Invasive cutaneous aspergillosis in a patient with anaplastic astrocytoma: a case report

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Abstract

Invasive aspergillosis is commonly encountered in immunosuppressed patients either primary through direct inoculation or secondary from blood dissemination. This report describes a case of 53 years old immunocompromised female patient who was diagnosed with frontotemporal anaplastic astrocytoma and developed nasal skin lesion turned to be invasive cutaneous aspergillosis.

Keywords

Invasive cutaneous aspergillosis, Anaplastic astrocytoma, Aspergillus.

Key Clinical Massage

Immunocompromised patients are subjected to life-threatening unusual infections, early diagnosis, and thorough investigations should be done to identify the underlying cause and offending organism concomitant with empiric treatment.

BackgroundAspergillosis referred to a spectrum of diseases caused by the aspergillus fungi species [1], aspergillus causes a wide array of diseases ranging from allergic conditions to invasive life-threatening diseases [2] as in patients with acute leukemia and recipients of allogeneic hematopoietic stem-cell transplants [3], Invasive pulmonary disease is the most common invasive disease as candida get inhaled [4]. Meanwhile, cutaneous aspergillosis tends to occur less frequently; the infection can be a primary infection at the site of skin trauma, surgery, burn, occlusive dressing or at the site of intravenous access[5,6], Secondary infection as a result of blood dissemination or through the direct extension of infection from contaminated nearby structures as sinuses [7,8].

Mortality and morbidity due to invasive aspergillosis are increasing due to the increasing number of patients with malignancies being treated with immunosuppressive therapy along with the survival of aggressive bacterial infections due to antibacterial therapy[4],Virulence and extent of the disease determined by host factors and microbial factors, with neutrophils play an essential role in host defense against filamentous fungi hence patients with neutropenia rendered more vulnerable to invasive disease caused by*Aspergillus* [1].

The most prevalent species causing invasive aspergillosis in immunocompromised patients is Aspergillus *fumigatus*[6], followed by *A. flavus* then *A. niger*as showed in a multicentric study in *218* patients with invasive aspergillosis [4].

Lesions of cutaneous aspergillosis can present as erythematous lesions, macules, papules, nodules, plaques, pustules, or lesions with purulent discharge, type of the lesion depends on the source of infection as dissem-

inated blood infections are different for others caused by an occlusive dressing which tends to present as hemorrhagic bulla[6].

Diagnosis of cutaneous aspergillus requires identification of the organism either directly by Potassium Hydroxide (KOH) preparation or through skin biopsy and identification of the aspergillus through culture and histopathologic examination [4,6], Galactomannan antigen detection implemented in the diagnosis of invasive aspergillosis in areas where there is a high chance of specimen contamination as blood and bronchoalveolar lavage (BAL) is expected[9].

Case PresentationA 53-year-old female patient who was diagnosed with frontotemporal anaplastic astrocytoma (WHO grade IV); the patient operated and started on post-operative radiotherapy and temozolomide; later admitted to the hospital multiple times for side effects related to her disease and chemoradiotherapy.

Patient suffered from saddle pulmonary embolism, received a full dose of heparin and respiratory support until her condition stabilized, later patient presented to the emergency department (ED) with heparin-induced thrombocytopenia; platelets 3000 (reference range 150000 – 400000/uL) and leukopenia WBC (White blood cells 1, Absolute Neutrophils count 0.4), heparin withheld, the patient admitted and started on aztreonam 2g Q8hours and vancomycin 20mg/kg Q8hours then shifted to cefepime 2 grams Q8hours as culture growth showed *Pseudomonas* for treatment of axillary cellulitis until resolved, temozolomide stopped.

Two days later, the patient developed a lesion near the ala of the left nostril and swelling of the left side of the face, ENT team consulted, the lesion was erythematous, hyperemic, and tender, nasal examination was limited due to tenderness elicited by exam maneuvers, clear discharge noted from the left nostril.

Sinus computed tomography (CT) scan with contrast done and showed clear paranasal sinuses, partial opacification of left maxillary and ethmoidal sinuses with left facial edema with no clear evidence of fungal sinusitis *(Figure 1).*

Patient started on empiric therapy set by the infectious medicine (ID) team with liposomal amphotericin B 3mg/kg Q24hours, tigecycline 100mg given as a loading dose followed by 50mg Q12hours, and ciprofloxacin 400mg Q8hours.

The patient did not show any signs of improvement and the lesion evolved into a black lesion with a central area of necrosis *(figure 2)* , biopsy taken and culture growth showed *Aspergillus flavis*meanwhile blood culture showed (*Stenotrophomonas maltophilia, Achromobacter xylosoxidans and Enterococcus casseliflavus*), plan of care discussed with the multi-disciplinary team (MDT) and the decision was to go for surgical debridement and endoscopic exploration of paranasal sinuses, but due patient electrolyte imbalance (Na 148, and K 5.5) abnormal coagulation profile (PT 16.7, INR 1.6 APTT 42.8) and low platelets (Plt 1000/uL)) surgery was delayed until normalization of patient lab values.

The patient received Granulocyte colony-stimulating factor (G-CSF); filgrastim 300mcg and platelets transfusion, patient received 6 units daily for 5 days but no significant improvement of platelets count as the count did not exceed 40000/uL.

The patient was taken into the theater, wide local excision of the lesion with 5 mm safety margin *(Figure 3)* and endoscopic exploration of the sinuses done which showed clear osteo-meatal complex and ethmoid air cells with no clear evidence of fungal sinusitis; the patient was planned for a frontonasal local flap, but due to patient abnormal coagulation profile plan was postponed until the patient condition improves.

The patient received 10 units of platelets on the day of surgery and continued empiric antimicrobial therapy with antifungal treatment and daily dressing on the surgical site; due to low platelet count patient tends to develop blood oozing from the surgical site, for that pressure dressing with hemostatic materials was done.

Unfortunately, the Patient had poor survival rate due to her disease, later she died of systemic complications of her primary disease.

Histopathology

"Biopsy and subsequent excision of the lesion revealed widespread necrosis of the skin, with extensive infiltration by numerous fungal organisms, composed of thin septate hyphae with branching at 45-degree angle. The morphological appearances were in keeping with aspergillosis." (Figure 4,5 & 6)

Discussion

It is estimated that invasive cutaneous aspergillosis represents up to 5% for all invasive aspergillosis [10], Invasive cutaneous aspergillosis represents a challenge in diagnosis, as lesions have no specific characteristics and tend to resemble lesions of any other skin pathologies [6] with secondary escharotic evolution [11], due to neutral behavior of lesions skin biopsy and culture may be delayed.

Early identification of invasive aspergillosis and initiation of antifungal therapy is crucial in the management of invasive, alleviation of immunosuppression and surgical intervention is needed to eradicate the infection when feasible, and the lesion is amenable to surgery.

Three classes of antifungals are available, azoles, polyenes, and echinocandins, with a Cochrane review showed the superiority of liposomal amphotericin B over azoles in the treatment of invasive aspergillosis in patients with persistent neutropenia[12], duration of treatment depends on the site of infection, immune status of the patient and response to therapy, a minimum duration of 6 – 12 weeks is needed but most of the time patients will require antifungal therapy for months or even years in some instances [13].

Surgery is advised in localized disease as our patient, but usually, immunosuppressed patients are less likely to tolerate surgery due to bleeding and increase the risk of superadded infections because of thrombocytopenia and leukopenia respectively.

Conclusion

Immunosuppressed patients are subjected to various types of infections due to their immunosuppression either due to primary disease or immunosuppressive therapy; disease presentation tends to be different and sometimes bizarre, the disease may develop in a way that not previously described or encountered, our patient developed invasive cutaneous aspergillosis without any evidence of primary blood infection, or aspergillus sinuses disease, skin break or burn, definitive diagnosis with biopsy is crucial in patients with neutropenia to identify the underlying pathology and offending organism and start the therapy accordingly.

Primary invasive cutaneous aspergillosis can develop in immunosuppressed patients with intact skin without any history of skin break, burn, or adhesive dressing, early intervention, and treatment will avoid serious complications related to the primary infection.

AbbreviationsKOH: potassium hydroxide

BAL: Bronchoalveolar lavage

WHO: World health organization

ED: Emergency department

WBC: White blood cells

ID: Infectious diseases,

CT: Computed tomography

Plt: Platelets

G-CSF: Granulocyte colony stimulating factor

Declarations

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Conflict of interest

None declared

Ethics approval and consent to participate

The article describes a case report. Therefore, no additional permission from our Ethics Committee was required.

Consent for publication

The consent for publication was obtained.

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Authors' contributionsAAA: Data collection, Literature search, Manuscript preparation, AS: Manuscript preparation and revision, MAP: pathology slides preparation, AJN: Manuscript preparation and revision, SG: Manuscript Preparation and submission.

All authors read and approved the final manuscript

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Figures:

Figure 1 - Coronal Cuts of Sinus CT scan with contrast

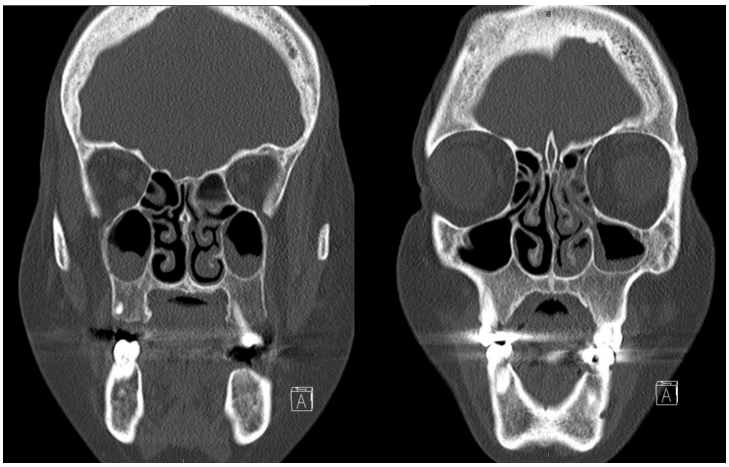
Figure 2 - Serial photos of patient's nasal lesion evolution.

Figure 3 - Post surgical image of the patient.

Figure 4 -Low power view showing marked cutaneous necrosis. H and E x 2

Figure 5 - Extensive infiltration by aspergillosis. Grocott stain x 2

Figure 6 - High power view displaying the typical fungal morphology. Note the thin septate branching hyphae. Grocott x 40



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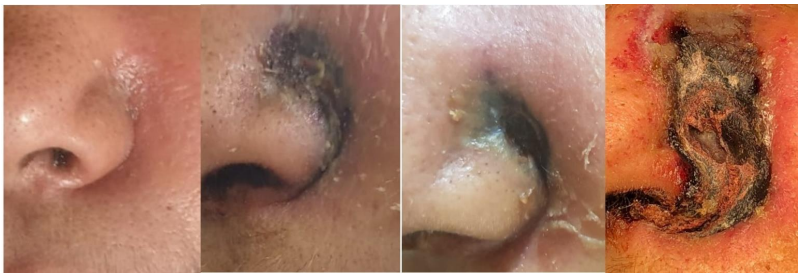


Figure 2 - Serial photos of patient's nasal lesion evolution.

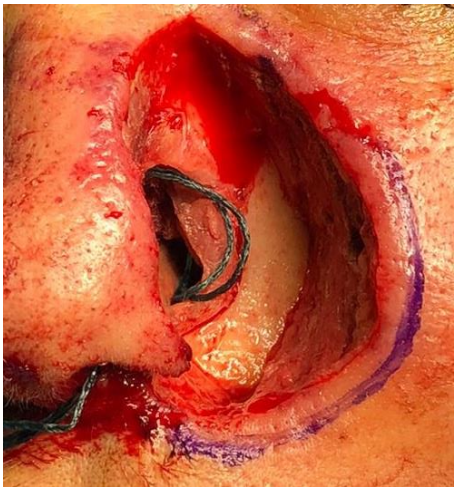


Figure 3 - Post surgical image of the patient.

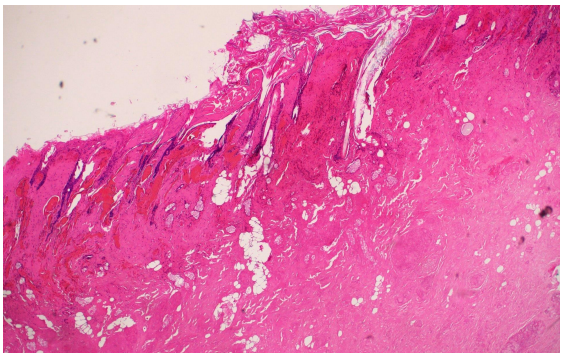
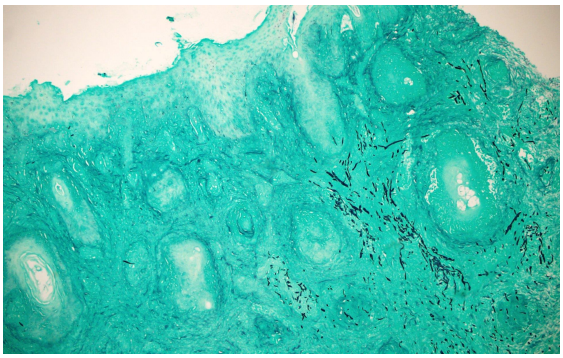


Figure 4 -Low power view showing marked cutaneous necrosis. H and E x 2



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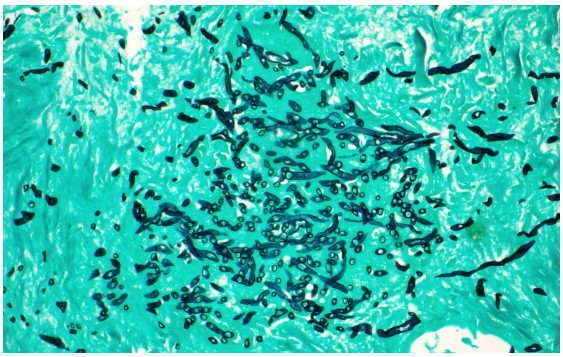

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