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CASE REPORT

A Unique Cytological Approach In Diagnosing A Case Of Invasive Aspergillosis Masquerading As Retro-Orbital Neoplasm

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ABSTRACT

Aspergillus is a fungal mould that is commonly present and may colonize the paranasal sinuses and lungs by virtue of large number of *Aspergillus* spores present in the inhaled air. Rare cases of invasive aspergillosis have been reported in immunocompetent individuals, although they are usually seen in immunocompromised individuals or diabetics.

The following is the description of a simple technique in the present case report of a young immunocompetent agricultural worker who presented with invasive aspergillosis as exophthalmos; where the diagnosis was made by isolating the pathogenic organism by employing the remnant material in the needle hub as the incubating material.

A 24 year old male presented to the ophthalmology OPD with the complaint of gradual and painless swelling of the right eye with accompanying loss of vision. A radiological opinion of orbital neoplasm was made, with differential diagnosis of benign fibrous histiocytoma and ?? lymphoma. A fine needle aspiration (FNA) was done and the May Grunwald Giemsa (MGG) stained smears revealed numerous foreign body type of giant cells, few epithelioid cell collections and scattered filamentous structures. To delineate the nature of the filamentous structures, Periodic acid Schiff (PAS) staining of the remaining smears was done, which showed that these filamentous structures were fragments of septate fungal hyphae with acute angle branching. A cytological diagnosis of fungal granulomatous lesion was given.

It was suggested that an attempt would be made to retrieve the fungal organism by means of culture from the remnant material in the hub of the needle which was used in the procedure. Both the needles were sealed and were sent to the mycology section of the microbiology department. A microbiological diagnosis of *Aspergillus flavus* was given.

The presentation of localized invasive aspergillosis can mimic infectious diseases such as mucormycosis and also neoplastic, vascular and neuro-ophthalmic diseases.

Key Messages

1. The presentation of localized invasive aspergillosis can mimic infectious diseases such as mucormycosis and also neoplastic, vascular and neuro-ophthalmic diseases.
2. This case is worth reporting because of its unusual presentation and the method employed to retrieve the fungal organism to conclusively reach a diagnosis. The exact causative organisms can be isolated from the remnant material in the needle hub, as observed in our study, which can in the end lead to specific managements.

Key words : *Aspergillus*, exophthalmos, needle hub , remnant.

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Introduction

Aspergillus is a fungal mould that is virtually ubiquitous. It may colonize the paranasal sinuses and lungs, as a large number of spores are present in the inhaled air. Under appropriate

conditions, the spores may become saprophytic within the host and multiply. Locally aggressive invasive fungal masses may develop, particularly if the host is severely immunocompromised. Rare cases have been reported in immunocompetent individuals, where it follows a chronic and slowly progressive course [3]. Aspergillosis often presents with vague complaints and clinical findings, making diagnosis difficult and subsequently, the treatment is delayed and the disease is accelerated [2]. The following is a case report of a young immunocompetent agricultural worker who presented with invasive aspergillosis as exophthalmos, where the diagnosis was made by isolating the pathogenic organism by employing the remnant material in the needle hub as the incubating material.

Case Report

A 24 year old male presented to the ophthalmology OPD with the complaint of gradual and painless swelling of the right eye, with accompanying loss of vision. On examination, the right eye had no perception of light. Further, the eye was found to be proptosed in an axial, lateral and downward direction [Table/Fig 1] (Figure-1 A, B). Slit lamp examination of the concerned eye showed pseudocornea formation. An ultrasound B-scan of the posterior segment was anechoic.

Apart from an eosinophilia (20%), the rest of his haematological, serological and biochemical profiles were within the normal range, including non reactive HIV and the Hepatitis B and C antigens. A CT scan of the orbit and paranasal sinuses revealed a moderately well defined, mildly enhancing mass lesion measuring 5x4.6x2cm in the retrobulbar region of right orbit involving intraconal and extraconal compartments along with loss of visualization of lateral wall of ethmoid sinus and a small polyp in maxillary sinus [Table/Fig 1](Figure 1 C). A radiological opinion of orbital neoplasm was made with differential diagnosis of benign fibrous histiocytoma and lymphoma. A fine needle aspiration (FNA) under radiological guidance was suggested to differentiate between the two. This was performed using 23G needle and two passes were given at two different sites.

The MGG stained smears revealed numerous foreign body type of giant cells, few epithelioid cell collections and scattered filamentous structures [Table/Fig 2] (Fig. 2 A, B). Periodic acid Schiff stain of the remaining smears showed these filamentous structures to be fragments of septate fungal hyphae with acute angle branching [Table/Fig 2](Fig. 2 C, D). A cytological diagnosis of fungal granulomatous lesion was given. No evidence of any orbital neoplasm was present.

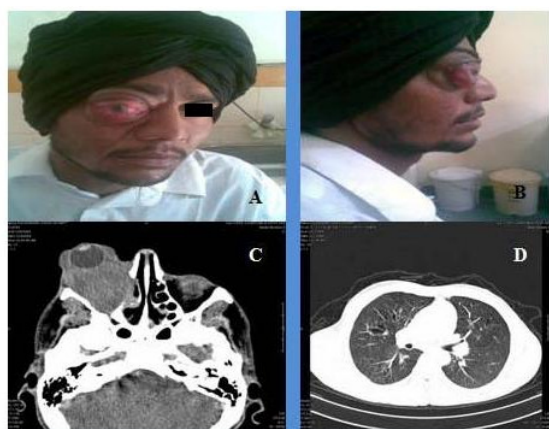
To reach a conclusive diagnosis and species identification for therapeutic purpose an intensive cross-departmental discussion was undertaken between the departments of pathology, microbiology, ophthalmology and maxillo-facial surgery and it was suggested that an attempt would be made to retrieve the fungal organism by means of culture from the remnant material in the hub of the needle used in the procedure. Both the needles were sealed and were sent to mycology section of microbiology department. The remnant in the hub of needle was taken with the sterile loop and inoculated in Sabouraud's dextrose broth. After overnight incubation subculture was done on Sabouraud's dextrose agar.

In view of the cytological findings a CT chest was further advised to rule out any evidence of allergic bronchopulmonary aspergillosis, which revealed central bronchiectasis and bronchocoele formation [Table/Fig 1] (Fig. 1 D).

Patient was then enquired for any past history of surgical procedure done in the nasal region owing to the absence of ethmoid bone on CT [Table/Fig 1](Fig. 1 C). He told about a surgery for nasal obstruction at another centre 2 years back, subsequent to which he was put on some long term oral treatment. Patient expressed his inability to procure any relevant documents regarding aforementioned treatment as they were lost over a period of time. Medical records retrieved from the other centre revealed that a polypectomy operation was done; the histopathological examination of the excised tissue suggested fungal infection for which he was put on anti-fungal therapy.

Meanwhile, the culture was kept at 22 degrees

and 37 degrees in separate BOD (biological oxygen demand) incubators. After 2 weeks velvety yellow to green colonies of fungal growth were obtained. The morphological characters were seen by preparing LCB (Lactophenol cotton blue) smears which showed, conidiophores of variable length, which were rough, pitted and spiny, the phialides were single and double covering the entire vesicle and pointing out in all directions. So a microbiological diagnosis of *Aspergillus flavus* was given. The case was finally diagnosed as that of invasive aspergillosis with an unusual presentation.



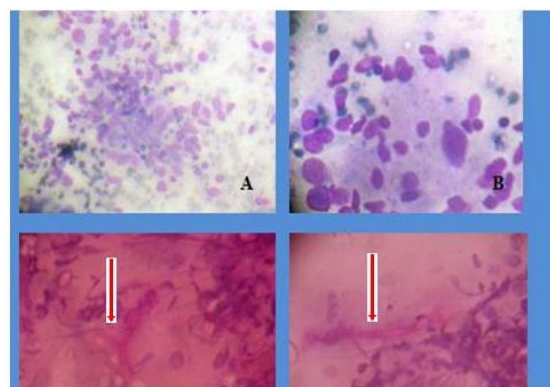
(Table/Fig 1)

(Fig. 1 A) Clinical Picture Of The Patient Showing Protrusion Of The Eye Ball (Front View)

(Fig. 1 B) Clinical Picture Of The Patient Showing Protrusion Of The Eye Ball (Side View)

(Fig. 1 C) CT Orbit And Paranasal Sinus Showing Protrusion Of The Eyeball And Loss Of Ethmoid Bone.

(Fig. 1 D) CT Chest Showing Bronchiectasis In The Lungs.



(Table/Fig 2)

(Fig. 2 A) Cellular Smears Showing Epithelioid Cell Granulomas (MGG 100x)

(Fig. 2 B) Higher Magnification Of The Same Smear (MGG 400 X).

(Fig. 2 C) Septate Fungal Hyphae With Acute Angle Branching (Pas 200 X).

(Fig. 2 D) Septate Fungal Hyphae (Pas 200 X).

Discussion

Aspergillus species rank closely behind *Candida species* in causing invasive fungal infections in humans. Primary lesions can be localized in the eyes, paranasal sinuses, external ears and larynx in apparently healthy individuals [4]. In an immunocompromised host, it occurs in the form of cutaneous, sino- orbital, pulmonary, central nervous system or disseminated infection [1]. There are more than 185 species of aspergillus and over 95% of all infections are caused by *A. fumigatus*, *A. flavus* and *A. niger*. *A. fumigatus* alone accounts for a large majority of cases of both invasive and non invasive aspergillosis. In the present case, however, *A. flavus* was isolated from the culture, which is also reported to be the cause in many case reports of sinus mycosis from India and Sudan [1]. *Aspergillus* organism has a characteristic microscopic appearance, but culturing the organism is necessary for its identification. *Aspergillus*, on being incubated on a fungal medium at 30 degree centigrade in 45% humidity, yields the growth. Colonial morphology and microscopic examination of sporulating forms allows the confirmation of the diagnosis [5].

Locally aggressive invasive fungal masses may develop, particularly if the host is severely immunocompromised with one or more predisposing factors such as neutrophil defects, corticosteroid use, HIV infection, diabetes mellitus, alcoholism, prosthetic devices or trauma and advanced age. But the clinical syndrome and the pathological spectrum depends on the underlying lung architecture, host immune response and the degree of inoculum [2], [6]. Rarely has invasive aspergillus infection been described in immunocompetent patients, as in the present case.

Invasive aspergillosis of the paranasal sinuses may present with rhinorrhoea, nasal obstruction or facial pain [7]. The paranasal sinuses offer the fungus good conditions for subsistence and chronic infection may lead to the development of mycetoma. The chronicity of sinusitis results from inflammatory mucosal swelling around the ostia which hampers ventilation and drainage [8]. In the present case, the orbital involvement was secondary to the infection of the sinuses, as elicited by the patient's past history. The extension of the sinus infection is either direct or through osseous structures like the lamina papyracea or through haematogenous spread by valve-less venous plexus to the orbit, brain or skin. Aspergillus has a propensity for vascular invasion which results in thrombosis, haemorrhage and the formation of mycotic aneurysm [7].

The presentation of localized invasive aspergillosis can mimic infectious diseases such as mucormycosis and also neoplastic, vascular and neuro-ophthalmic diseases [1]. In our case, the patient presented with proptosis and loss of vision, which is a very atypical presentation and so the clinical and radiological diagnosis of orbital tumour was made. CT scans usually reveal enhancing soft tissue masses, sometimes with bone destruction [8]. Invasive aspergillus infection of the sinuses involving the adjoining structures is a well documented cause of morbidity and mortality in an immunocompromised host [7].

A long term follow up is advocated due to the high recurrence rate of the infection. The reason of poor response to treatment in our case could be the invasion of the bone and the walls of the blood vessels which affected the poor penetration of the drugs and also the past non-complaint behaviour of the patient towards the anti-fungal treatment [1]. However; early diagnosis of the orbital involvement of fungal sinusitis continues to be a challenge. Any type of paranasal aspergillosis may progress to or may be associated with a more aggressive disease, illustrating the importance of the early recognition of this increasingly encountered disease. While the imaging of the sinuses and the adjoining structures provide complementary diagnostic evidence, the demonstration of fungus in the tissues guides the treatment and the isolation of fungi confirms the diagnosis. There is no uniformly accepted, completely effective treatment. Management often involves surgical debridement and amphotericin B local irrigation, followed by systemic administration of intravenous amphotericin B usually. Response to treatment depends on the early diagnosis and the initiation of antifungal treatment [6].

This case is worth reporting because of its unusual presentation and the method employed to retrieve the fungal organism to conclusively reach a diagnosis. It is therefore proposed by our observations that the protocol of immediate disinfection of the needles used after an FNA procedure (either by incinerating them in a needle destroyer or in hypochlorite solution) be desisted from. A time gap of discarding the needles used in the procedure by a few minutes (time required in staining the smears and viewing them) can go a long way in reaching an appropriate diagnosis, especially in cases of lesions of infective aetiology.

The exact causative organisms can be isolated from the remnant material in the needle hub as was observed in our study, which can in the end, lead to specific managements.

However, more and larger sample studies have to be undertaken regarding the utility of this retrieval method in employing it for isolating the

causative organism in cases of frank or suspected infective lesions. This case highlights the importance of clinico-pathological correlations where inter departmental discussions led to a conclusive diagnosis of invasive aspergillosis which alleviated the patient's anxiety regarding the suggested neoplastic nature of the lesion he was suffering from.

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