



## ORIGINAL RESEARCH PAPER

## General Medicine

### A RARE CASE REPORT OF INVASIVE ASPERGILLOSIS: SUCCESSFULLY TREATED WITH VORICONAZOLE IN IMMUNOCOMPETENT PATIENT

**KEY WORDS:** Aspergillosis, Voriconazole, Immunocompetent

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#### ABSTRACT

14 years old Female with no known co-morbidities reported in Emergency Department with Left periorbital swelling, Breathlessness and Fever since 1 days. Patient desaturated on the next day of admission and was shifted to Medical ICU. HRCT Thorax were done suggestive of multiple variable sized nodular consolidation in bilateral lung parenchyma and perifocal GGOs present. Patient was referred to Ophthalmic and ENT surgeon for an opinion and was advised CT PNS suggestive of iso dense collection in posterior ethmoid sinus, spheno-ethmoid recess & sphenoid sinus. FESS (functional endoscopic sinus surgery) was performed and aspirated fluid was sent for histopathological analysis. Histopathological appearance was suggestive of Aspergillosis. Aspergillus lung nodule with Paranasal sinus involvement in young Female without any risk factor is rare. Patient was managed with Intravenous voriconazole for 10 days followed by Oral voriconazole 200 mg bd for 5 weeks. On follow up patient was asymptomatic with no residual swelling.

#### INTRODUCTION-

Fever, breathlessness and periorbital edema may be the symptoms of a broad spectrum of diseases. Both infectious and non-infectious diseases can all lead to fever and periorbital edema. Since some of these diseases might be emergent, differential diagnosis is critical for proper and immediate intervention. A careful history and physical examination should be performed in order to decide which further tests are needed to clarify the diagnosis. In this case report, we aimed to present association of periorbital and fever in a patient finally diagnosed with Aspergillosis. Swelling aspergillosis fumigates is common pathogen in human airway causes various diseases ranging from mild hypersensitivity reaction to more severe invasive disease that is rapidly progressive and carries 50 % mortality despite treatment.<sup>(1)</sup> This disease normally occurs in immunocompromised hosts, however immunocompetent patient rarely develop invasive aspergillosis.<sup>(2,3)</sup> Invasive aspergillosis should be considered in differential diagnosis of an otherwise undiagnosed culture negative febrile respiratory illness.<sup>(1)</sup>

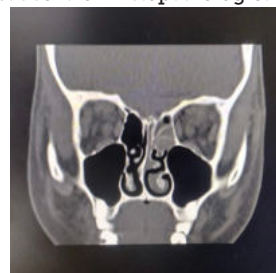
Histopathological examination along with microbiological confirmation remains the gold standard in diagnosis.<sup>(4,1)</sup> Assay estimating the components of the fungal cell wall may assist in establishing diagnosis of invasive aspergillosis.<sup>(4,5)</sup> Appropriate anti-fungal therapy when administered early in the illness may cure the disease.

#### Case report

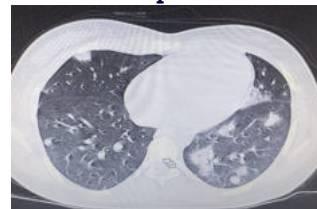
A 14 years old female admitted with complaint of high grade fever and left periorbital swelling, difficulty in breathing since 2 days. She had history of taking anti-inflammatory medicines over the counter for same. Suspecting drug reaction the patient was admitted but her periorbital swelling increased on day 2 of hospitalization. Her body temperature was 38.7 °C. Quick swab for Strep A was negative. Complete blood count revealed that white blood cells: 11,890 / mm<sup>3</sup>, lymphocytes (69%) and PMN (27.3%). There was no eosinophilia and thrombocytes were 1,96,000 / mm<sup>3</sup>. BUL: 27 mg/dL, Sr. Creatinine: 0.57 mg/dL. AST: 46 IU/L, ALT: 37 IU/L, LDH: 550 U/L, CRP: 1.87 mg/dL. On inspection, extra-oral examination revealed a diffuse swelling that was present on the left side of the face involving the periorbital region. The skin on the center of the swelling was erythematous with no

pus discharge. No scar or redness, but mild hyper pigmentation of left periorbital region was seen. No diminution of vision or diplopia was observed in the patient. Ophthalmic Surgeon opinion was taken and for further evaluation CT PNS was done suggestive of iso dense collection seen in left posterior Ethmoid sinus, Spheno-ethmoid recess and sphenoid sinus. Further we took an opinion of ENT specialist where FESS (Functional endoscopic sinus surgery) was advised.

On day 3 patient desaturated and was immediately shifted to Medical ICU on Non Invasive NIV Ventilation. Considering persistent Hypoxia (ABG PaO<sub>2</sub>- 80 mmHg) HRCT was done. It revealed multiple variable sized nodular consolidation in bilateral lung parenchyma with perifocal Ground Glass Opacities. Covid 19 RT PCR was done which came out to be negative. FESS ( functional endoscopic sinus surgery ) procedure was done on the same day. Fluid aspirated from ethmoid sinus was sent for histopathological analysis.



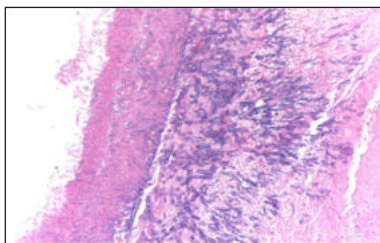
**Figure 1. Coronal section of CT PNS suggestive of iso-dense collection seen in left posterior ethmoid sinus, sphenoethmoid recess and sphenoid sinus.**



**Figure 2. Axial section of HRCT Thorax suggestive of variable sized nodular consolidation in bilateral lung parenchyma with perifocal Ground Glass Opacities.**

Histopathological evaluation showed septate hyphae with dichotomous branching suggestive of the *Aspergillus* spp, suggestive of aspergillosis.

Next day patient was posted for bronchoscopy. BAL (Broncho alveolar lavage) sent for histopathology suggesting of aspergillosis. Further serum galactomannan level was analyzed and ODI came to be 0.62.



**Figure 3. Histological examination (hematoxylin and eosin stain) shows abundant septate fungal hyphae with dichotomous branching suggestive of the *Aspergillus* spp, eosinophils and giant cells are also seen.**

As per guidelines in immune competent host, patient was treated with Intravenous voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h for 10 days). Patient responded to the treatment very well and was discharged with oral voriconazole 200mg BD for 5 weeks. Patient came for follow up after 5 weeks asymptomatic with reduction in orbital swelling.

## DISCUSSION :

A high index of suspicion in otherwise undiagnosed culture negative invasive febrile respiratory illness to diagnosis of invasive aspergillosis which was confirmed by histopathological analysis. Aspergillosis in immunocompetent patient is rare. Recently, the incidence of invasive pulmonary aspergillosis in immunocompetent patient with critical illness seen in those with postinfectious condition or in immunocompetent patients with occupational exposure to dust such as those who work at construction site.<sup>(6,7)</sup>

Clinical symptoms in patients with invasive pulmonary aspergillosis include fever, cough, dyspnoea, hemoptysis, perifocal chest pain. These symptoms without classical risk factor are non specific . Accurate diagnosis could be often delayed fungal hyphae is considered gold standard. Whereas non invasive test for serological marker such as galactomannan testing or aspergillosis polymerase chain reaction assay are other good options for the diagnosis of invasive aspergillosis. although the exact mechanism by which the aspergillosis species causes invasive aspergillosis in immunocompetent patient is not understood, the species may inhibit antigen presenting cell functions & suppress T cell response by a toxic substance , gliotoxin which aspergillum fumigatus produces<sup>(8)</sup>.

Most invasive aspergillosis is caused by *A. fumigatus* [80-90%]; *A. flavus* [5-10%], *A. niger* [1-5%] and *A. terreus* [1%] are less common<sup>(9)</sup>. *Aspergillus fumigatus* is the most common organism in immunocompetent patients too. Predisposing factors that promote fungal infections in the sinuses include polyps and stagnant secretions besides other factors like neutropenia, inappropriate use of antibiotics, immunosuppressive drugs, corticosteroids, uncontrolled diabetes mellitus, human immunodeficiency virus infection, trauma, burns, and radiation therapy<sup>(10)</sup>. Because of its rarity in immunocompetent patients, accurate recognition is critical in order to achieve optimal results. Delayed diagnosis and treatment of invasive maxillary sinus aspergillosis may lead to a poor therapeutic outcome. Management of invasive aspergillosis therapy is still controversial and depends on several factors such as the nature of the disease, host immunity and degree of tissue invasion. Response to

treatment depends on early diagnosis and initiation of antifungal therapy augmented by surgical debridement. Surgical debridement of abnormal tissue in the sinus is recommended for pharmacological therapy to reach the infected area. Surgery may improve the control of fungal disease and patient survival. The Infectious Diseases Society of America [IDSA] released updated guidelines for the treatment of invasive aspergillosis in 2018. Voriconazole [broad-spectrum triazole] has now become the drug of choice for invasive aspergillosis. This is due to a better tolerance, increased efficacy [with a greater likelihood of a complete or partial response], improved survival [with a lower mortality rate], and significantly less toxicity when compared with amphotericin B.<sup>(11)</sup> The recommended dosing regimen of voriconazole is 6 mg/kg IV every 12 hours on day one followed by 4 mg/kg IV twice daily, and after, 200 mg orally twice daily. The most frequent adverse events are visual disturbances, such as blurred vision, altered visual and colour perception, and photophobia. Treatment with voriconazole therapy our patient improved drastically.

## CONCLUSION

Invasive sinus aspergillosis should be considered as differential diagnosis in cases of immunocompetent host with periorbital or face swelling with fever . Early diagnosis and therapeutic intervention, with selection of an appropriate antifungal agent and surgical debridement, is the key to successful treatment of invasive aspergillosis. Voriconazole is recommended for the primary treatment of invasive aspergillosis in most patients; this is due to a better tolerance, increased efficacy, improved survival, and significantly less toxicity with fewer drug-related adverse events.

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