HIV-ASSOCIATED CONDITIONS OCCURRING IN MULTIPLE HEAD & NECK ANATOMIC SITES

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OUTLINE

- HIV/AIDS
- Kaposi’s Sarcoma (KS)
- Non-Hodgkin’s Lymphoma
- Lymphoid Hyperplasia
- Herpes Zoster
- Case Report
- Conclusion
HIV/AIDS

- **Structure of HIV**
  - 2 copies of positive single-stranded RNA
  - Reverse transcriptase
  - Enclosed by capsid (p24)
  - Viral envelope (phospholipid bilayer)
HIV/AIDS

- HIV life cycle:
  - HIV infects CD4+ T cells, macrophages and microglial cells
    - Entry into cells is mediated by gp120 (virus) and CD4 molecules and CCR 5 receptors on target cells
    - Macrophages are the first cells to become infected and are the source of HIV production when CD 4+ T cells become depleted
    - Macrophages fuse into multinucleated giant cells in tonsils and adenoids of HIV+ patients and produce a huge amount of virus
  - HIV RNA, reverse transcriptase, and various enzymes are transported into nucleus and ssRNA → dsDNA, which is then integrated into host DNA
  - New HIV particles are synthesized and released
HIV/AIDS

- Incidence as of 2008:
  - 33.4 million people are living with HIV/AIDS
    - 15.7 million are women
    - 2.1 million are children
  - 2.7 million were newly infected with HIV
  - 2.0 million AIDS related deaths

- Median survival without treatment is about 10yrs

- HAART has reduced death rate from disease by 80%, and raised life expectancy for a newly diagnosed HIV infected person 20-50yrs

- AIDS:
  - CD4 < 200/ul
  - Presence of opportunistic pathogens
KAPOST’S SARCOMA

- Most common malignancy associated with advanced HIV/AIDS
- It is an AIDS defining illness (CD4+ <200/ul)
- Occurs in:
  - 43% of homosexual or bisexual men
  - 4% of IVD
- KS is caused by HHV-8
- AIDS related KS is very aggressive and affects:
  - Oral and pharyngeal mucosa
  - Neck masses appear secondary to lymph node infiltration
  - Cutaneous lesions of face, trunk, and lower extremities
KAPOST’S SARCOMA

- Typical KS lesions are pink-purplish and slightly raised or nodular and non-tender
  - Slow progression, many lesions regress with HAART
  - Secondary Infection is a major complication
- Diagnosis is made by history and characteristic appearance of lesion, biopsy allows confirmation
- Treatment:
  - Low-dose radiation therapy, chemotherapy, and immunotherapy
  - Low-dose radiation therapy is effective for dermatologic lesions, mucosal lesions are more resistant to therapy
  - Painful mucositis occurs at much lower radiation doses in HIV/AIDS patients
ORAL AND OROPHARYNGEAL KAPOSI’S SARCOMA

• KS is the most common oral malignancy in HIV disease
  • 95% occur on the palate and tongue
  • gingival surfaces and the oropharynx

• In one study, 44% of patients with dermatologic KS also had submucosal lesions of their aerodigestive tract

• Lesions are initially flat and asymptomatic but they often become exophytic and ulcerated
ORAL AND OROPHARYNGEAL KAPOSI’S SARCOMA

- Secondary infection produces severe odynophagia, dysphagia and difficulty in maintaining good oral hygiene.
- In rare cases, KS has resulted in airway obstruction that requires emergent tracheotomy
- Treatment:
  - A newer and very effective technique is the use of intralesional Vinblastine
  - Photodynamic therapy
  - Low-dose radiation → Painful mucositis
  - HAART
  - Systemic therapy (doxorubicin or daunorubicin +/- vinblastin, bleomycin) with extensive mucocutaneous involvement (>10 new lesions in 1 month)
Kapostis Sarcoma in the External Ear

- Dermatologic lesions occur in the EAC and/or the pinna
- Symptoms occur secondary to infection or obstruction, leading to conductive hearing loss
- Tumors can also extend onto the tympanic membrane or into the middle ear

Treatment:
- **HAART**
- Rarely necessary
  - Carbon dioxide laser is used to excise canalicular KS
  - Argon laser is used when involvement of TM is present
    - Argon laser spares more normal tissue
OTHER LOCATIONS FOR KAPOSI’S SARCOMA

- **Sinonasal KS**
  - Is very rare and usually associated with concurrent cutaneous lesions of nose and face
  - Symptoms include:
    - Nasal obstruction
    - Intermittent epistaxis
    - Rhinorrhea

- **Cervical Lymphadenopathy**
  - KS can initially present as an enlarging cervical mass or parotid gland swelling
  - FNAB of lymphnodes can diagnose KS but its differentiation from bacillary epitheliod angiomatosis (cat-scratch disease) may require an open biopsy
Non-Hodgkin’s Lymphoma

- NHL is the second most common malignancy associated with HIV
  - 100-fold increase risk if HIV+

- NHL is much more aggressive and high grade (Large B-cell) in HIV patients
  - Extra-nodal sites are involved in 89% of patients
    - 10% of patients have involvement of the Head and Neck
    - 42% have CNS extension

- Patients present with a non-tender, rapidly enlarging neck mass, fever, night sweats and significant weight loss

- Diagnosis:
  - multiple FNABs because NHL can present in the background of benign follicular hyperplasia (HIV lymphadenopathy)
  - Open biopsy
NON-HODGKIN’S LYMPHOMA

Criteria for open excisional biopsy

- Constitutional Symptoms
- Localized lymphadenopathy
- Disproportionately large node in a patient with persistent generalized lymphadenopathy
- Cytopenia or elevated erythrocyte sedimentation rate or both in a patient with otherwise negative evaluation
NON-HODGKIN’S LYMPHOMA

- Oral/Oropharynx manifestations
  - Oropharynx is the most common extra-nodal site
    - Tonsils, tongue > gingiva
  - Lesions may be ulcerative or nodular
- Nasal/Paranasal Sinus Manifestations
  - Nasal obstruction
  - Epistaxis
  - Rhinorrhea
- Parotid enlargement
- Conjunctival lymphoma
- Cervical lymphadenopathy
- Treatment:
  - Chemotherapy or Radiation therapy
Lymphoid Hyperplasia

- Lymphoid hyperplasia found in the nasopharynx is a manifestation of HIV-associated lymphadenopathy seen in peripheral lymph nodes.
- Lymphoid hyperplasia commonly affects the entire Waldeyer’s ring (adenoids, lingual tonsils and palatine tonsils).
- Adenoidal Hypertrophy in an otherwise asymptomatic adult should raise the suspicion of a possible underlying HIV infection.
LYMPHOID HYPERPLASIA

- Nasopharyngeal lymphoid hyperplasia results in nasal obstruction, serous otitis media, recurrent acute otitis media and oropharyngeal airway compromise (very rare).

- Diagnosis is based on history and physical exam including indirect laryngoscopy.
  - MRI or CT scan of the nasopharynx is recommended to rule out an erosive skull base process or asymmetric adenoid hypertrophy which can suggest Lymphoma/KS.
  - FNAB is helpful to establish a diagnosis but does not rule out lymphoma

- Treatment:
  - Systemic antibiotic and topical steroid sprays
  - Adenoidectomy
Herpes Zoster-Ramsay Hunt Syndrome

- **Etiology:**
  - Reactivation of VZV in Geniculate ganglion
  - Initial encephalomeningomyelitis that secondarily spreads from the CSF to the labyrinth
  - Inflammatory neuritis of facial, cochlear and vestibular nerves
    - Severe facial nerve paralysis+SNHL+vertigo
    - Painful vesicular lesions in the concha or EAC
      - Often misdiagnosed as otitis externa
    - Dysgeusia (chorda tympani)
    - Hyperacusis (stapedius)
  - More common in HIV than non-HIV patients
    - In a prospective study of 48 high-risk patients with VZV revealed that 73% were seropositive for HIV and 17% developed AIDS during 10-24 month follow-up
HERPES ZOSTER-RAMSAY HUNT SYNDROME

- Diagnosis is based on history and physical, virus isolation from vesicles, acute and convalescent serum titers (4-fold increase)

- Treatment:
  - Acyclovir
  - High dose corticosteroids (concurrent opportunistic infections contraindicate use of systemic steroids)
  - Eye protection
Herpes Zoster in the Oral Cavity

- Occurs along the dermatomal distribution of CN V
- Crops of vesicular lesions are commonly found on the hard or soft palate, lips and gingiva
- Viral dissemination occurs in severely immunocompromised patients
Zoster ophthalmicus

- Lesions along CN V1 distribution
- Herald infection of the cornea is common
- Zoster ophthalmicus is an indication for aggressive management with IV Acyclovir
**Case Report**

**HPI:** A 33-year old, 13 weeks pregnant female presents with shortness of breath and noisy breathing. She also has odynophagia, bilateral neck swelling, sore throat and night sweats for the past 3 days. She has a discharging ear and a chronic non-productive cough for 3-6 weeks. She was started on Distaclor (Cefaclor) and discontinued when she was confirmed to be pregnant. She is a non smoker and social drinker. No history of IVD or other risk factors of HIV infection.

**PE:** She is febrile, has inspiratory stridor, tachycardia and tachypnea

**Oral cavity/Oropharynx:** Extensive candidiasis

**Neck:** Bilateral Lymphadenopathy

**Fiberoptic laryngoscopy:** Very large, edematous and inflamed epiglottis with extensive white patches. Vocal cords could not be visualized only the posterior portion of arytenoids were seen

**Lateral x-ray of the neck:** enlarged epiglottis and a normal trachea

**U/S:** nonviable pregnancy

**Labs:** WBC 6.1x10³/ul, Hb 13.2g/dl, PLT 215x10³/ul, 

**CD4⁺ 44/mm³**

**Assessment:** Patient tested positive for HIV and is diagnosed with severe fungal/bacterial epiglottitis.

**Plan:** Patient is started on IV fluconazole, cefuroxime, metronidazole, nystatin mouth washes, HAART, Bactrim, azithromycin and dapsone.
CASE REPORT

Patient is examined 2 weeks later

Flexible fiberoptic laryngoscopy: Epiglottis still appeared inflamed and grossly swollen

CT scan of neck and upper thorax: Showed a 4 cm swelling of the epiglottis extending down into the aryepiglottic folds and into the vestibule. Bilateral cervical lymphadenopathy was also noted.

In view of her slow recovery, a biopsy of her epiglottis was obtained.

Histopathology: Necrotic inflammatory tissue with ulceration and dense proliferation of anastomosing vascular channels. Patient was diagnosed with Kaposi’s Sarcoma.

Patient continued on HAART and 8 weeks after her initial presentation her larynx appeared normal, her viral load was undetectable and CD4 count increased.
Conclusion

- About 80% of patients with HIV infections present with otolaryngological symptoms.
- Often, the otolaryngologist is the primary physician who diagnosis the HIV infection.
- Oropharyngeal findings are the most common and seen in 59% of patients, followed by cervical lymphadenopathy in 42% of patients.
- Combination of findings are common in some patients particularly cervical lymphadenopathy coexisting with oral and nasal manifestations this should be a clue that HIV ought to be ruled out.
Sharon, that was a nice review of ENT manifestations of HIV. It certainly highlights the fact that many of these patients are going to get a problem in the head and neck and these can range from commonplace issues to the exotic. The causes of most otolaryngologic manifestations of HIV disease fall into the following three categories: infections, neoplasms, and primary neurologic damage caused by HIV.

As otolaryngologists we certainly see our share of patients with HIV and even full blown AIDS. There are certain things like seeing adenoids in adults that should raise your suspicions about underlying HIV disease. Large parotid cysts or unexplained persistent adenopathy should also make you think possible HIV.

A word of caution: If you order tests, be prepared to follow up the results. Especially with sensitive things like HIV testing, make sure you are willing to be responsible for following up the results.

Instead of being a death sentence, having HIV is now quite manageable if found early and treated aggressively. An astute otolaryngologist can pick up on things during a routine head and neck exam that can lead to an early diagnosis and treatment for the patient.

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REFERENCES

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