidiobolomycosis in the Indian subcontinent.

Materials and Methods: We conducted a review of literature using the terms “conidiobolomycosis”, “conidiobolus”, “entomophthoromycosis” and “entomophthoromycosis” in the Pubmed database combined with the following: India and publication language (English).

Results: A total of 75 cases of conidiobolomycosis were reported from 12 states of India, between October 1966 and December 2017, who presented with centropacial swelling

(males-62, females-13). The mean age of presentation was 35 years. Majority of the patients were immunocompetent with only one patient being immunosuppressed (acute leukaemia). A total of 21 patients were diagnosed only on the basis of culture, while the rest of them were diagnosed either on histopathology alone (n=33) or a combination of histopathology and culture (n=21). Saturated solution of potassium iodide (SSKI) was the most common drug (alone or in combination) used for treatment. Except one mortality, which was unrelated to the disease, all patients (n=56) responded to therapy.

Conclusion: Conidiobolomycosis is reported from most parts of the country, primarily in immunocompetent males and has an excellent response to anti-fungals.

Keywords: *Conidiobolus coronatus*, *Conidiobolus incongruus*, Entomophthoromycosis

INTRODUCTION

Conidiobolomycosis is a chronic subcutaneous rhino facial entomophthoromycosis [1]. Although, it is histopathologically indistinct from *Basidiobolus* spp., the other genera in the order entomophthorales, both of them are clinically and mycologically separate entities. There are three main species in the *Conidiobolus* genera-*C.coronatus*, *C.incongruus* and *C. lamprauges*. A new species, *C.thermophilus* has been isolated from the environment in India, but no human cases have been reported [2]. It is an uncommon disease, with few cases being reported from the tropical and subtropical zones of Africa, Asia and Americas [1]. The epidemiology of this disease in India is not well understood as most of the literature is in the form of case reports. Thus, the purpose of this study was to perform a systematic review of clinico-epidemiological characteristics of conidiobolomycosis cases from India.

MATERIALS AND METHODS

We conducted a comprehensive search of English medical literature via the PubMed database to search for articles between October of 1966 and December of 2017. We used “conidiobolomycosis”, “conidiobolus”, “entomophthoromycosis” and “entomophthoromycosis” as the search terms. The search terms in the Medline database were combined with the following: India and publication language (English) and subject (human). The titles, affiliations, and abstracts of the selected articles were reviewed. Compatible clinical symptoms and either histopathology or culture positivity was taken as conidiobolomycosis. Those reports with at least the following details were included-state/region of residence where the case was reported, age, sex, immune status of the patient, diagnostic modality, treatment received and response to the treatment. Cases of mucormycosis, basidiobolomycosis and any other fungi were excluded. Repeated reports and non-case studies were excluded.

RESULTS

A total of 307 articles were included for title/abstract screening. Out of this, 282 articles were excluded based on the inclusion and exclusion criteria. A total of 27 studies were included for full text review. A total of 75 cases of conidiobolomycosis were found who presented with centropacial swelling [3-29]. Most number of cases were reported from West Bengal, Punjab, Delhi and Tamil Nadu. Male: female distribution was 62:13. The mean age of presentation was 35 (SD-14) years.

Majority of the patients were immunocompetent with only one patient being immunosuppressed (acute leukaemia) [7]. Most of the patients were diagnosed on histopathology alone (n=33) while culture alone was positive in 21 patients. Rest 21 patients were identified by a combination of histopathology and culture. Of the 58 patients, whose treatment details were known, only 22 patients were treated with monotherapy while the rest of 36 patients were treated with various combination of drugs. Majority of the patients responded to the therapy (n=56) with mortality reported in only one patient (Acute leukaemia patient) [7]. Follow-up details were not mentioned for 14 patients while four were lost to follow-up. The state-wise distribution is tabulated in [Table/Fig-1].

DISCUSSION

Conidiobolomycosis is a rare disease that has been reported from tropical areas around the world. A total of 75 cases were reported from India in a time span of over 50 years. It was reported from most parts of the country (12 states). The germination of *Conidiobolus* spp. requires high amount of humidity and this is probably the reason why majority of the cases were reported from the hot and humid states of West Bengal, Tamil Nadu and Punjab [1]. It is a chronic inflammatory granulomatous disease that involves the nasal mucosa and presents as nasal obstruction and centro-facial swelling of the nose [1]. It is seen

State	No.	Gender	Age range (in years)	Diagnosis	Treatment	Follow-up
Himachal Pradesh [8]	1	M1	20	C-1	SK-1	R-1
Delhi [7,12,13,27,28]	12	M11, F1	1-70	H-11, C 1	A-1, AFSI-1, ASI-1, S-2, SI-2, K-1, SF-3, SK-1	R-10, NR-1, LFU-1
Punjab [9,11]	15	M13, F2	25-50	H-10, H+C-5	SI-10, S-1, NM-3, AK-1	R-14, LFU-1
Uttar Pradesh [11,21,22],	4	M4	16-50	H-1, H+C-3	ASI-1, S-1, A-1, SI-1	R-4
Uttarakhand [10]	1	M	18	H+C-1	IT-1	R-1
Assam [11]	1	M	27	H+C-1	SC-1	R-1
Orissa [5,19]	2	M2	19-45	H+C-2	S-1, SI-1	R-2
West Bengal [3,14-16]	20	M18, F2	20-65	H-1, C-17, H+C-2	SKC-1, SFKC-1, S-5, SK-2, SF-2, SI-1, NM-8	R-12, NM-8
Maharashtra [25]	1	M	20	H+C-1	I-1	R-1
Karnataka [23,24,26]	6	M3, F3	22-50	H-6	I-1, A-1, C-1, NM-3	R-2, LFU-1, NM-3
Kerala [18]	1	M	60	H+C-1	SF-1	R-1
Tamil Nadu [4,6,11,17,20,29]	11	M6, F5	15-55	H-4, C-2, H+C-5	IT-1, S-4, SC-2, F-1, NM-3	R-7, LFU-1, NM-3

[Table/Fig-1]: State wise distribution of cases of conidiobolomycosis from October 1966- December 2017 in India.

M: Male; F: Female; H: Histopathology; C: Culture; A: Amphotericin B; S: Saturated solution of potassium iodide; K: Ketoconazole; F: Fluconazole; I: Itraconazole; T: Terbinafine; C: Cotrimoxazole; R: Response present; NR: No response present; LFU: Loss to follow-up; NM: Not mentioned

in immunocompetent individuals and no known risk factors are described. Out of the 75 cases in our review, except one, all cases were immunocompetent [7]. It is hypothesised that the acquisition of spores of *Conidiobolus* spp. occurs via respiratory route or after minor trauma [1]. Males in the third and fourth decades of their life having more likelihood of being in contact with spores are most commonly affected [9,15,16].

Since, it is acquired by inhalation, the disease usually starts with the involvement of nasal cavity (unilateral to bilateral) and later extends to the surrounding area leading to facial swelling. The diagnosis of conidiobolomycosis is usually based on clinical presentation and the histopathology alone [27,28]. The culture of the causative fungus is confirmatory, although often unsuccessful. Most of the cultures was identified as *C. coronatus*, except one, which was identified as *C. incongruus* based on the culture and micro-morphological features (non-villose conidia) [8]. Histopathologically, aseptate hyphae along with granulomatous infiltrate consisting of eosinophils and multinucleated giant cells are seen. The star like eosinophilic projections has been described as Splendore hoespli phenomenon [1]. Splendore hoespli phenomenon is described with other fungal and parasitic diseases, but presence of aseptate hyphae along with this phenomenon is usually enough to make a diagnosis of entomophthoromycosis. Although, aseptate hyphae is also seen with mucormycosis, but splendore hoespli phenomenon is rarely described in mucormycosis.

The treatment modalities include either surgical excision or medical treatment. In a meta-analysis by Choon SE et al., it was observed that, once diagnosed, conidiobolomycosis is a fairly easy disease to treat with a very good response rate (83%), irrespective of the anti-fungals used [30]. In the reported cases that we reviewed from India, most of the cases had good response with anti-fungals. We observed that SSKI followed by itraconazole were the most commonly used drug either alone or in combination. In absence of clinical trials comparing the efficacy of the drugs, it would be difficult to classify SSKI or itraconazole as the preferred drug for treatment [15]. Although, the response can be evident in as early as one week, the total duration of therapy has not been clearly defined.

CONCLUSION

Conidiobolomycosis should be considered among middle aged immunocompetent males, presenting with painless centofacial swelling and symptoms of nasal obstruction. Culture or presence of aseptate hyphae and splendore hoespli phenomenon on histopathology helps in clinching the diagnosis in most cases. It can be treated with azoles or SSKI with a good response rate. We report

this review of literature to bring a rarely diagnosed but very easily treated fungus into the light from the Indian perspective.

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Date of Submission: **Nov 03, 2018**

Date of Peer Review: **Jan 03, 2019**

Date of Acceptance: **Jan 07, 2019**

Date of Publishing: **Mar 01, 2019**

FINANCIAL OR OTHER COMPETING INTERESTS: None.