

HIV manifestations in the head and neck

The human immunodeficiency virus (HIV) and AIDS continue to create major changes in the practice of medicine.

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South Africa has the highest incidence of HIV- and AIDS-infected individuals in the world, with 5.3 million living with HIV and AIDS.^{1,2} The interpretation of HIV prevalence trends in South Africa is increasingly complex due to the simultaneous implementation of both preventive and treatment programmes. The number of individuals on antiretroviral treatment (ART) is rising, leading to improvement in survival rates.³ The longer survival rate influenced the way HIV-associated manifestations present, including the manifestations in the head and neck region.

Head and neck manifestations can be subdivided into different groups: (i) oral; (ii) sinonasal; (iii) neuro-otological; (iv) neck and salivary gland pathology; and (v) HIV-associated neoplasms.

Multiple oral lesions in a patient on ART might indicate treatment failure.

Oral manifestations

Candida, oral hairy leukoplakia, herpes stomatitis, periodontal and gingival disease, aphthous ulcers and xerostomia are some of the most common manifestations in cases of HIV and AIDS, although initiation of ART has significantly reduced their incidence.⁴ Multiple oral lesions in a patient on ART might indicate treatment failure. Common HIV-associated neoplasms still present in the oral cavity and physicians should have a low threshold for biopsy if there is no response to empiric therapy.



Fig. 1. A case of acute necrotising ulcerative gingivitis a year after presentation.

Oral candidiasis is present in 70 - 90% of patients with AIDS.⁴ The pseudomembranous type presents as white, cheese-like plaques that can be scraped off, revealing an erythematous, bleeding base. Hyperplastic candidiasis is identified by raised white plaques on the buccal mucosa that cannot be scraped off. A biopsy or potassium hydroxide solution is often necessary to confirm the diagnosis and exclude malignancy. Atrophic candidiasis presents as hyperaemic mucosa commonly found on the hard palate or dorsal tongue, and angular cheilitis presents as tender erythematous fissured oral commissures. The management of oral candidiasis includes the use of topical antifungals (nystatin or clotrimazole). Occasionally, the use of systemic antifungals (ketoconazole or fluconazole) might be necessary.

Gingivitis and periodontal disease are very common, even with good oral hygiene.

Xerostomia associated with chronic mouth breathing (enlarged adenoids), autoimmune salivary gland disease, and iatrogenic causes (antidepressants) worsens the risk of gingivitis, periodontitis and dental caries. Gingivitis presents as a red line at the gingival margin that bleeds with minimal trauma. Periodontitis, however, presents as loosening teeth and deep dental pain, which is caused by the spread of infection



Fig. 2. Sequestrum removed from the palatal lesion.

HIV manifestations



Fig. 3. A case of oral hairy leukoplakia.



Fig. 4. A case of an aphthous ulcer.



Fig. 5. A case of a herpetiform ulcer.

to the periodontium. As the CD4 count decreases, the risk of rapidly progressive acute necrotising ulcerative gingivitis (ANUG) and stomatitis increases.⁴ Gram-negative anaerobes play a major role in the development of ANUG. In gingivitis, plaque removal and a 10% povidone-iodine with 0.2% chlorhexidine gluconate mouthwash are sufficient, but in ANUG and necrotising stomatitis only parenteral antibiotics (clindamycin or metronidazole) are effective. Owing to the necrotising nature of ANUG, there is extensive soft tissue loss that leads to bone destruction and sequestration, which needs to be debrided (Figs 1 and 2).

Oral hairy leukoplakia results from an infection with the Epstein-Barr virus (EBV). It presents as a white corrugated lesion most commonly found on the lateral side of the tongue (Fig. 3). It affects 17 - 25% of HIV patients and its presence indicates an increased risk of developing AIDS within 6 months.⁴ No management is necessary but leukoplakia and carcinoma *in situ* should be excluded with a biopsy.

Aphthous ulcers (AUs) can be divided into herpetiform (0.2 mm), minor (<6 mm) and major ulcers (>6 mm) ulcers (Figs 4 and 5). AUs affect the unattached mucosal surfaces. Management of ulcers should focus on symptomatic relief, support of nutritional status and ruling out of malignancy.

Management includes a combination of topical steroids (triamcinolone) and a local anaesthetic spray (lidocaine (Xylocaine)). A mouthwash with either tetracycline (250 mg/5 ml qid for 4 days) or chlorhexidine (0.2% bd for 7 days) should be added. Intra-oral herpes infection usually affects the attached mucosal surfaces such as the hard palate, gingiva and tongue and is characterised by small round ulcers without an erythematous halo. Extra-oral herpes infection (fever blisters) remains very common but in HIV the blisters are numerous, larger in size, persist longer and recur more frequently than in the normal population. Acyclovir 200 mg 5 times/d for 5 days is needed in herpetiform ulcers to prevent a coalescent stomatitis in cases of a CD4 count below 100.⁴

Hyperplastic candidiasis is identified by raised white plaques on the buccal mucosa that cannot be scraped off.

Sinonasal infections

The most common symptom among HIV-infected patients is of sinonasal origin – a blocked nose. Adenoid hyperplasia and allergic rhinitis are the most common pathogenic mechanisms. Any adult with a chronic blocked nose and an effusion in the middle ear who does not respond to conservative management should be referred to an ENT specialist for a nasopharyngoscopy and biopsy. If the nasopharyngeal biopsy confirms lymphoid hyperplasia, the diagnosis of possible HIV can be confirmed with an ELISA blood test. If the biopsy reveals a lymphoma, the patient should be referred to an oncologist. An adenoidectomy can be performed to relieve the nasal obstruction while a myringotomy and ventilation tube insertion can be done for the middle-ear effusion.

Sinusitis. There is a 70% risk of acute sinusitis and a 60% risk of recurrent acute

HIV manifestations

or chronic sinusitis. Three mechanisms might explain this: HIV patients have a 87% increase in atopy and allergic rhinitis leading to swollen mucosa and decreased ventilation, impaired systemic and local immunity, and decreased mucociliary clearance.⁴ The spectrum of organisms involved appears to be broader than in the normal population and might be explained by multiple previous courses of antibiotics, or prophylaxis. As the CD4 count drops, the risk of chronicity increases and there is a greater propensity to develop complications such as periorbital cellulitis and invasive fungal rhinosinusitis. The main goal in the management of sinusitis in HIV patients is to treat bacterial sinusitis promptly and to identify lymphoma or fungal rhinosinusitis. Antibiotics, decongestants and intranasal steroids for 10 days should be used as the first line of treatment in bacterial sinusitis.

Any adult with a chronic blocked nose and an effusion in the middle ear who does not respond to conservative management, should be referred to an ENT specialist for a nasopharyngoscopy and biopsy.

Invasive fungal rhinosinusitis is uncommon in HIV patients but progression to AIDS decreases the neutrophil function. Neutrophils and macrophages are our main protection against *Aspergillus* and other fungi. Physicians should consider invasive fungal rhinosinusitis in a feverish patient who does not respond to antral lavage and antibiotics. They present with pale, necrotic nasal mucosa, periorbital swellings and proptosis, especially if associated with perforations in the septum and hard palate. Emergency referral to an ENT specialist is essential.

Neuro-otological presentations

Sensorineural hearing loss (SNHL), otitis externa and otitis media are very common in HIV and AIDS. The neurotropic nature of HIV, autoimmune demyelination and antibodies produced against peripheral nerves lead to clinical signs of neurological disease in 40% of patients.⁴ Trigeminal (CN5), facial (CN7) and vestibulocochlear (CN8) nerve signs might be the only presenting symptoms and work-up should include serology for HIV, particularly of a CN7 palsy. Opportunistic infections such as cryptococcosis, syphilis and the central effects of HIV and ototoxic effects of antiretroviral drugs should not be ignored as possible causes of SNHL. A neuro-otological presentation necessitates an ENT and audiology referral owing to the differential diagnosis.

Neck and salivary gland disease

Most HIV-infected patients will present with a neck mass during their illness. The differential diagnosis includes neoplasms, infections, HIV lymphadenopathy and parotid disease. Idiopathic follicular hyperplasia is the most common cause but multiple conditions may co-exist. Persistent generalised lymphadenopathy (PGL) should be differentiated from more serious conditions. A sketchy history and a low yield from microbiological and histological testing often complicate the diagnostic process. A thorough history, an examination, a CD4 count, fine needle aspiration (FNA) and open biopsies might be needed in the work-up of a suspicious lesion. An infectious or a malignant lesion should be suspected if it is larger than 2 - 3 cm, asymmetric, unilateral, deep and painful. Tender lymphadenopathy is usually infectious while non-tender nodes tend to be malignant. A low CD4 count (<100) tends to be associated with infectious or malignant causes of the lymphadenopathy, but a CD4 >500 is usually associated with PGL. Infectious causes of the lymphadenitis, such as mycobacteria (Figs 6 and 7), Pneumocystis, EBV, toxoplasmosis and cat scratch disease, should be excluded.

Parotid enlargement mostly results from benign lympho-epithelial cysts (BLCs) that develop secondary to a benign



Fig. 6. A case of *Mycobacterium avium intracellulare* – soft palate.

lymphoproliferative disease. It is common in adults and children not on ART. BLCs usually present as bilateral, painless parotid swellings. The differential diagnosis includes Sjögren's disease, Whartin's tumour and branchial cleft cysts. A unilateral, solid mass with involvement of the skin, CN7, fixed nature or development of pain should lead to an ultrasound and FNA to exclude an infectious or malignant process.⁴ BLCs tend to be managed conservatively until they produce cosmetic deformities or chronic pain. Management options include low-dose radiation, sclerosis, repeated aspiration or superficial parotidectomy. Sclerosis with 70 - 90% alcohol or doxycycline can easily be done as an outpatient.



Fig. 7. A case of *Mycobacterium avium intracellulare* – nose.

Head and neck neoplasms

Kaposi's sarcoma (KS) and non-Hodgkin's lymphoma are AIDS-defining conditions but other tumours are also associated with HIV, including basal cell carcinoma, squamous cell carcinoma (SCC) and Hodgkin's lymphoma.

HIV manifestations



Fig. 8. A case of Kaposi's sarcoma of the hard palate and gingiva.



Fig. 9. A case of Kaposi's sarcoma of the tongue.

Non-Hodgkin's lymphoma. The risk of developing lymphoma is increased 40-fold

in HIV-positive patients, especially if the CD4 count drops below 200. Ninety-five per cent of cases are high-grade B-cell tumours.⁴ The extranodal site presentation doubles in HIV patients and 60% of these cases occur in the head and neck region.⁴ Symptoms are dependent on the site of presentation, but usually constitute decreased functionality owing to a growing mass or an ulcer. FNA can aid the diagnostic process but for subtyping one needs a tissue sample. Lumbar punctures are frequently necessary due to the high risk of asymptomatic CNS lymphoma.

Kaposi's sarcoma. This HHV-8-derived mesenchymal tumour involving blood and lymphatic vessels probably needs no introduction. KS is almost pathognomonic with AIDS. AIDS-KS is more aggressive and less responsive to chemotherapy than the classic form (Figs 8 and 9). There is a 60% predilection for the head and neck region (50% cutaneous and 50% mucosal).⁴ Lesions are frequently multiple, non-tender, and blue-purple and do not blanch to touch. They tend to coalesce and can become symptomatic, especially in the oral and sinonasal cavities. Treatment is indicated when these lesions become symptomatic or aesthetically disfiguring. Symptoms include bleeding due to ulceration, difficulty

in eating, pain or even obstructive airway symptoms. The diagnosis should be confirmed with a biopsy. Treatment remains palliative (local or systemic) as no cure is known. Management includes starting the patient on ART. The introduction of ART has resulted in a clear decline in the incidence of KS. Local therapies include alitretinoin gel, intralesional chemotherapy, radiotherapy with less than 20Gy, laser and cryotherapy. Systemic chemotherapy is reserved for visceral disease and liposomal anthracyclines as a single agent are now considered as first-line treatment in advanced AIDS-KS.

Squamous cell carcinoma. The incidence of SCC is not increased in HIV, but a high rate of human papillomavirus (HPV) infection and an increased survival due to ART might explain the higher prevalence. HIV-SCC has a high predilection for the tonsils, oral cavity and larynx. These lesions present earlier and are more aggressive. A low threshold for biopsy is indicated. Management of these patients is challenging owing to comorbidities.

References and Further reading available at www.cmej.org.za

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- The prevalence of HIV individuals on ART is expected to rise because of the improvement in survival rates.
- Initiation of ART significantly reduced the incidence of oral lesions. Multiple oral lesions might indicate failure of the treatment regimen
- Physicians should have a low threshold for biopsy in head and neck lesions if there is no response to empiric therapy.
- The management of ulcers should focus on symptomatic relief, nutritional support and excluding malignancy.
- Facial nerve paralysis might be the only presenting symptom and work-up should include serology for HIV.
- The most common symptom among HIV-infected patients is sinonasal in origin.
- If a blocked nose is associated with a middle-ear effusion, the physician should suspect possible nasopharyngeal malignancy and the patient should be referred to an ENT specialist for biopsy.
- A parotid swelling should be suspected as being infectious or malignant if the mass is larger than 2 - 3 cm, asymmetrical, unilateral, deep, and involves the facial nerve or skin.
- The risk of developing lymphoma is increased up to 40 times in HIV-positive patients, especially if the CD4 count decreases below 200. Sixty per cent of these cases occur in the head and neck region.
- Treatment of Kaposi's sarcoma in the head and neck region is indicated in symptomatic or aesthetic disfiguring lesions.