Chapter 8. Otolaryngological Manifestations of AIDS

Acquired immunodeficiency syndrome (AIDS) first came to medical attention in the early 1980s, when an isolated number of deaths from rare lung infections (Pneumocystis carinii pneumonia (PCP)) and unusual skin tumors (Kaposi's sarcoma) were noted in previously healthy homosexual men in California and New York. In the 1990s, AIDS has become an epidemic. As of January 1990, the Centers for Disease Control (CDC) has reported more than 121,500 cases of AIDS and approximately 72,500 AIDS-related deaths in the United States. Fifty-nine percent of all reported cases of AIDS as of October 1989 have died, with current estimates of a 100% mortality rate between 3 and 5 years after diagnosis.

I. HIV

The causative agent of AIDS is the human immunodeficiency virus (HIV). HIV infection manifests itself in a wide range of diseases processes: constitutional abnormalities (Table 8-1), opportunistic infections (Table 8-2), and secondary cancers (Table 8-3).

A. Pathophysiology

HIV is a retrovirus that attacks CD4 receptors found on T-helper cells, macrophages, central nervous system (CNS) cells of monocytic origins, and other antigen-presenting cells. As a result, a T cell immunodeficiency occurs and the host becomes susceptible to many opportunistic infections and neoplastic conditions.

Because of the multiple systemic manifestations of AIDS, the CDC divided the spectrum of HIV infections into four stages (Table 8-4).

Other classification systems for HIV infection do exist, such as the Walter Reed staging system, which uses both clinical and laboratory indicators (number of peripheral CD4+ lymphocytes and levels of HIV antigen) to monitor disease progression. To date, CD4+ cell count is the most clinically useful measure of immune function in the HIV-infected individual. When the count falls below 200 cells/mm³, the host becomes most susceptible to opportunistic infections.

B. Transmission

HIV has been isolated from a number of body fluids, including blood, semen, saliva, tears, urine, cerebrospinal fluid, breast milk, and cervical and vaginal secretions. Transmission of the virus has been reported from sexual intercourse (anal and vaginal), parenteral inoculation (eg, IV drug abuse, blood transfusion, organ transplantation), and from HIV-infected mother to child. Latency between HIV infection (seropositivity) and full-blown AIDS has a reported mean of 10 years.

C. Epidemiology

As of January 1990, the CDC reported more than 121,645 cases of AIDS in the United States; 97.9% of these cases occurred in adults, 0.4% in adolescents (aged 13 to 19 years), and 1.7% in children (aged < 13 years). Approximately 72,500 of reported cases have ended
in death as of January 1990. The current estimates predict that 31% of persons with AIDS have died within 1 year of initial diagnosis, 56% at 2 years, 76% at 3 years, and nearly 100% at 5 years.

Table 8-1. Constitutional abnormalities associated with HIV

- Diarrhea
- Fever
- Generalized lymphadenopathy
- Hepatosplenomegaly
- Night sweats
- Weight loss/wasting syndrome.

Table 8-2. Opportunistic infections associated with AIDS and HIV infection

- *Pneumocystis carinii* pneumonia
- *Candida albicans* (bronchial, esophageal, or pulmonary)
- *Cryptococcus neoformans* (extrapulmonary)
- *Coccidioides immitis* (extrapulmonary)
- Disseminated histoplasmosis
- Disseminated toxoplasmosis (after 1 month of age)
- Disseminated *Mycobacterium tuberculosis*
- Disseminated *Mycobacterium* species (*M. avium intracellulare* or *M. kansasii*)
- Chronic isosporiasis
- Extraintestinal strongyloidosis
- Nocardiosis
- Cytomegalovirus infection outside of liver, spleen, and lymph node (after 1 month of age)
- Progressive multifocal leukoencephalopathy.

Table 8-3. Secondary cancers associated with AIDS and HIV infection

- Kaposi’s sarcoma
- Primary lymphoma of the brain
- B-cell non-Hodgkin's lymphoma.

Major risk groups for HIV infection include male homosexuals, IV drug abusers, persons receiving unscreened blood transfusions or blood products, and sexual partners of the above groups. As of 1990, the breakdown of AIDS cases reported in the United States was 68% homosexual men (7% with history of IV drug abuse), 21% heterosexuals with a history of IV drug abuse, 5% heterosexuals without a history of IV drug abuse, 2% associated with blood transfusions or blood products, and 1% were hemophiliacs.

African-Americans and Hispanics represent greater than 40% of AIDS cases. Women and children of minority populations are markedly over-represented among persons with AIDS.
Cumulative data based on three large cohort studies including more than 1200 health care workers with HIV exposure due to accidental needlestick injury estimate the rate of infection as 0.4%. Additionally, case reports of transmission from HIV-infected doctors to patients have also been reported. More data are needed on this aspect of transmission and epidemiology.

**Table 8-4. CDC stages of HIV infection, 1986.**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Acute infection (often and EBV-like syndrome with or without aseptic meningitis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Group 3</td>
<td>Persistent generalized lymphadenopathy</td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
</tr>
<tr>
<td>Subgroup A</td>
<td>Constitutional disease (eg, with weight loss, fever, diarrhea)</td>
</tr>
<tr>
<td>Subgroup B</td>
<td>Neurological disease</td>
</tr>
<tr>
<td>Subgroup C1</td>
<td>Secondary infectious diseases (12 specific diseases), including PCP pneumonia, toxoplasmosis, and esophageal or pulmonary candidiasis</td>
</tr>
<tr>
<td>Subgroup C2</td>
<td>Secondary infectious disease (another 6 specified diseases), including hairy leukoplakia and oral candidiasis</td>
</tr>
<tr>
<td>Subgroup D</td>
<td>Secondary cancers, including Kaposi's sarcoma, Hodgkin's lymphoma, and non-Hodgkin's lymphoma</td>
</tr>
<tr>
<td>Subgroup E</td>
<td>Other conditions, eg, chronic lymphoid interstitial pneumonitis.</td>
</tr>
</tbody>
</table>

* Only patients in group 4, subgroup C1 fulfill the criteria for AIDS.

**II. Manifestations of AIDS in otolaryngology**

Patients with AIDS often present with diseases of the head and neck. Different studies have indicated that greater than 40% of patients with HIV present initially with otolaryngological manifestations.

A University of California at San Francisco study conducted from 1980 to 1984 revealed that out of 399 AIDS presentations, 165 (41%) initially presented with head and neck manifestations. Of the presenting symptoms, 35% had cutaneous, oral, and pharyngeal lesions of Kaposi’s sarcoma; 22% had chronic cough and shortness of breath; 8% had rapidly enlarging neck masses; and 4% had herpes simplex virus. Two additional European studies revealed that 68% and 88% of AIDS patients manifested head and neck symptoms.

Manifestations of AIDS can be classified into three groups: (1) opportunistic infections caused by immunosuppression, (2) tumors resulting from immunosuppression, and (3) direct effects of HIV infection. This section examines the otologic, rhinologic, and oral manifestations of HIV, as well as lymphadenopathy in AIDS patients. Many patients with the listed conditions may follow a similar clinical course as the immunocompetent individual.

**A. Otologic manifestations**

HIV infection may predispose to a variety of otologic infections by immunosuppression, hastening preexisting disease or development of opportunistic infections.
However, most otologic diseases associated with AIDS parallel disease in the immunocompetent host.

1. Infections

   a. **External otitis.** *Pseudomonas aeruginosa* is a common pathogen. Cases of fungal external otitis have been reported.

   b. **Acute otitis media.** As in the immunocompetent host, *Pneumococcus* and *Haemophilus influenzae* are the organisms most frequently cultured in HIV-infected patients.

   c. **Serous otitis media.** Increased eustachian tube dysfunction is HIV-infected patients may occur secondary to nasopharyngeal masses, recurring viral infections, and allergy.

   d. **Chronic otitis media.** Cases of extrapulmonary PCP-infected aural polyps have been reported.

   e. **Herpes zoster oticus (Ramsay Hunt syndrome).** Bullous myringitis-type lesions have been reported.

   f. **Otosyphilis.** Accelerated development of otosyphilis from its latent state may occur in HIV-infected patients.

2. Neoplasms

   a. **Kaposi’s sarcoma.** Prior to HIV, Kaposi’s sarcoma was a rare malignant disease found mainly in elderly Caucasian men. It is a mesenchymal tumour, and clinically appears as red-purple plaques and nodules. The sarcomatous lesions may involve the external auricle, nasopharynx, or both.

3. HIV-induced hearing loss

   The hearing deficit in HIV-infected individuals can be divided into sensorineural and conductive hearing losses.

   A. **Sensorineural hearing loss.** This is the most frequent cause of hearing loss in HIV-infected patients, usually in the high-frequency range. Possible causes include:

      (1) CNS and end-organ involvement, with tumors, infections (CNS toxoplasmosis, neurosyphilis, tuberculosis, and bacterial, viral or cryptococcal meningitis), or HIV drug regimen side effects.

      (2) HIV virus neurotropism could conceivably involve the eighth cranial nerve.

      (3) Central demyelination from HIV infection. Auditory brainstem-evoked responses with conduction delays greater than two standard deviations and a degraded waveform have been noted in patients with AIDS and in healthy seropositive patients.
b. **Conductive hearing loss.** This is less common. Causes include PCP granulomas and Kaposi’s sarcoma of the external auditory canal, external otitis, and otitis media.

B. **Rhinologic manifestations**

1. **Infections**

   a. **Sinusitis.** The incidence of sinusitis has ranged from 10-68% in AIDS patients. Because the frequency of sinusitis is so high in this population, patients presenting with fever, headache, or URI symptoms should be evaluated for sinusitis. The most common pathogens are *Staphylococcus aureus, Pneumococcus*, and *Pseudomonas aeruginosa*.

   **Immunological factors.** B-cell dysfunction also occurs in AIDS patients, and patients are therefore at higher risk for recurrent bacterial infections than the general population. IgG subclass deficiencies found in some AIDS patients have been associated with increased frequency of infections, including otitis media, sinusitis, and bronchopneumonia. Deficiencies in the subclasses IgG2 and IgG4 exist in a subgroup of AIDS patients, predisposing this population to recurrent bacterial sinopulmonary infections. In addition, progressive elevation of IgE levels in association with an increase in histamine release has been reported in certain AIDS patients. This may be relevant when considering the frequent drug reactions seen in this population; this may also predispose patients to recurrent rhinosinusitis.

   b. **Herpes reactivation.** Seventy-three percent of patients at high risk for AIDS who presented with herpes zoster were found to be HIV seropositive upon testing, and an additional 15% became HIV positive during follow-up. Latent activation of varicella zoster virus in the dorsal root ganglion, thought to be secondary to deficient cell-mediated immunity, may occur more often than in the immunocompetent host. Here, patients may present with giant herpetic nasal ulcers that begin in the vestibule and extend onto the septum or face.

   c. **Candidiasis.** Nasopharyngeal candidiasis is often part of a spectrum of diffuse pharyngeal candidiasis (see II.C.).

2. **Neoplasms**

   a. **Nasopharyngeal lymphoid masses.** Nasopharyngeal masses, which on biopsy reveal benign lymphoid hypertrophy, have been reported. Patients may present with nasal obstruction and otitis media with serous effusion.

   b. **Lymphoma.** Cases of high-grade, undifferentiated, large-cell lymphomas and high-grade, small, noncleaved, B-cell lymphomas in the nasal cavity and antrum have been reported. Patients present with nasal obstruction, foul-smelling nasal discharge, and alar flaring.

   c. **Kaposi’s sarcoma.** This malignancy has been reported on the nasal skin, vestibule, cavity, septum, and nasopharynx.
3. HIV-associated diseases with rhinologic manifestations

**Idiopathic thrombocytopenia.** Patients with this complication can present with epistaxis.

C. Oral manifestations

Oral lesions appear to represent an early indication of immunosuppression. Because HIV-infected people are immunocompromised, these lesions may represent the first presentation of AIDS.

1. Infections

   a. **Candida.** Candida is the most common intraoral fungal infection in HIV-positive patients and may represent the earliest sign of HIV infection. Prevalence is 30-90% among HIV-positive patients. Forms of this infection include:

      (1) **Pseudomembranous infection (thrush).** Clinically, it appears on the oral mucosa as a creamy plaque resembling mild curd; it wipes off easily, but often leaves a bleeding surface.

      (2) **Hyperplastic candidiasis (leukoplakia candidiasis).** Clinically, this appears as a white firm plaque that cannot be wiped off.

      (3) **Erythematous candidiasis (atrophic candidiasis).** Patients present with red patches on the buccal mucosa, hard and soft palate, or dorsum of tongue.

      (4) **Angular cheilitis.** This is a perioral manifestation of the disease and presents as a fissuring, cracking erythema, or ulceration, at the corner of the mouth.

   b. **Cryptococcus neoformans**

   c. **Histoplasmosis.** Cases have been reported.

   d. **Bacterial infections.** Streptococcal species, *Staphylococcus aureus*, and less commonly *Klebsiella pneumoniae, Enterobacter cloacae, Mycobacterium avium intracellulare, Actinomyces*, and *Escherichia coli* have been reported. These bacterial infections cause severe periodontal and gingival disease in the oral cavities of AIDS patients. Clinically, these infected, colonized patients experience severe pain, hyperemic gingiva, and spontaneous bleeding that results in gross destruction of soft tissue and bone.

   e. **Hairy leukoplakia (associated with Epstein-Barr virus).** Oral hairy leukoplakia is an asymptomatic hyperkeratotic lesion often found in the oral cavity and oropharynx of the immunocompromised, including HIV-infected patients. Clinically, it appears as a white patch, sometimes corrugated, usually on the lateral margins of the tongue. Cases have been reported on the floor of the mouth, buccal mucosa, oropharyngeal mucosa, and soft palate. Candida overgrowth occurs frequently on the surface of these lesions.
f. **Herpes simplex virus.** Symptoms differ in HIV-infected patients and healthy patients. In the immunocompetent host, lesions are usually restricted to attached tissues and appear as small vesicles that coalesce in a few days to shallow ulcers, most lasting 7 to 14 days. However, lesions in HIV-infected patients may occur throughout the mouth, especially on the palate, lips, and perioral areas. Ulcers are deep and painful and may persist for several weeks.

g. **Other herpes viruses.** Few cases of herpes zoster and cytomegalovirus (CMV) have been reported.

h. **Human papilloma virus.** This virus is common in the HIV-infected patient and produces oral manifestations of focal epithelial hyperplasia, warts, and condyloma acuminatum.

2. **Neoplasms**

a. **Kaposi's sarcoma.** Kaposi’s sarcoma is the most common intraoral neoplasm associated with AIDS. The hard palate is most commonly involved; however, cases involving the gingiva, buccal mucosa, and soft palate have been reported. Candida-infected sarcomatous lesions have been reported.

b. **Non-Hodgkin's lymphoma.** The location and symptoms can mimic Kaposi's sarcoma.

c. **Squamous cell carcinoma.** Although this is the most common intraoral malignancy in non-HIV-infected patients, it is less common than both Kaposi’s sarcoma and non-Hodgkin's lymphoma in AIDS patients. The tongue is the most frequently involved site in HIV-positive patients.

3. **HIV-associated diseases with oral manifestations**

a. **Parotid disease.** Parotid enlargement is very common in HIV-infected patients, and evidence of xerostomia has been reported in 6-10% of this population. Clinically, a cystic enlargement of the parotid gland, which often accompanies a syndrome of persistent generalized lymphadenopathy, is observed. Parotid masses caused by HIV infection usually occur as unilateral or bilateral multicystic, nontender parotid enlargements.

b. **Sjögren's-like syndrome**

c. **Recurrent aphthous stomatitis.** These ulcers are larger and more painful in the HIV-infected individual. They can interfere with speech and swallowing.

d. **Idiopathic thrombocytopenia.** Like the rhinologic manifestations of epistaxis, patients may present with oral ecchymosis, petechiae, and spontaneous gingival bleeding.

e. **Oral mucosal hyperpigmentation.** These lesions are spots or striations in buccal mucosa, hard palate, gingiva, and tongue often seen in HIV-infected patients.
f. **Tonsillar abnormalities.** Tonsillar abnormalities, secondary to tumour (Kaposi's sarcoma and lymphoma) and infections have been reported.

g. **Vocal cord edema.** Hoarseness, secondary to true vocal cord edema usually from chronic cough, previous radiation therapy, or lymphatic obstruction from Kaposi's sarcoma has been reported.

h. **Recurrent laryngeal nerve paralysis.** CMV infection of the recurrent laryngeal nerve can occur.

**D. Lymphadenopathy in AIDS**

Most HIV-infected patients have marked lymphadenopathy, seen mainly in the head and neck (Table 8-5).

### Table 8-5. Head and neck sites of adenopathies in HIV-infected patients

<table>
<thead>
<tr>
<th>Site</th>
<th>Percentage</th>
<th>Site</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior cervical</td>
<td>86</td>
<td>Submandibular</td>
<td>37</td>
</tr>
<tr>
<td>Preauricular</td>
<td>51</td>
<td>Submental</td>
<td>26</td>
</tr>
<tr>
<td>Postauricular</td>
<td>47</td>
<td>Supraclavicular</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jugular</td>
<td>17</td>
</tr>
</tbody>
</table>

Lymph node enlargement, a hallmark of HIV infection, occurs in all stages of the disease. Causes for lymphadenopathy range from benign lymphadenopathy to neoplastic and opportunistic infections. Causes include:

1. **Persistent generalized lymphadenopathy (PGL).** PGL is found in early HIV infection and is an unexplained lymphadenopathy of 3 or more months' duration involving two or more extrainguinal sites in an individual at risk for developing AIDS.

2. **Non-Hodgkin's lymphoma.** The majority of HIV-positive patients with lymphoma have high-grade B-cell tumors, including immunoblastic lymphoma, diffuse large-cell lymphoma, and small noncleaved Burkitt's and non-Burkitt's lymphoma.

3. **Hodgkin's lymphoma.** Cases have been reported in HIV-positive patients, but do not appear to occur in increased frequency compared to non-HIV-positive patients.

4. Kaposi's sarcoma

5. Mycobacterium avium intracellulare

6. Mycobacterium tuberculosis

7. Histoplasma capsulatum
III. Pediatric AIDS: Specific ENT problems

HIV infection has been well documented in children. Like adults, children suffer the ravages of this disease, including:

A. Cervical adenopathy. Nodes are soft, regular, and nonadherent (see II. D.).

B. Parotid gland enlargement. This enlargement is common, usually bilateral and painful. Course waxes and wanes. See II.C.

C. Oroesophageal candidiasis. Most HIV-infected children develop mucocutaneous candidiasis (thrush). As in adults, the most common form is pseudomembranous candidiasis. See II.C.

D. Oral hairy leukoplakia. This has also been noted in the pediatric setting. See II.C.

E. Bacterial infections. There is an increased incidence of bacterial infections in children with AIDS. Otitis and sinusitis occur frequently. See II.A. and II.B.

F. Viral infections. Upper respiratory tract infections caused by viruses are common in HIV-infected children and usually run a self-limited course. Herpes simples and varicella zoster have been reported in HIV-infected children. See II.C.

G. Thrombocytopenia. As in adults, some children with HIV have associated thrombocytopenia and may present with petechiae of the palate and head and neck, as well as epistaxis. See II.B. and II.C.