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Systemic Hylohyphomycosis caused by Acremonium Species, *Cylindrocarpon lichenicola* and *Apispora montagnei*

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ABSTRACT: The hyalohyphomycosis are a group of diseases caused by filamentous fungi that are present in tissues as hyaline septate hyphae. Apart from causing cutaneous infections, disseminated infections affecting particularly immune suppressed patients have been widely reported. Here, we report interesting cases of such infections, two due to *Acremonium* species and one each caused by *Cylindrocarpon lichenicola* and *Apispora montagnei*. These fungi were isolated from peripheral blood of the respective patients. The direct microscopic observations of the blood samples revealed hyaline, thin to thick, septate, branched mycelium in all the four cases. The patients were between the age group 20-48 years. Two were post operative cases, one with acuate renal failure and the other had mitral stenosis with pulmonary hypertension. *Acremonium* species and *Cylindrocarpon lichenicola* are known to cause infections in both immuno-competent and immuno-suppressed patients. However, *Apispora montagnei* is for the first time documented as causal agent of disseminatd infection. Emergence of such cases in contemporary medicine is alarming. It presents management problems and thus such cases be viewed cautiously by the clinicians.

Key words: Hylohyphomycosis, hyaline, disseminated, contemporary, immune suppressed.

I. INTRODUCTION

The term Hyalohyphomycosis was proposed by Ajello [1] and Mc-Ginnis in 1986 to accommodate mycotic infections in which the tissue form of the etiologic agents is septate hyphae with no pigment in the wall. It is usually causes infections affecting highly immunosuppressed patient. Hylohyphomycosis are many ranging from harmless saprophytic colonization to acute invasive disease. The list of opportunistic agents of hylohyphomycosis continue to grow as does the number of immunocompromised patients, however, mycoses also are manifested in patients who appear immunocompetent by current methods of detection[5]. Predisposing factors include prolonged neutropenia, especially in leukemia patients or in bone marrow transplant recipients, corticosteroid therapy, cytotoxic chemotherapy and to a lesser extent patients with AIDS. The typical patient is granulocytopenic and receiving broad spectrum antibodies for unexplained fever.

Apart from causing cutaneous infections, disseminated infections affecting particularly immunosuppressed patients have been widely reported. Cylindrocarpon genus contain 35 species is world spread isolated mostly from soil as an occasional human pathogen. Here we report interesting cases of such infections, two due to *Acremonium* species and one caused by *Cylindrocarpon lichenicola* and *Apispora montageni*. These fungi were isolated from peripheral blood of the respective patients. Important human pathogens included in this group are *Aspergillus, Penicellium, Fusarium, Scopulariopsis, Pscudallescheria, Scedosporium, Acremonium, Paecilomyces* and *Trichoderma* species [13,3,2,15]. Hyaline moulds uncommonly cause human disease. Most severe cases of hyalohyphomycosis occur in patient with hematologic malignancies or in solid organ transplant recipients. *Acremonium* species are primarily pathogens of plants and insects and only rarely cause invasive disease in humans [13]. The skin lungs and gastrointestinal tract are the apparent portals of entry *Acremonium* species cause infections ranging from posttraumatic to mycetoma in normal hosts [6,8]. *Cylindocarpon lichenicola* also known as *C. tonkinense Bugn*, is a hyaline filamentous fungus belonging to the hyphomycetes. Cylindrocarpon genus contain 35 species is world spread isolated mostly from soil as an associated human pathogen. It rarely infects humans, but is able to affect both immuno-competent and immunocompromised hosts.

It has been associated with corneal infections, disseminated infection, peritonitis in connection with continuous ambulatory peritoneal dialysis and cutaneous lesions [4,14,9]. *Acremonium* species and *Cylindrocarpon lichenicola* are known to cause infections in both immunocompetent and immuno suppressed patients. However *Apispora montageni* for the first time documented as causal agent of disseminated infection. *Apispora montagnei* is an ascomycete that is commonly isolated worldwide for a variety of soil types and from diverse dead plant material. Henrique pereira *et al* [7] investigated, the effect of culture conditions on the production of bioactive secondary metabolites by the endophytic fungus *Arthrinium* state of *Apispora montegnei* sacc.

Case Reports

Case-1: A 38 year old female was admitted in the hospital with the complaint of vomiting, giddiness and ulcers in the mouth. She was unconscious and had decreased renal output. Her blood urea-28 mg/dl, sugar creatinine-1-4mg/dl and blood sugar 180 pp. She was diagnosed as a case of Acute Renal Failure.

Case-2: A 22 year old female was admitted in the hospital for eight months amenorrhoea with labour pains, she had repeated urinary tract infection scissarian section was done 2 days before the date of collection of sample for cephalopelvic disproportion.

Case-3: A 20 year old female was admitted in the hospital for nine months amenorrhoea with labour pains. Caesarian section was done for cephalopelvic disproportion. She was primy.

Case-4: A 48 year old male was admitted in the hospital with the complaints of breathlessness and oedema all over the body and cough since last 4 months. On examination, diastolic murmur was present. Heart sound was loud bilateral crepetation present. X-ray showed cardiac enlargement. He was diagnosed as a case of Mitral Stenosis with pulmonary hypertension.

Case No.	Clinical Sample	Direct microscopic examination	Culture on SDA with Chloramphenicol
1	Blood	Positive	*Acremonium* species
2	Blood	Positive	*Acremonium* species
3	Blood	Positive	*Cylindrocarpon lichenicola*
4	Blood	Positive	Arthrinium State of *Apispora montagnei*

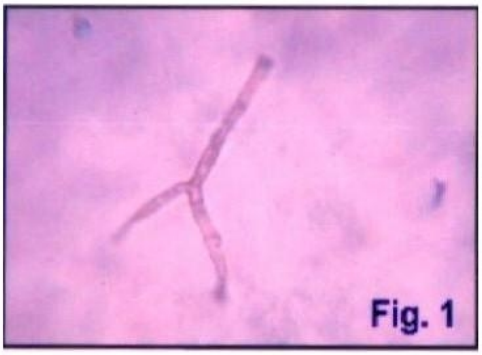
II. MATERIALS AND METHOD

The fungi were isolated from peripheral blood of the respective patients. 2 ml. of blood from the patient was collected by means of vein puncture using sterilized needle and syringe. The blood was immediately transferred to a previously sterilized bottle containing 3 ml of Sabouraud's dextrose broth and coated with heparin as anticoagulant. The bottle was incubated at $28\pm1^{o}C$ for 2-3 weeks. The direct microscopic examination was done by preparing smear of blood and staining it with lactophenol cotton blue solution. Sabouraud's dextrose agar medium was used for the primary isolation of fungus in culture from the blood sample. Approximately 5 ml of the SDA medium was poured in each test tube and sterilized in autoclave at $120^{o}C$ at 15 lbs pressure per square inch for 15 minutes and then slants were prepared. A loopfull of previously incubated blood sample of the patients was streaked on SDA slants with chloramphenicol and incubated at $28\pm1^{o}C$ for 7 days. The fungi were identified on the basis of thermotolerence, macro and micromorphological characteristics. *Apispora montagnei* was reffered to Dr. J. Guarro, Deptt of Microbiology, University of Barcelona, Spain for specific identification.

III. RESULTS

Direct microscopy of blood sample of case No.1 and 2 showing branched septate mycelium (Fig.1 and 2).

On SDA at $28^{o}C$ after 3 days of incubation, the colony was cream coloured, soft mucoid with wavy margin. Reverse of the colony was pale leuteous. The cells were ovoid and pseudohyphae were not observed in both the cases of *Acremonium* sp. Direct microscopy of *Cylindrocarpon lichenicola* showed brown septate and broad mycelium. Colonics on SDA at $28^{o}C$ after 7 days of incubation grew rapidly. It was cottony, fluffy, off white, regular and myceloid. Reverse of the colony was cinnamon to chesthut enormous radial folds were present. Mycelium was wide, hyaline and septate (Fig. 3).



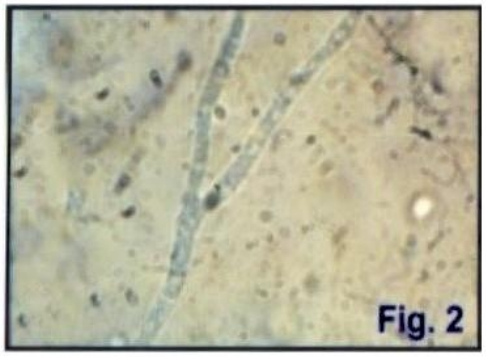


Fig. 1 & 2. D.M. of Blood Sample of Case No. 1 & 2 showing branched, septate hyaline mycelium (Cotton Blue Stained, 1000X). Fungi isolated *Acremonium* sp.

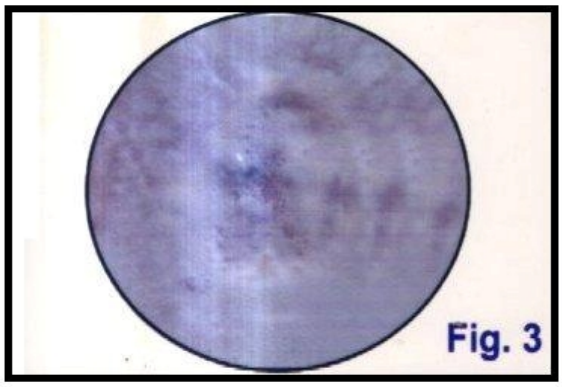


Fig. 3. Colony characteristics of case No.3 on SDA after 7 days of incubation at 28^{o}C Fungi isolated *C. lichenicola.*

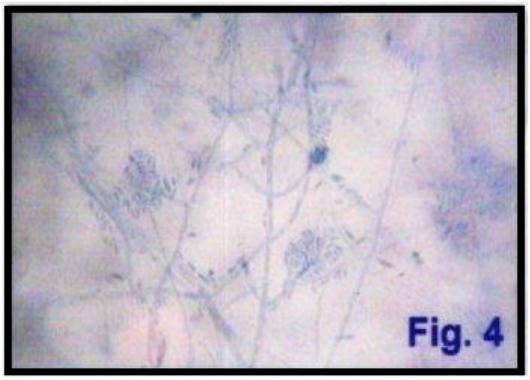


Fig. 4. Slide culture of case No. 3 in cotton blue stained, 400X Fungi isolated *C. lichenicola*.

Blood sample revealed mycelium which were septate and branched in the direct microscopic examination of *Apispora montagnei* (Fig. 4). On SDA medium after 7 days of incubation, the colony showed good growth at 28^{o}C.

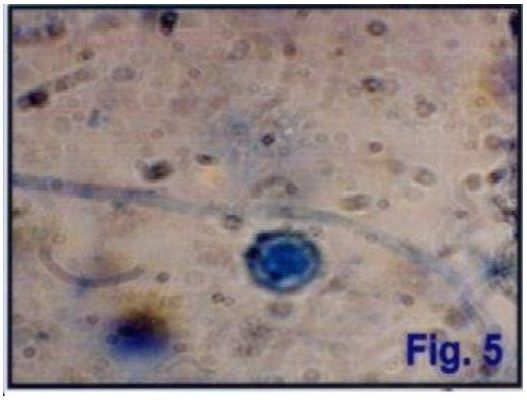


Fig. 5. D.M. of blood sample of Case No. 4 showing septate branched and hyaline mycelium in Cotton Blue stained.

The colony was fluffy, raised and the colour was white, brownish, reverse pigmentation of the colony was brownish in colour. Hyphae branched, colourless to oval or barrel shaped (Fig. 5).

IV. DISCUSSION

The hyalohyphomycosis are a group of disease caused by filamentous fungi that present in tissue as hyaline septate hyphae. Apart from causing cutaneous infections, over the past twenty years, disseminated infection affecting highly immunosuppressed patients has been widely reported. *Acremonium* sp. is a cause mycetoma and ocular infection in immuno-competent individual. The population at risk for disseminated infection includes cancer patient and transplant recipients. The present investigation documents an interesting case of *Cylindrocarpon lichenicola* isolated from blood sample of a post-operative patient.

Though this species is rarely isolated but is, however, reported to infect both healthy [10] and immunocompromised patients [9]. Another significant isolation from the blood sample is of *Apispora montagnei* in a patient with cardiac disease. This is possible the first report of disseminated infection due to *A. montagnei* which is reported to be a plant pathogen [12]. Rai S., *et al* 2012 [11] also reported two cases of chronic fungal sinusitis in immunocompetent adult male infected with with hylohyphomycosis, which are opportunistic soil saprophytes uncommon to humans.

V. CONCLUSION

Hylohyphomycoses mycotic infection have increased significantly on the global basis and is the clinical entity of great public health importance in modern era. A particular problem to these infections in their poor prognosis is a consequence of the combination of severe immunosuppressant and poor sensitivity of these fungi to available agents. Present study reports an interesting case of *Acremonium* sp. being isolated from the blood sample of a patient with acute renal failure. Infection due to hyalohyphomycosis is a major challenge for clinicians because their incidence has increased. The diagnosis is difficult and prognosis is poor. Emergence of such case in contemporary medicine is alarming. It presents management problems and thus such cases be viewed cautiously. To our knowledge *Apispara montagnei* is for the first time implicated as a human pathogen. Infection due to hyalohyphomycetes is a major challenge for several reasons: (i) Their incidence has increased; (ii) the diagnosis is largely based on the demonstration of tissue invasion, and (iii) The prognosis is poor because most therapeutic agents are ineffective and the host is usually severly immunocompromised.

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