

Fruiting bodies of *Aspergillus*: An unusual finding in histopathology

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ABSTRACT

A-62-year-old lady presented with complaints of cough, dyspnea and hemoptysis of 3 months duration. A radiological evaluation revealed a mass lesion in the left lung along with significant lymphadenopathy. With a clinical and radiological diagnosis of carcinoma of the lung, the patient was taken up for biopsy. The specimen consisted mainly of grey-white friable soft-tissue, which on histopathological evaluation showed small cell carcinoma, which was confirmed with immunohistochemistry. Apart from the carcinomatous component, many hyphae and fruiting bodies of *Aspergillus* were also seen. We are reporting this case because, though the finding of hyphal forms of *Aspergillus* is not so uncommon in lung biopsies, detection of fruiting bodies of *Aspergillus* in histopathological section is an extremely rare finding. The hyphal forms of *Aspergillus* can be confused with the hyphal forms of other fungi, but when fruiting bodies are present a definite diagnosis is possible at the histopathology level itself. We would also like to highlight that contamination should be excluded before labeling a case as Aspergillosis because of the potentially toxic medication implicated in the treatment.

KEY WORDS: *Aspergillus*, fruiting body, lung

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INTRODUCTION

Aspergillus is a ubiquitous fungus belonging to the ascomycete molds. The *Aspergillus* genus of molds was probably first described by Micheli in 1729.^[1] The name is thought to come from the similarity between fruiting heads of this particular fungus and the brush or aspergillum, used for sprinkling of holy water. The spores of the *Aspergillus* fungus are ubiquitous, usually introduced by inhalation and are frequent inhabitants of the human upper respiratory tract. *Aspergillus fumigatus* is the species most frequently isolated from patients with invasive or disseminated infections.^[2] Aspergillosis is the second most common opportunistic mycosis in patients with malignant diseases.^[3] The hyphal forms show regular, progressive, dichotomous branching at acute angles from

parent hyphae. The anamorphic (asexual) form produces conidial (fruiting) heads in situations of high oxygen tension such as pulmonary cavities, skin, bronchial mucosa etc. The finding of anamorph of *Aspergillus* in histopathology sections is however rare with only very few case reports in the literature.^[4,5]

CASE REPORT

A 62-year-old female patient who was an agriculturist presented to us in a critically ill-condition and had complaints of cough and hemoptysis since 3 months and also had respiratory distress at presentation. A chest X-ray was performed, which showed a left sided hilar mass. A computed tomography scan of the thorax revealed a moderately enhancing soft-tissue density lesion measuring 6 cm × 4.9 cm × 4 cm. in the left hilar region extending to apicoposterior segment of left upper lobe. A bronchoscopy was performed, which revealed a mass lesion in the left main bronchus. With a clinical and radiological diagnosis of lung carcinoma, a biopsy was carried out.

The specimen obtained for histopathological examination consisted of greywhite, friable soft-tissue aggregate measuring 0.5 cm × 0.5 cm. Examination of Hand E stained

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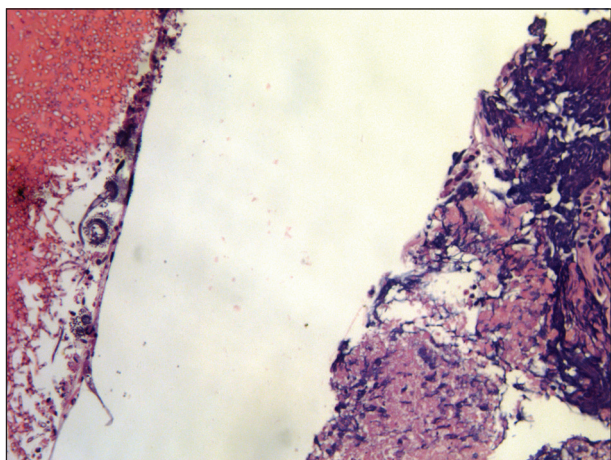


Figure 1: Hyphal form as well as fruiting bodies of *Aspergillus* species along with cluster of tumor cells (H and E, x100)

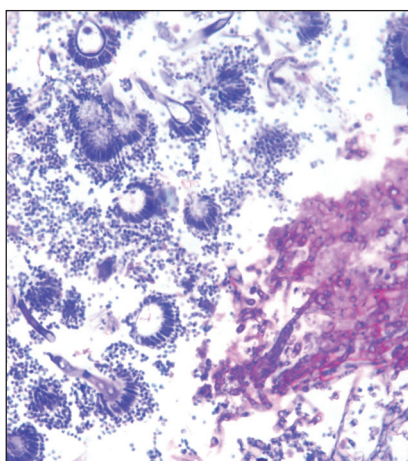


Figure 2a: Higher power view of hyphae and fruiting bodies of *Aspergillus* (H and E, x400)

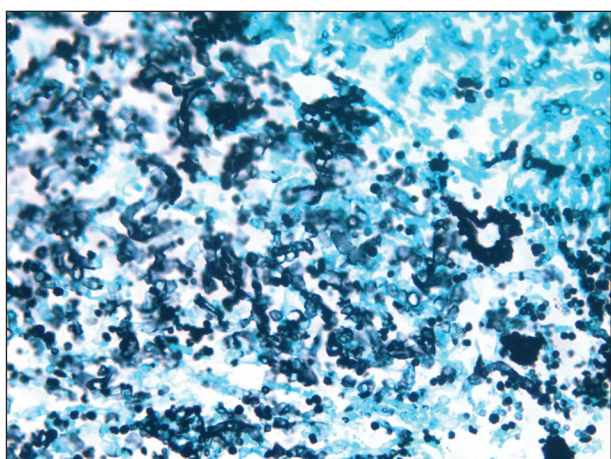


Figure 2b: Methenamine silver stain highlights the fungi (H and E, x400)

sections revealed mainly necrotic tissue and clusters of tumor cells with crush artefact [Figure 1]. Amidst the necrotic material were seen branching septate hyphae of *Aspergillus*. Apart from hyphal forms, many fruiting bodies

of *Aspergillus* were also seen [Figure 2a]. A methenamine silver stain was carried out, which highlighted the fungi [Figure 2b]. On immunohistochemistry, the tumor cells were positive for cytokeratin and synaptophysin. A diagnosis of small cell carcinoma of lung with co-existent *Aspergillosis* was made. Our patient was then lost to follow-up and hence culture and species identification could not be carried out.

DISCUSSION

Though classically hyphae of *Aspergillus* are described as acute branching septate hyphae, sometimes it becomes difficult to differentiate them from hyphal forms of other fungi such as *Pseudallescheria boydii*, the *Fusarium* Spp. and occasionally with the *Candida* spp. Thus, a microbiological isolation by culture is often required for confirmation, which considering the ubiquitous nature of *Aspergillus* is difficult to get. However when fruiting bodies of *Aspergillus* is seen diagnosis can be considered and even species sub typing can be attempted at the histopathology level.

Fruiting bodies (Conidia) of *Aspergilli* develop from mycelia in areas of high oxygen tension, or severe infections. They are not usually seen in histopathology sections. The fruiting body is composed of a vesicle and either 1 or 2 layers of phialides that produce conidia, and the morphology of the fruiting body may allow *Aspergillus* species to be subtyped *insitu*. However accurate species diagnosis requires confirmation by culture. The presence of a single row of phialides over the upper one-third of the vesicle is seen in *A. fumigatus* while *A. flavus* and *A. niger* have two rows of phialides covering the entire vesicle. Other species of *Aspergillus* may also show bi or mono-seriate heads; hence, species sub typing based on the number of row of phialides may not be accurate.

Veress *et al.* reported that two factors may play an important role in *Aspergillosis*.^[6] Secretion of a toxic substance by fungi that penetrates into tissues under appropriate conditions and secondly the induction of tissue necrosis caused by an immune mechanism. Most recent clinical classification of *Aspergillosis* has been put forth by Rowe-Jones and Moore-Gillon in 1994.^[7] These include non-invasive, invasive and destructive non-invasive types of *Aspergillosis*. Destructive non-invasive type has been further classified into *Aspergilloma*, fungus ball and mycetoma.

It is difficult to isolate *Aspergillus* in culture because of the ubiquitous nature of its spores. Hence, culture is often negative. No skin sensitivity or serum reactivity tests are useful because most of the affected patients are immunodeficient.^[8] Early diagnosis of invasive *Aspergillosis* may be possible in high-risk patients by using Galactomannan (GM) test. Serial screening of circulating GM, an epitopic determinant of several antigens secreted

by the *Aspergillus* early in its growth, has been shown to be sensitive and specific in the diagnosis of invasive aspergillosis. This test helps to spare febrile patients without evidence of fungal infection other than prolonged fever from unnecessary and potentially toxic therapy.

The diagnosis of Aspergillosis in humans is made after taking into consideration the clinical, radiological and microscopic findings. Our patient had two predisposing factors one of which was the underlying malignancy, which caused an immune compromised state and secondly her profession as an agriculturist, which offered a damp environment favorable for fungal growth. Our patient was lost to follow-up and did not report for treatment.

Early recognition of Aspergillosis is mandatory since it is a potentially life-threatening infection requiring an immediate intervention and treatment with toxic drugs.^[9,11] It is also essential to rule out contamination before labeling a case as Aspergillosis. There is a case report of detection of *Aspergillus* including the fruiting bodies in routine cervical Pap smear in a non-symptomatic lady.^[10] This case on further investigation and follow-up was found to be due to contamination. This report once again underlines the need for clinical correlation and ruling out contamination before labeling a case as *Aspergillus* infection.

Pulmonary Aspergillosis is a saprophytic infection caused by colonization of pre-existing cavitory lesions.

The cavitory lesions may result from treated tuberculosis, bronchiectasis, sarcoidosis, cysticfibrosis, emphysematous bullae and other necrotizing infections. There are case reports in the literature of Aspergillosis co-existing with lung cancer.^[12,13] The co-existence of these two pathologies is thought to be due to colonization of *Aspergillus* in bullous airspaces that were obstructed or contained within the tumor. Our case is that of small cell carcinoma of lung with co-existent Aspergillosis. Unlike other cases where the hyphal forms of the fungus were noted, in our case many

fruiting bodies were noted in the histopathologic sections which is a rare finding.

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