

Nasal-alar 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 primarily 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

ala, anaplastic astrocytoma, Aspergillus, invasive cutaneous aspergillosis

1 | BACKGROUND

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

Aspergillosis referred to 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 diseases² as patients with acute leukemia and recipients of allogeneic hematopoietic stem cell transplants.³ Invasive pulmonary disease is the most common invasive disease as conidia get inhaled.⁴ Meanwhile, cutaneous aspergillosis tends to occur less frequently; this can be a primary infection at the site of skin trauma, surgery, burn,

and occlusive dressing or at a site of intravenous access^{5,6}; and 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 because of 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* and then *A. niger* as shown in a multicentric study in 218 patients with invasive aspergillosis.⁴

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Lesions of cutaneous aspergillosis can present as macules, papules, nodules, plaques, pustules, or lesions with purulent discharge, and type of the lesion depends on the source of infection as disseminated blood infections are different from 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 with identification of aspergillus through culture and histopathologic examination.^{4,6} Galactomannan antigen detection is used to diagnose invasive aspergillosis in areas with a high chance of specimen contamination as blood, and bronchoalveolar lavage (BAL) is expected.⁹

2 | CASE PRESENTATION

A 53-year-old female patient was diagnosed with a frontotemporal anaplastic astrocytoma (WHO grade IV); after the surgery, she was started on postoperative radiotherapy and temozolomide, then she was admitted to the hospital multiple times for side effects related to her disease course and chemoradiotherapy.

The patient suffered from saddle pulmonary embolism, treated with a therapeutic dose of unfractionated heparin (UH) and respiratory support until her condition stabilized. Later, the patient presented to the emergency department (ED) with heparin-induced thrombocytopenia, her laboratory results showed platelet number 3000 (reference range 150 000-400 000/ μ L), leukopenia, and neutropenia (white blood cells 1, absolute neutrophil count 0.4), so heparin was withheld, then patient admitted to inpatient ward and started on aztreonam 2 g Q8 hours and vancomycin 20 mg/kg Q8 hours and thereafter shifted to cefepime 2 g Q8 hours

as culture growth showed *Pseudomonas* for the treatment of axillary cellulitis until infection resolved, and temozolomide was stopped.

Two days later, the patient developed a lesion near the ala of the left nostril and swelling of the left side of the cheek, the ENT team was consulted, and physical examination showed a small lesion at the left nasal-alar crease; it was hyperemic, erythematous, and tender, about 1 cm in size with no fluctuation, but the nasal examination was limited due to tenderness elicited by examination maneuvers; meanwhile, it showed clear discharge from the left nostril.

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

The patient started on empiric antimicrobial therapy set by the infectious medicine (ID) team with liposomal amphotericin B 3 mg/kg Q24h hours, tigecycline 100 mg given as a loading dose followed by 50 mg Q12 hours, and ciprofloxacin 400 mg Q8 hours.

The patient failed to show any signs of improvement and the lesion evolved into a black lesion with the central area of necrosis within 5 days that progressed as shown within 10 days (Figure 2); biopsy taken and culture growth showed *Aspergillus flavis*; and meanwhile, blood culture showed *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, and *Enterococcus casseliflavus*. Plan of care was discussed with a multidisciplinary team (MDT) and the decision was to go for surgical debridement and endoscopic exploration of paranasal sinuses, but due to patient's 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/ μ L), surgery was delayed until normalization of patient laboratory values.

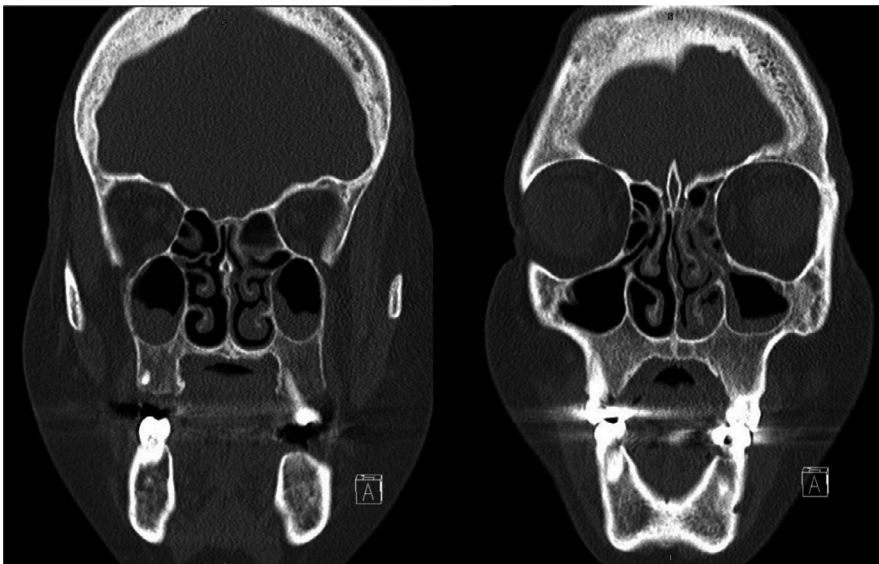


FIGURE 1 Coronal cuts of sinus CT scan with contrast



FIGURE 2 Serial photographs of the patient's nasal lesion evolution

She has received Granulocyte Colony-Stimulating Factor (G-CSF); filgrastim 300 mcg with no satisfactory response (platelet count 2000/ μ L after filgrastim); thus, she has received 6 platelets units daily for 5 days, with no significant improvement of platelets counts as it did not exceed 40 000/ μ L.

The patient was taken into the theater 10 days after the appearance of the primary lesion, wide local excision of the lesion was done with safety margin until viable skin and subcutaneous tissue noted (Figure 3), and endoscopic exploration of the sinuses was 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 with low

platelet count, 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; hence, pressure dressing with hemostatic materials was applied.

Unfortunately, the patient had a poor prognosis due to her disease; later she died of systemic complications of her primary disease.

2.1 | Histopathology

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

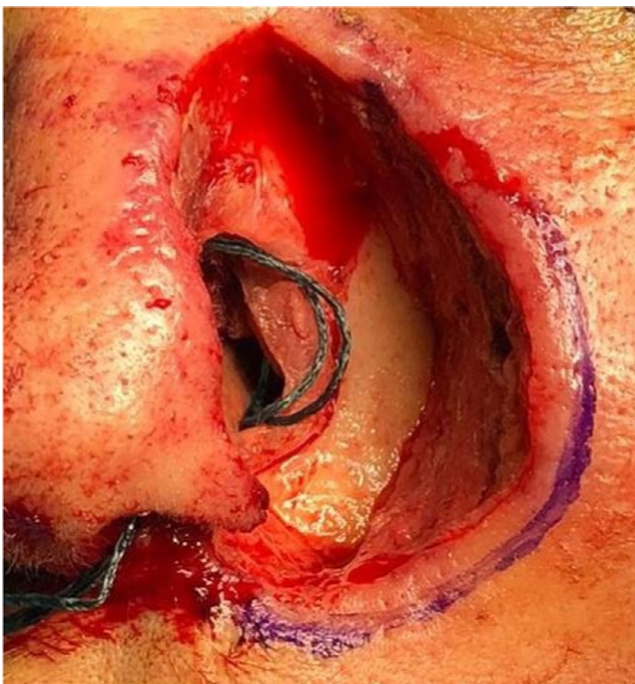


FIGURE 3 Postsurgical image of the patient

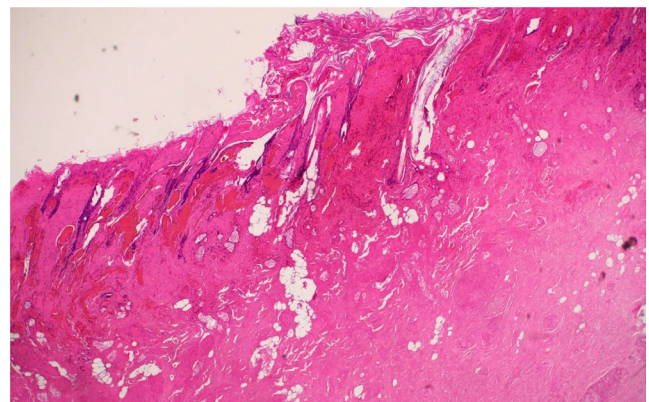


FIGURE 4 Low power view showing marked cutaneous necrosis. H and E $\times 2$

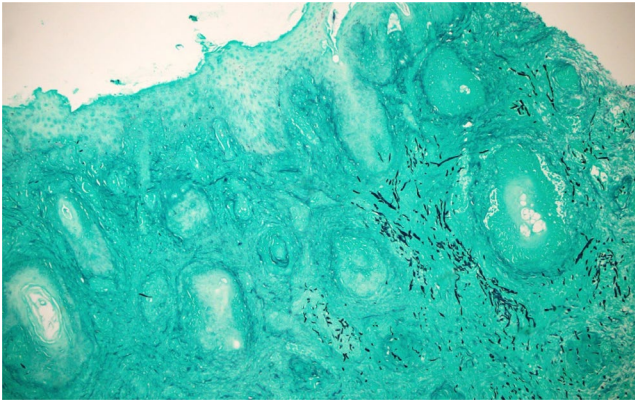


FIGURE 5 Extensive infiltration by aspergillosis. Grocott stain $\times 2$

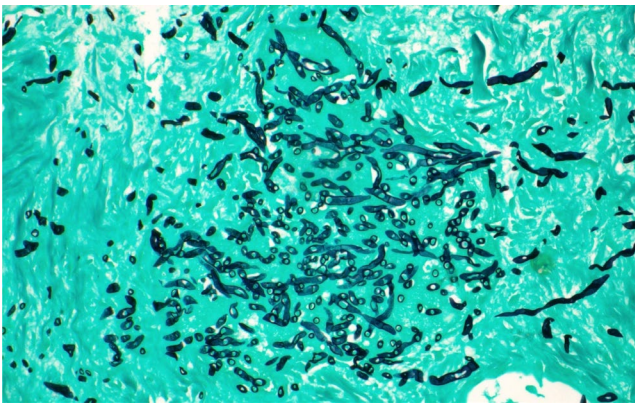


FIGURE 6 High power view displaying the typical fungal morphology. Note the thin septate branching hyphae. Grocott $\times 40$

3 | DISCUSSION

It is estimated that invasive cutaneous aspergillosis represents up to 5% for all invasive aspergillosis¹⁰ and invasive cutaneous aspergillosis represents a challenge in diagnosis, as lesions have no specific characteristics and tend to resemble lesions of any other skin pathologies⁶ with secondary escharotic evolution,¹¹ due to neutral behavior of lesion skin biopsy and culture may be delayed.

Early identification of invasive aspergillosis and initiation of antifungal therapy is crucial in the management of invasive infection, 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 showing 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 increased the risk of superadded infections because of thrombocytopenia and leukopenia, respectively; treatment of choice in cutaneous aspergillosis is a medical treatment with the elimination of the source of infection surgically if possible.¹⁴

4 | CONCLUSION

Immunosuppressed patients are subjected to various types of infections due to their immunosuppression due to either 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; and our patient developed invasive cutaneous aspergillosis without any evidence of primary blood infection, or aspergillus sinus 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.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

AAA: collected the data, performed the literature search, and prepared the manuscript. AS: prepared and revised the manuscript. MAP: prepared pathology slides. AJN: prepared and revised the manuscript. SG: prepared and submitted the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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