***Case report***

INVASIVE HEMIFACIAL MYCOSIS MIMICKING FACIAL MALIGNANCY-CASE REPORT.

ABSTRACT

Invasive facial fungal infections are confusing disease processes that can involve one, or more regions of the face, presenting with varied clinical features that mimic other clinical conditions that range from benign disease conditions to malignancies. While typically exhibiting characteristic features of fungal disease, facial mycosis can sometimes present in an unusual manner, having improbable localization to different aspect of the face such as the eyelids, cheeks, ear, etc. We present a -year-old retired military man from the rural aspect of the southern part of Nigeria who presented with left hemifacial growth and deformity, and ptosis of the left upper eyelid. Tissue biopsy analysis yielded Histoplasmosis which treated with the use of oral and topical anti-fungal medications leading to complete resolution of all presenting complaints.

Key words: Histoplasmosis, Hemifacial mycosis, Mycotic masquerade.

INTRODUCTION

Histoplasmosis, also known as “Darling disease”, “Cave disease”, and “Ohio valley disease” is a systemic fungal infection caused by the thermally dimorphic fungus Histoplasmosis capsulatum.1 The causative agent H.capsulatum is found globally in the soil, especially in soil containing high concentrations bird and bat droppings.2 The clinical manifestations of histoplasmosis are of three main types: pulmonary, progressive disseminated, and chronic cavitary forms. Following exposure to the fungus, the disease process is self-limiting and restricted to the lungs in 99% of the individuals, while the remaining 1% progress to either disseminated, or chronic disease involving the lungs, liver, spleen, lymph nodes, bone marrow, and sometimes, the skin and mucous membrane.3 Skin lesions may occur with all the three forms of histoplasmosis or rarely, as a primary cutaneous histoplasmosis.1 Cutaneous lesions occur in about 17% of patients with disseminated histoplasmosis. This can present as popular or pustular skin lesions, plaques, ulcers, molluscum or wart-like lesions, and rarely, as erythema nodosum-like skin lesions.2

The common routes of infection are through direct inoculation of spores through the skin, mucous membranes, and thorn pricks injury. Our patient had several unique characteristics in the sense that he was an immunocompetent individual who lives in a non-endemic region of the southern region of Nigeria. Also, the primary hemifacial skin lesions had mimicry of a malignant cutaneous ulcer with raised everted edges, invasion of the left upper eyelid causing ptosis with its consequent misdiagnosis.

CASE PRESENTATION

The patient is a 75-year-old man who presented with a 2-month history of left hemifacial swelling, ptotic left upper eyelid and wound. There is no history of weight loss or anorexia, no history of excessive exposure to ultraviolet radiation, he doesn't smoke cigarettes He presented to dermatology clinic from where he was referred to plastic surgery clinic. He was a recently diagnosed diabetic patient on oral euglycemic drugs. On examination elderly man afebrile, not pale, anicteric, well hydrated. His vital signs were within normal.

Examination of his face revealed a large plaque 7cm X 5cm over the left temporo-frontal-zygomatic region with a central necrotic patch, crusty margin and raised and everted edge. There was associated drainage of serous fluid, oedematous left eyelids and ptosis of the left upper eyelid (figure 1).

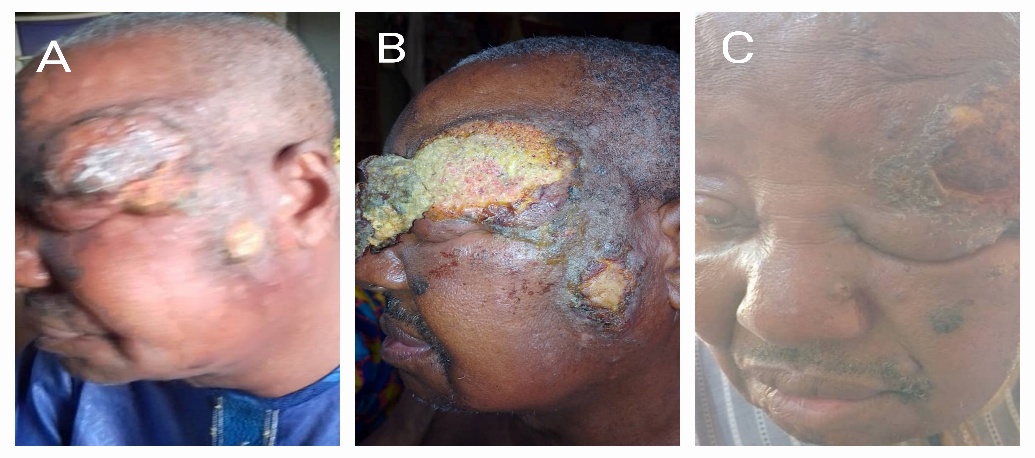
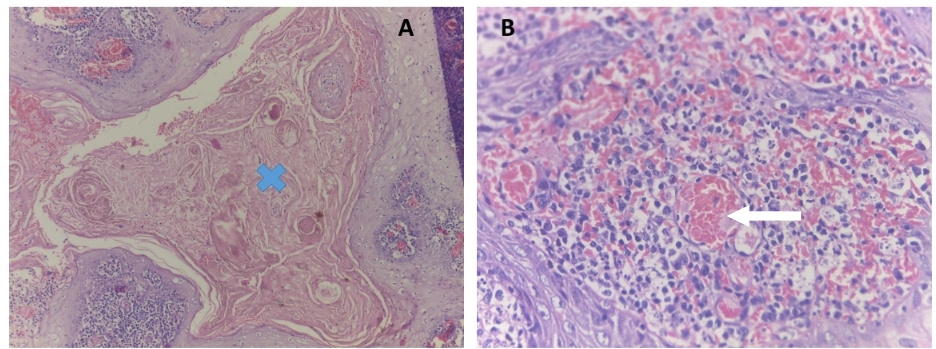


Figure 1: Pre-intervention photographs. A: Left hemifacial mass with ulcerated crater, and elevated edge. B: Ulcerated crater at the epicentre of the mass following debridement of the necrotic floor. C: Ptosis of the left upper eyelid.

A clinical diagnosis of left hemifacial squamous cell carcinoma was made. He had wound debridement and tissue samples sent for histopathological analysis, microscopy, culture and sensitivity (MCS), and fungal study. The MCS result yielded mixed growth of Enterobacter spp and Staphylococcus aureus, fungal study yielded growth of Histoplasmosis capsulatum. Macroscopic analysis of the tissue showed a skin fragment with an irregular epidermal surface. Histopathological examination revealed a chronic diffuse lympho-plasma-histiocytic infiltrate (figure 2).



**Fig 2 A:** X4 magnification of H&E stain showing keratin horn cysts, marked blue-**X** within a hyperplastic squamous epithelium with infection and hemorrhage. **B.** Larger magnification (X40 magnification H&E stain) showing dense acute inflammation and congested new vessels (white arrow), and intact basement membrane of the keratinocytes.

Periodic Acid Schiff (PAS) stain showed numerous spore-like fungal structures, having regular morphology, presenting as 2-4mm oval-shaped yeasts in rows and stained in red and brown colours (figure 3).4

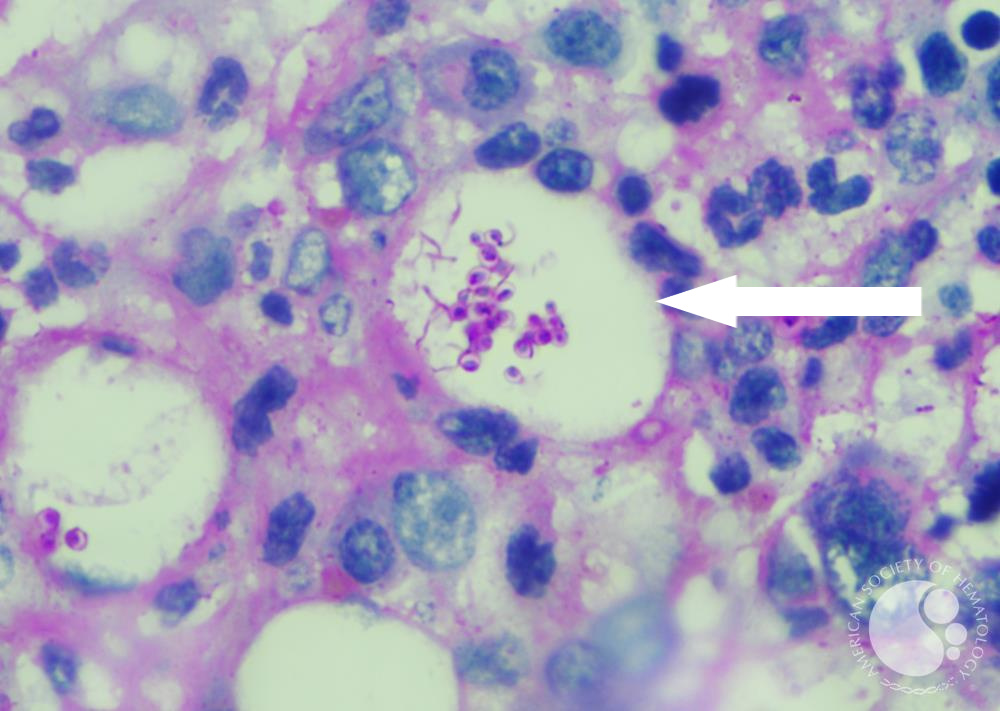


Figure 3: Periodic Acid Schiff (PAS) stain showing numerous intracellular yeasts with retraction of the cytoplasm (white arrow), i.e., the classical “halo” appearance.

Serological tests (anti-hepatitis C, anti-hepatitis B, VDRL, anti-HIV) were negative. Blood tests (full blood count, lipid profile, clotting profile, fasting blood glucose showed no abnormalities. He was intravenous Fluconazole 200mg 12 hourly for 5 days thereafter oral fluconazole 200mg daily the facial wound dressing the face performed daily using 2% Salicylic acid (Nixoderm) cream. Patient problems resolved remarkably with complete resolution of the facial lesions and ptotic left upper eyelid (figure 4).



Figure 4: A: 2 months post antifungal therapy. B: 4 months post antifungal therapy. C: 6 months post antifungal therapy

DISCUSSION

Masquerades are an integral part of surgical practice, and oncological surgery is no exception.2 Primary cutaneous histoplasmosis is very rare and can present with papules, nodules, plaques, pustules, acneiform eruptions, ulcers, abscesses, or umbilicated papules resembling molluscum contagiosum-like lesions.2,5,6 The route of infection is through direct inoculation of spores through the skin, and mucous membranes, and thorn pricks are the most common mode of acquiring this variant of histoplasmosis.2,6,7 The disease occurs commonly in immunocompromised individuals, more so, in HIV-infected persons having CD4+ count <75cells/ml. In immunocompetent individuals, about 95% of histoplasmosis infections are asymptomatic.2,5 However, prolonged exposure to high number of spores may lead to acute or chronic infection.3 The clinical spectrum of histoplasmosis is variable, ranging from a severe multisystemic illness involving the bone, liver, spleen, and lungs, to an indolent infection localised to the gastrointestinal tract (GIT), skin, adrenal glands, brain, meninges, or extrapulmonary tissues.2 There are many clinical presentations of histoplasmosis infection which usually starts as a primary lung histoplasmosis. This primary lung histoplasmosis can evolve to compromise the central and lateral regions of the face. Other areas of the head reported in the literature include oral mucosa, upper eyelids, and the nasal septum.1,5,6

Delineating histoplasmosis from malignancies requires a high index of suspicion and an apt cognizance from the physician and the pathologist involve in the evaluation of the tissue biopsy. Clinically, histoplasmosis lesions are seen as firm, painful ulcers with verrucous, necrotic and polypoid proliferations which may be accompanied by regional lymphadenopathy, with a close resemblance to cutaneous squamous cell carcinoma.5,8 The destruction of tissues is the result of hematogenous dissemination of the fungus spores, triggering a cascade of proinflammatory cytokines and the cytogenetic effects generated by tissue macrophages, lymphocytes, and neutrophils that progressively destroy the fine and delicate tissues.6 Definitive diagnosis should be made by culture of the organism. Periodic Acid Schiff (PAS) and Grocott Methamine Silver (GMS) are used in the screening of tissues for the presence of histoplasmosis.6 A classic “halo” appearance caused by retraction of the cytoplasm from the cell wall is helpful in the identification of the organism. Specific stains like PAS and GMS stains highlight the fungus, its capsule consisting of a polysaccharide and stains poorly with hematoxylin and eosin (H & E) stain.1

The histologic findings of histoplasmosis are equally perplexing, with features of pseudoepitheliomatous hyperplasia (PEH) of the overlying epithelium. PEH is the common histologic feature of histoplasmosis that misleads unsuspecting pathologists due to its close resemblance to squamous cell carcinoma.1 The distinctive feature of PEH from squamous cell carcinoma in a biopsy is hyperplasia of the epidermis. This is a benign feature seen in variety of conditions such as inflammatory conditions and trauma. It is also known that atypical mitosis, lymphovascular invasion and perineural invasion are features seen in squamous cell carcinoma, but not in PEH.1

The first line agent of treatment of histoplasmosis is amphotericin given at a dose of (3-5mg/day). However, poor response to amphotericin has reported in the literature.9,10 The patient in this report was treated with daily topical 2% salicylic acid (Nixoderm), intravenous fluconazole 400mg/day for one week, and had the oral fluconazole (50mg/day) for the next six months. His symptoms resolved remarkably during the course of the treatment and by the end of 6th months, he had achieved complete remission of his symptoms.

CONCLUSION:

Every growth is not cancer, and all cancer is not a growth. Cutaneous mycosis is a rare but emerging fungal infection of the skin which can present with features that mimic cutaneous malignancies. Thus, it should be considered in most cutaneous lesions that appear like a malignancy. This report elaborates the mimicry of hemifacial histoplasmosis to cutaneous malignancy. The unusual location, complex presentation and dramatic remission following treatment with 2% salicylic acid and systemic fluconazole emphasizes the importance of a high index of suspicion of cutaneous mycosis in skin lesions with malignant characteristics.

Declaration of patient’s consent for use of his clinical photography: The authors certify that they have obtained the appropriate patient consent forms for use of their image in the scientific community. In the form the patient gave his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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