

Otolaryngological Manifestations of HIV/ AIDS : A Review

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INTRODUCTION, EPIDEMIOLOGY AND PATHOLOGY

Human immunodeficiency virus (HIV) infection may be referred to as the epidemic of the 20th century. It was estimated that by the end of the 1990s, 10 million people worldwide would have become HIV-positive[1,2]. In the United States HIV seroprevalence varied between 0.45% - 27.5% while it is 1.2% - 12% in Nigeria, and estimated to have caused 0.25million deaths in the year 1999 [2,3].

HIV preferentially infects cells of the nervous and lymphatic systems. The most important cell infected is the T-helper cell, through the CD4 receptor, resulting in both functional impairment and numeric depletion of T helper cells.

It was reported initially that 41% of patients with AIDS had head and neck manifestations however, as awareness increased, recognition of these lesions also increased and now nearly 100 percent of patients with AIDS develop head and neck manifestations[4,5]. The otolaryngologic manifestations of HIV disease can be classified as infections, neoplasms, and primary neurological damage caused by HIV. The common complications are tabulated in Table 1 [6].

NECK

An enlarging neck mass was reported in up to 91% of HIV-infected patients with head and neck manifestations[7]. The etiology of these neck masses

can be HIV lymphadenopathy, infectious processes or neoplasms[8,9].

HIV Lymphadenopathy

Persistent generalized lymphadenopathy, also known as HIV lymphadenopathy, is defined as unexplained generalized lymphadenopathy involving two or more extra-inguinal sites and lasting more than three months¹. It is one of the major criteria and the axilla and neck are the most common sites. Patients often have no symptom other than neck swelling. Tissue sampling should be performed when malignancy is suspected [10]. Indications for biopsy include recent weight loss and rapid increase in size.

Infectious Process of the Neck Related to HIV

Tuberculosis

Extrapulmonary disease has been reported to be predominant accounting for 50 to 67% of tuberculous infections in these patients[10,11]. The common sites include the cervical nodes, larynx and the bone marrow[12, 13, 14, 15]. The majority of the patients have no symptom other than an enlarging neck mass which is usually firm and nontender but 10% may be inflamed[14, 15, 16].

In the HIV-infected population, however, *Mycobacterium avium* complex (MAC) infection is the most common mycobacterial infection. MAC infection appears to originate from the lungs, but it can be isolated from lymph nodes, and other sites in up to 50% of affected patients[17, 18]. Histopathology of the involved tissue usually reveals poorly formed granulomas or no granulomas at all. Unlike *M. tuberculosis*, the response of atypical mycobacterial infections to traditional antimycobacterial drugs

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TABLE
Head Neck Manifestations of AIDS

| Otologic | Nasal and sinus | Oral | Neck |
|-----------------------------|-----------------------------|---------------------------|---|
| Otitis externa | Cutaneous | Recurrent aphthous ulcers | Generalized lymphadenopathy |
| Serous otitis media | Kaposi's sarcoma | Condyloma | Neck mass (due to infection with Mycobacterium tuberculosis, Mycobacterium avium complex, cryptococcosis, histoplasmosis or coccidioidomycosis) |
| Kaposi's sarcoma | Herpes simplex ulcers | Candidiasis | Parotid gland cyst |
| Eustachian tube dysfunction | Herpes zoster | Hairy leukoplakia | |
| Sensorineural Hearing loss | Noncutaneous | Herpes simplex | |
| | Adenoid hypertrophy | Gingivitis | |
| | Eustachian tube Obstruction | Stomatitis | |
| | Acute/chronic sinusitis | Periodontitis | |
| | | Kaposi's sarcoma | |
| | | Non-Hodgkin's lymphoma | |
| | | Squamous cell carcinoma | |

is often poor [17, 18]. Newer regimens including azithromycin or clarithromycin are effective [19].

Laryngeal tuberculosis remains the most common granulomatous disease of the larynx. Studies linking laryngeal TB to AIDS have estimated the incidence to be up to about 30% [6, 18, 19, 20], however, as the epidemic continues, more cases are expected. A high index of suspicion and differentiation from cancer or other granulomatous diseases are crucial to management.

Pneumocystis Carini

Extrapulmonary *Pneumocystis* was previously associated only with overwhelming, often fatal, disseminated infection but the incidence is rising now due to the use of prophylactic treatment for pulmonary *Pneumocystis* [20]. More recently, reports have described cervical infections without systemic or pulmonary involvement including an enlarging cervical mass from *Pneumocystis* infection of lymph nodes or the thyroid gland [21, 22]. Thyroid involvement produces a diffuse goiter-like swelling and the patient can be clinically hypothyroid. The diagnosis should prompt a search for both pulmonary and systemic disease. These cervical infections usually respond rapidly to medical therapy as used for pulmonary infections.

Mycosis

Fungal infections, including cryptococcosis, histoplasmosis, and coccidioidomycosis, can manifest as a cervical mass in the HIV-infected patient. *Cryptococcus neoformans* is the most prevalent cause of deep-seated fungal infections in the HIV-infected population, occurring in 5 to 10% of these patients and commonly involves the lungs and the meninges [23]. Pulmonary and disseminated forms of histoplasmosis and coccidioidomycosis are becoming more widespread in patients with advanced HIV disease as the incidence of HIV infections increases in areas in which *Histoplasma* or *Coccidioides immitis* is endemic [23, 24, 25, 26].

Serum and cerebrospinal fluid antigen titers correlate well with active cryptococcal disease although the typical granulomatous lesions of fungal infections may be absent [26]. Therapy with amphotericin B is moderately effective.

Malignancies

The most common malignancy associated with HIV disease is Kaposi Sarcoma (KS), an idiopathic multiple sarcoma of the skin. The incidence reported is 47% [27]. The oral cavity is the most common

site, nearly 95% are found on the palate. Other sites include gingival surfaces of the oropharynx, external ear, larynx and nose. The clinical course is unpredictable. They may be asymptomatic, but some may become exophytic and ulcerated. Secondary infection often occurs, producing severe, increasing pain, difficulty with mastication and swallowing, and increasing difficulty maintaining good oral hygiene[28, 29]. The involvement of the pinna or the external auditory canal may lead to conductive hearing loss especially with tumor extension to the tympanic membrane or into the middle ear.

Treatment includes low-dose radiation therapy which is usually very effective, although the risk of radiation intolerance and mucositis is high in HIV-infected patients. Alternative therapy that has been successful in some cases of oral and epiglottic KS is intralesional injection of vinblastine[28, 30, 31]. Carbon dioxide and argon laser have been used in excision of canalicular or tympanic membrane lesions[32]. The goals of therapy are to relieve symptoms and improve cosmesis.

Non-Hodgkins Lymphoma is the second most common HIV-associated malignancy. It commonly presents as a nontender, rapidly enlarging neck mass. The histopathologic findings are variable, but the majority of these lymphomas are high grade[33]. The precise relationship between these and HIV disease has not been defined, however, in the HIV-infected patient, NHL, Hodgkin's disease and squamous cell carcinoma tend to be more aggressive and less responsive to treatment[33, 34]. The work-up is the same as for the general population. The treatment includes surgery and chemotherapy, because HIV-infected patients tolerate radiotherapy very poorly.

Parotid

Xerostomia is a common complaint in AIDS. It is present in 10% of a group of patients with HIV infection, ARC and AIDS [30, 31, 32, 33, 34]. The cause is unknown, although CMV has been implicated in several studies. Treatment includes frequent saline rinses, sialogogues and topical fluoride applications. Cystic parotid enlargement is a well documented finding in AIDS. This may occur early in the disease prior to diagnosis of HIV infection..

The parotid masses are typically unilateral or bilateral multicystic, nontender enlargements resembling lymphoepithelial cyst. Needle aspiration is indicated for symptomatic relief and to rule out malignancy. Surgery should be avoided due to the refractoriness of the lesion and its underlying benign nature, as well as the risk of facial nerve damage.

Oral Cavity

The oral cavity represents one of the most common sites for HIV-related pathology. The spectrum includes infectious, benign inflammatory, neoplastic, and degenerative processes.

Candidiasis (Oral Thrush)

Oral candidiasis is by far the most common oral condition in HIV/AIDS patients. It occurs even in patients with CD4 counts from 200 to 500 mm³. Typically, it is a recurring problem which presents as tender, white, pseudomembranous or plaque-like lesions with underlying erosive erythematous mucosal surfaces; however, the less typical atrophic or chronic hypertrophic form is also often encountered. Angular cheilitis is a variant of oral candidiasis which typically presents as a nonhealing fissure at the oral commissure. Diagnosis is usually made by potassium hydroxide preparation of scrapings from these lesions[35, 36].

Topical therapy with nystatin or clotrimazole can be effective. Systemic therapy with ketoconazole, fluconazole, Amphotericin B and prophylactic antifungal may be indicated in severe cases of immunosuppression[37, 38].

Herpes Simplex

Herpes labialis most commonly presents as crops of fever blisters on the palate, gingiva, or other oral mucosal surfaces. The lesion tend to be larger and more numerous, recur more frequently, and often persist longer than in non-HIV subjects. They can also extend onto adjacent skin and coalesce to form giant herpetic lesions[39, 40].

Treatment may not be necessary if the lesions are small, relatively asymptomatic, and beginning to heal. Otherwise, treatment consists of oral acyclovir for large or symptomatic lesions.

Hairy Leukoplakia

This usually presents as a white, vertically corrugated lesion along the anterior lateral border of the tongue. It occurs almost exclusively in HIV-infected patients, and is associated with more rapid progression to the full-blown AIDS. Epstein-Barr virus is associated with these lesions and is the probable cause. It is primarily an asymptomatic condition requiring little more than recognition and observation. Treatment is generally unnecessary [41, 42, 43].

Recurrent Aphthous Ulceration

This is typically a painful condition of the oral cavity formed by the coalescing of the smaller lesions into large ulcers and can present anywhere in the oral cavity or pharynx [40]. They are often associated with severe odynophagia leading to anorexia and dehydration, and thus contribute to AIDS morbidity and wasting. It may be worsened by secondary infection [41]. Surgical or laser excision of these lesions is the treatment of choice [18].

Otologic Manifestation

Sensorineural Hearing Loss

Sensorineural hearing loss has also been reported between 21 to 49% of HIV-infected patients [42, 43, 44]. It may be unilateral or bilateral, usually worsens steadily with increasing frequencies, but speech discrimination is usually preserved. The possible etiologies are a primary infection by HIV of the central nervous system or peripheral auditory nerve, cryptococcal meningitis and idiopathic [45, 46, 47].

Smith and Canalis [47] reported cases of otosyphilis in patients with HTLV III, they proposed that the virus alters the course and hastens the development of otosyphilis leading to sensorineural hearing loss, therefore, diagnostic work-up should include serologic testing for syphilis.

Otitis Externa

The epidemiological parameter of otitis externa is not different in the AIDS population, although the course could be more dramatic [48]. Predisposing factors are excessive irritation or mechanical trauma [8]. Patients usually present with hearing loss, otalgia and inflamed external auditory canal with purulent debris within it. Treatment requires prolonged suctioning of

the exudate in the ear and topical antibiotic treatment [49].

As in other immunocompromised patients, persons with HIV/AIDS are predisposed to malignant otitis externa or osteomyelitis of the skull base. Clinical evidence suggesting malignant otitis externa includes severe, progressive pain, fever and granulation tissue within the ear canal. The causative agent is usually *P. aeruginosa*, although *Pneumocystis carinii*, *M. tuberculosis* and other common pathogens have been reported [49]. Treatment requires combination of prolonged intravenous antibiotics and, possibly, surgical debridement.

Otitis Media

The most common otologic problems reported in HIV-infected patients are serous otitis media and recurrent acute otitis media. These conditions frequently affect paediatric patients with HIV disease because eustachian tube dysfunction typical of this age group combined with depressed cell-mediated immunity markedly increases their susceptibility to middle ear infection [45, 50].

In HIV-infected adults, eustachian tube dysfunction can result from nasopharyngeal lymphoid hyperplasia, sinusitis, nasopharyngeal neoplasms, or allergies and their associated mucosal changes. In most of these patients with nasopharyngeal lymphoid hyperplasia, an adenoidectomy will improve eustachian tube function [50].

Rhinosinusitis

The prevalence of rhinosinusitis ranges from 20 to 70% in patients with AIDS [4]. Causative organisms include atypical opportunistic and common organisms responsible for sinusitis in hosts without AIDS. Opportunistic fungal sinusitis is caused by organisms such as *Alternaria alternata*, *Aspergillus*, *Pseudallescheria boydii*, *Cryptococcus* and *Candida albicans* [9, 15, 36, 48, 49, 50, 51, 52]. The features of sinusitis are similar to findings in non-HIV subjects. Medical therapy is effective while surgery is often indicated to facilitate sinus drainage and to obtain tissue specimens to diagnose other infections and malignancies [52].

Nasal Allergy

Contrary to what would be expected, there is B – cell activation leading to increased production of circulating immune complexes and immunoglobulins A, G and E. The excessive IgE production is associated with increased IgE-mediated allergic symptoms, including allergic rhinitis. Sample et al and others[53, 54, 55] have reported raised Ig E level and a two-fold increase in the incidence of allergic symptoms in HIV-infected men. Profuse rhinorrhoea and congestion is similar to the general population although the intensity may suggest chronic persistent bacterial rhinosinusitis.

Topical nasal steroid sprays and systemic antihistamines are effective. The newer, second-generation antihistamines are preferred in HIV-infected patients because of lesser anticholinergic activity resulting in decreased viscosity and surface adhesiveness of nasal secretions[55]. However, specific environmental allergens should be identified and avoided if possible[56].

The multiplicity of these pathologies may suggest enormous challenges to the otolaryngologists in the management of these patients however patient care also requires special considerations. These include the risk of transmission of the infection, recommendations for surgical procedures and concepts of post - exposure prophylaxis[56, 57].

In conclusion, with increasing incidence of HIV, more cases will be encountered by otolaryngologists in Nigeria and research into otolaryngologic peculiarities of HIV/AIDS will expectedly be an issue for the future.

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