Reverse masquerade syndrome: Fungal adnexal infection mimicking carcinoma in a HIV-positive patient

Bipasha Mukherjee, Raka Chatterjee, Jyotirmay Biswas

A known HIV-positive male patient presented with a rapidly progressive ulcerative lesion involving the conjunctiva, lids, and anterior orbit along with a decrease in vision in the right eye. He was on anti retro-viral and anti-tubercular therapy. In view of the clinical features, our provisional clinical diagnosis was a malignant lesion of the eyelid with orbital involvement, possibly squamous cell carcinoma. However, incisional biopsy revealed absence of malignant cells. On Gomori Methenamine Silver staining, plenty of fungal filaments were seen, which was confirmed by culture as Candida albicans. Hence, it turned out to be a case of fungal adnexal infection mimicking carcinoma in a HIV-positive patient. The patient responded well to systemic anti-fungals.

Key words: AIDS, Candida albicans, reverse masquerade syndrome

Fungal infections of the lid and orbit may resemble ocular inflammation and neoplasia. However, to the best of our knowledge, a periorcular Candida infection presenting as a rapidly progressive ulcerated lesion mimicking a malignant neoplasm in an HIV-positive patient has hitherto not been reported.

Case Report

A known HIV-positive, 48-year-old male patient on Highly Active Anti Retroviral (HAART) therapy for the last 4 months and anti-tubercular therapy (ATT) since the last 3 months, presented with a painless, rapidly progressive ulcerated lesion involving the conjunctiva, lids, and anterior orbit of the right eye for past 3 weeks. According to the patient, the lesion started as a small boil over the right upper lid, which rapidly increased in size. Then, he developed a swelling over the medial canthal area. Both the lesions bled to touch. The patient gave history of decrease in vision in the right eye over the last 10 days. Best corrected visual acuity in the right eye was perception of light with inaccurate projection of rays and that of the left eye was 6/6; N6 (Snellen). The anterior segment examination of the left eye was within normal limits. Fundus examination of left eye revealed cotton-wool-spots and flame-shaped hemorrhages in the periphery suggestive of AIDS-related retinal microvasculopathy.[1] The right eye conjunctiva was congested with a sloughed-out area measuring 1 × 0.5 cm with underlying scleral thinning. The cornea showed an epithelial defect and thinning with extensive keratinization. The upper lid showed a 2.5 × 1 cm full-thickness defect with an overlying black eschar and a medial canthal ulcerative lesion [Fig. 1]. Ultrasound B scan of the right eye was within normal limits. Routine blood investigations were within normal limits, except mild decrease in hemoglobin levels (8.6 mgm/dl). Erythrocyte Sedimentation Rate was raised to 128 mm/h. CD4 lymphocyte count was 100 cells/µl and viral load of 101 copies of RNA/ml.

Magnetic resonance imaging (MRI) revealed a soft tissue lesion in the right supero-medial extra-conal space associated with thickening of extra-ocular muscles [Fig. 2a]. Considering the above findings in this immuno-compromised patient, the differential diagnoses were squamous cell carcinoma of the lid with extension into the orbit and zygomycosis. The patient was accordingly taken up for incisional biopsy of the periocular lesion for definitive histopathological diagnosis. Surprisingly, no malignant cells were found in the biopsy specimen. Gomori methenamine silver stain (GMS) staining showed plenty of fungal filaments [Fig. 3a]. Part of the specimen was also sent for microbiological analysis that showed presence of numerous budding yeast cells on KOH/Calcofluor-white stain [Fig. 3b]. Culture confirmed it as Candida albicans. The patient was started on IV fluconazole 600 mg once daily for 14 days after discussion with an infectious disease specialist. Topical antibiotic drops and lubricants were continued. HAART therapy and ATT were continued.

On his next follow-up visit, the patient had responded significantly to this therapy. The lid defect had healed. There were symblepharon and lagophthalmos of 7 mm. Cornea was opaque and keratinized [Fig. 4]. Temporary tarsorrhaphy was performed, and he was advised to undergo symblepharon release with amniotic membrane transplantation with full thickness skin graft of right upper lid. Repeat MRI revealed significant resolution of the lesion [Fig. 2b].

Discussion

Acquired immunodeficiency syndrome (AIDS) is a potentially lethal multisystem disorder caused by human immunodeficiency virus (HIV) that infects T-lymphocytes resulting in profound immunodeficiency leading to opportunistic infections and neoplasms.[2] Ocular lesions can occur in 70% of cases; whereas, ocular adnexal complications, seen in 25% of cases, can be a sign of severe immunodeficiency.[3]

Various opportunistic infections that occur in eye and its adnexa in HIV-positive patients are bacterial (Staphylococcus sp.), viral (Molluscum contagiosum, HZV), and fungal (Aspergillus...
The common neoplastic lesions occurring in Indian subcontinent are basal cell carcinoma, squamous cell carcinoma, and Non-Hodgkins lymphoma. HIV infection is associated with increased risk for eye lid and conjunctival squamous cell carcinoma. A total of 5–10% of all cutaneous squamous cell carcinomas in AIDS occurs in eye lid.[4] Clinically, it looks like a painless, nodular, plaque-like lesion. Chronic scaling, fissuring of skin, or central ulceration is frequently present. Histopathology confirms the diagnosis. A case of histoplasmosis presenting as an eyelid cutaneous malignancy has been reported.[5] In HIV-positive patients, Aspergillus spp. is the commonest fungi to invade the orbit. Mucormycosis is the commonest fungus invading the orbit in immunocompromised patients. It is a life-threatening infection causing thrombosis and tissue infarction by direct vascular invasion. Mucormycosis presents as progressive orbital and facial cellulites. Black necrotic eschars can be noted in the nasal cavity, on the hard palate, or as facial lesions. Fungating skin lesions are not seen in mucormycosis. Cutaneous disease manifests as cellulitis, which progresses to dermal necrosis and black eschar formation. Candida albicans is a normal commensal commonly found in skin and mucus membrane and causes mild superficial infections in moist and warm skin and mucosa. For this normal human commensal to become a significant pathogen, there must be some disruption of normal host defense mechanisms as in AIDS. Both Periodic Acid Schiff (PAS) stain and Gomori methenamine silver (GMS) stain are used to screen tissue for the presence of the distinctive yeast, but culture remains the gold standard. Candida appears as large, round, white, or creamy colonies with a yeasty odor on agar plates. In HIV-infected patients, Candida albicans can cause both ocular (keratitis, endophthalmitis) and periocular (blepharitis, cellulitis) infections. However, a combined orbital and eyelid infection by Candida spp., without any systemic involvement in an immunocompromised patient is unprecedented. Cases of candidal orbital necrotizing fasciitis has been reported in immunocompetent adults.[6] Our PUBMED search did not reveal any report of Candida orbital cellulitis in absence of any adnexal or systemic involvement in an HIV patient. The management of periocular Candida infection in a HIV-positive patient can be medical as well as surgical. Various antifungal
that act against *Candida albicans* are amphotericin B, ketoconazole, fluconazole, and, recently, posaconazole.[7] But, the key to proper infection control remains in thorough debridement, with the ultimate aim being prevention of spread of infection to the central nervous system.

In conclusion, rapidly progressive periocular lesions in an immunocompromised patient are typically malignant. Fungal infections have a slow and progressive clinical course. Fungal infections mimicking a carcinoma is called “reverse masquerade syndrome.”[8] A thorough examination and appropriate investigations are needed to differentiate between these two entities. Timely and correct diagnosis will prevent needless aggressive intervention.

**Acknowledgments**

Dr. Olma Veena Noronha, Consultant Radiologist, VRR Scans, Chennai, India.

**References**

1. Banker AS. Posterior segment manifestations of human immunodeficiency virus/acquired immune deficiency syndrome. Indian J Ophthalmol 2008;56:377-83.

2. Govendra P, Hansraj R, Naidoo KS, Visser L. Ocular manifestations of HIV/AIDS: A literature review (Part 1). S Afr Optometrist 2010;69:193-9.

3. Biswas J, Sudarshan S. Anterior segment manifestations of HIV/AIDS. Indian J Ophthalmol 2008;56:363-75.

4. Neves-Motta R, Ferry FR, Basílio-de-Oliveira CA, Carvalho Rde S, Martins CJ, Eyner-Silva WA, et al. Highly aggressive squamous cell carcinoma in an HIV-infected patient. Rev Soc Bras Med Trop 2004;37:496-8.

5. Merin MR, Fung MA, Eisen DB, Lin LK. Histoplasmosis presenting as a cutaneous malignancy of the eyelid. Ophthal Plast Reconstr Surg 2011;27:e41-2.

6. Rath S, Kar S, Sahu SK, Sharma S. Fungal Periorbital necrotizing fascitis in an immunocompetent adult. Ophthal Plast Reconstr Surg 2009;25:334-5.

7. Groll AH, Walsh TJ. Posaconazole: clinical pharmacology and potential for management of fungal infection. Expert Rev Anti Infect Ther 2005;3:467-87.

8. Karcıoğlu ZA. Reverse masquerade syndrome. Orbital Tumors: Diagnosis and Treatment. New York City: Springer; 2005. p. 324-5.