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Magnusiomyces capitatus : Rising Colonisation, A Concern?

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ABSTRACT

Background: *Magnusiomyces capitatus* is an emerging yeast that has been increasingly isolated from clinical samples nowadays which warrants the need for surveillance of its isolation, clinical significance as well as drug resistance**. Material and Methods:** The present observational study was conducted (January 2016 to June 2017) on various clinical samples. All isolates confirmed as *Magnusiomyces capitatus* by MALDI-TOF MS were included in the study. The antifungal susceptibility testing was done as per the CLSI guidelines. **Results:** Among 4038 samples, 37 *M. capitatus* were isolated. All these strains were from pulmonary samples. The male: female ratio was 2.3:1. The age range was 21 -85 years. Risk factors were tuberculosis (35.1%), COPD (16.2%), diabetes mellitus (10.8%), carcinoma (5.4%), immunosuppressive drug therapy (5.4%) and HIV (2.7%). MIC values were very high for caspofungin and fluconazole in all of our isolates. **Conclusion:** *M. capitatus* is establishing itself as an emerging pathogen and so, should not be ruled out just as an insignificant finding in mycology laboratories.

INTRODUCTION

Magnusiomyces capitatus, telemorph of *Saprochaeta capitata*, previously known as *Blastoschizomyces capitatus*, *Geotrichum candidum*, and *Trichosporon candidum* is an ascomycetous yeast [1]. It forms blastospores, true hyphae, and annelloconidia which look like arthrospores so is easily confused with arthrosporic yeast like Trichosporon and Geotrichum [2].

Known to be isolated from environmental sources like wood and soil and also from the human commensal flora, this has been reported from clinical samples mainly from Europe, namely Italy, Spain, and France, and some from India and other Asian countries [1, 2, 3, 4]. The infection with this yeast was majorly found in the immunocompromised host, in neutropenic patients with hematologic malignancies but in many instances, it has also been isolated from immunocompetent hosts also [5]. Tanabe *et. al.* have reviewed such cases in immunocompetent patients with the recovery of *Magnusiomyces capitatus* from respiratory samples, five of whom were from India [5]. He referred to this group of patients as 'immunocompetent'.

Ours is an observational study of *Magnusiomyces capitatus* isolated from respiratory samples which was started after the sudden isolation of this yeast, starting from November 2015, which were not isolated earlier. Though a pathogenic role could not be established but we recorded the associated risk factors in these patients and also performed the antifungal susceptibility to understand the epidemiology of this fungus. Colonization is the first step for the making of a pathogen in a favorable setting with risk factors, which was our concern [5]. A major concern with this fungus is its inherent resistance to caspofungin and quite high MICs for fluconazole which are mostly the drug of choice in yeast infections [1, 2]. The mortality rate with this fungus has been reported to be quite high despite the antifungal treatment [2]. Prompt and accurate identification is necessary to provide the targeted treatment in an infectious state. PCR sequencing of internal transcribed spacer and/ or matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) is considered accurate in identifying this fungus [5]. So in this study, we present the risk factors associated and antifungal susceptibility profile of *Magnusiomyces capitatus* isolated from pulmonary samples.

METHODOLOGY:

The present observational study was conducted in the Department of Microbiology over 18 months from January 2016 to June 2017. The study was conducted after obtaining ethical approval from the Ethical Clearance Committee of the Institute Government medical college and hospital, Chandigarh (GMC/IEC/2015/0056), and is a part of postgraduate thesis project. The present research was conducted based on the ethical guidelines for biomedical research on human subjects According to the Central Ethics Committee on Human Research of Indian Council of Medical Research, New Delhi, India, in 2006 [6] and the Declaration of Helsinki' of 2008 [7].

Various samples which were received in the mycology laboratory during this time were processed using standard mycological techniques [3]. All samples were initially examined microscopically by performing potassium hydroxide (KOH) wet mounts followed by putting culture on Sabouraud's dextrose broth and inoculation on two tubes of Sabouraud's dextrose agar (SDA) kept at 25ºC and 37ºC. The cultures were examined daily for one week. The yeast-like growth was further identified by standard mycological techniques namely morphology on cornmeal-tween 80 agar (Fig 1), color and colony characteristics on CHROM agar Candida medium (Hi-Media Laboratories, Mumbai, India), urease test and thermotolerance test at 42°C, growth in the presence of cycloheximide at 25°C [8]. The final identification of all these fungal strains as *Magnusiomyces capitatus* (*Saprochaeta capitata*) was done by MALDI-TOF Vitek MS (Biomerieux, France).

The antifungal susceptibility testing of the isolates was performed for amphotericin B, azoles namely fluconazole, voriconazole and echinocandins namely caspofungin, (procured from the Sigma- Aldrich) as per Clinical and laboratory standard institute (CLSI) micro broth dilution method M27-A3 [9]. Briefly, RPMI supplemented with 2% glucose was inoculated with 10^5 CFU/ml of yeast in flat-bottom trays with antifungal agents and incubated at 30◦C for 48 h. The reading was taken with the help of a spectrophotometer. Quality control strains used were *Candida parapsilosis* ATCC 22019 and *Candida krusei* ATCC 6258.

RESULTS AND DISCUSSION

RESULTS

A total of 37 *M. capitatus* were isolated over 18 months, all from pulmonary samples. During the said period, the number of pulmonary samples namely sputum, broncho-alveolar lavage

(BAL), bronchial washings, pleural fluid, etc received was 425. So, the prevalence of *M. capitatus* in pulmonary samples was calculated to be 37 (8.7%). The male: female ratio was 2.3: 1 (males being 26 and females11 in number). The age group affected varied from 21 years to 85 years with the median age being 61years. Most of the isolates (36) were from sputum samples with one isolated from broncho-alveolar lavage of a patient with MDR TB. Various underlying factors found to be associated are shown in Table 1. The risk factors associated with these patients were prior antibiotic therapy (100%), tuberculosis (35.1%), COPD (16.2%), diabetes mellitus (10.8%), carcinoma (5.4%), immunosuppressive drug therapy (5.4%), and HIV (2.7%).

Antifungal susceptibility test results are shown in Table 2. The isolates had low MIC values for amphotericin B and voriconazole but had high MIC values for fluconazole and caspofungin.

DISCUSSION

Magnusiomyces is a colonizer of the respiratory tract and gastrointestinal tract. However, recently, it has been identified to be an opportunistic pathogen as well. Serious systemic infections in form of fungemia by *Magnusiomyces* have been reported [10].

Mostly, the laboratories put this isolate in the category- yeast and do not go for further identification. Mycologically, it is a yeast-like fungus that grows on Sabouraud's dextrose agar. It is commonly confused with *Trichosporon* or *Geotrichum.* (Figure 1) However, it can be easily differentiated based on growth in presence of cycloheximide and its characteristic feature of the production of annelloconidia which in the routine laboratory can be well appreciated on Cornmeal tween 80 agar (Figure 1). It is urease negative and does not assimilate nitrogen. It assimilates glucose and galactose and does not ferment any sugars. It is capable of growing at a high temperature of 42^{o}C. As genetic sequencing is not easily available and is not cost-effective, MALDI-TOF MS can be a good option for the final identification of the isolates as observed by other authors too [11].

Mostly, in clinical samples, it has been isolated from respiratory specimens and that too sputum [2]. Similarly in our study, all isolates were from sputum except one, where it was isolated from broncho-alveolar lavage. It has long been considered a contaminant or colonizer of the respiratory tract. But its isolation in conditions such as diabetes, solid organ transplants, endocarditis, and chronic obstructive pulmonary disease should be considered

with caution, as it is emerging as a significant yeast pathogen. Initial respiratory colonization along with underlying lung pathology with decreased lung protection barriers can lead to infection [5].

In our study, about 72% of these patients were associated with risk factors/co-morbidities namely tuberculosis (35.1%), COPD (16.2%), diabetes mellitus (10.8%), carcinoma (5.4%), immunosuppressive drug therapy (5.4%) and HIV (2.7%). All (100%) of our patients had undergone at least one course of broad-spectrum antibiotic therapy in the last six months. A review on pulmonary cases of *M. capitatus* showed an association of 27.3% with tuberculosis and 54.5% with COPD [5].

There are still no guidelines regarding the importance of its isolation from respiratory samples especially sputum. Are they pathogenic in any way or do they simply represent colonization? If we consider them to be colonization only, there are few points regarding this to be considered. One, the normal flora is changing; two, there is a lack of specific clinical and radiographic findings associated with these patients making it extremely difficult to make a proper diagnosis or establish their pathogenicity; three, *M. capitatus* colonization may precede invasive infection and hematogenous dissemination. Four, the organism shows the presence of various virulence factors like slime production which help in escaping host immune response [4]. Fifth, it has also been reported as a breakthrough infection in patients on echinocandins [12]. Sixth, the yeast is not easy to identify mycologically in the isolates. Seventh; if not suspected or timely diagnosed, it may have serious complications as treatment choices are limited. The pathogen is considered inherently resistant to echinocandins and high MICs to fluconazole.

As observed in our isolates, the MIC to caspofungin was very high. Fluconazole, is an oral, cheap, and easy available antifungal is often used as first antifungal drug given in suspected patients but we found MIC values to be very high to fluconazole in all of our isolates (Table 2). Tanabe et al suggested azole compounds and amphotericin B as first-line agents but based on our MIC results this needs to be reconsidered [5]. Supram HS et al have also reported an MIC of 2µg/ml for amphotericin B and fluconazole for their seven isolates [2]. High MICs for fluconazole have also been reported by other studies [10, 13].

The present study has its main strength that we were able to pick up so many *M. capitatus* isolates which are usually missed. The limitation has been that it is primarily an observational

study in the laboratory set up and we were not able to follow these patients. Further studies where we can observe the therapeutic and clinical outcomes in such patients can be planned.

CONCLUSION:

M. capitatus is establishing itself as an emerging pathogen with difficulty in diagnosis and treatment both. Further studies correlating its isolation with the clinical condition are required before labeling it as only a colonizer.

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Conflict of Interest- None

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Figures:

Figure 1

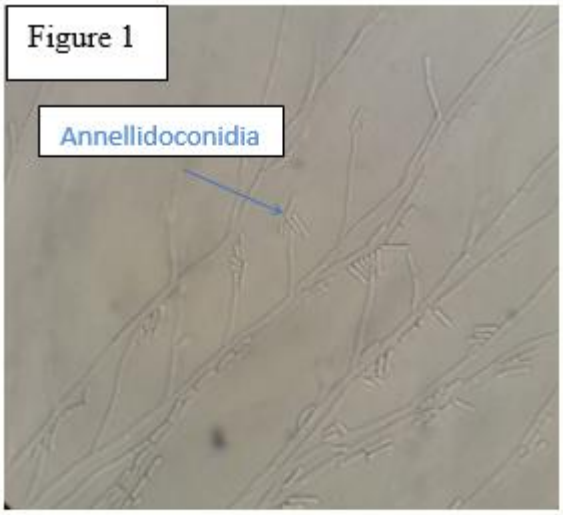

Figure 1:Annellidoconidia in clusters at the tip of pointed annelid in *Magnusiomyces capitatus* on Corn meal by Dalmau technique

Figure 2

Figure 2 :- Colony morphology of *Magnusiomyces capitatus* species on SDA.

Tables:

Table 1: Characteristics of patients with isolation of *Magnusiomyces capitatus*

Various characters	Total cases (37)
Age, years, median (range)	61 years (21-85 years)
Male, sex, n (%)	26 /37 (70%)
History of smoking, n (%)	11 / 37 (42%), all male
Department/ward, n (%)	Pulmonary, 27 /37 (73%)
Underlying disease:	27 (72.9%)
Tuberculosis	13(35.1%) Out of this MDR TB (2)
COPD (Chronic obstructive pulmonary disease)	6 (16.2%)
Diabetes mellitus	4(10.8%)
Carcinoma	2(5.4%)
Immuno-suppressive drugs/steroids	2(5.4%)
HIV	1(2.7%)
Specimen of isolation, n (%)	Sputum 36, BAL 1
Concomitant microorganism isolated, n(%)	6 (16.2%) namely *Klebsiella pneumoniae* (3), *Staphylococcus aureus* (2), *Enterococcus faecalis* (1)
Prior antibacterial/antibiotic therapy (last six months)	37
Prior antifungal therapy, n (%)	3 (8.1%)
Catheterization	7
Outcome (Mortality) of patients, n (%)	4 (10.8%). Not attributed to isolation of *Magnusiomyces capitatus* as such

Table 2: Antifungal susceptibility results of the *Magnusiomyces capitatus* isolates

Antifungal agent	**MIC Range**	**MIC50**	**MIC90**
Amphotericin B	0.0313-0.5	0.25	0.25
Fluconazole	2-32	8	8
Caspofungin	16-64	32	32
Voriconazole	0.0313-0.5	0.125	0.25