Burn Baby Burn!
The Evaluation and Diagnosis of Oral Lesions

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I do not have any financial relationships with any Pharmaceutical Companies

Learning Objectives

- Describe the appropriate history, physical exam, and additional testing if indicated, required for the appropriate evaluation of oral lesions.
- Recognize the symptoms and exam findings that indicate a malignancy or other life threatening process as the cause of oral lesions.
- Identify infectious, inflammatory, allergic, and autoimmune processes that feature oral lesions as a component of their presentation.

Phil

Presentation

47 y/o male presents to Otolaryngology office for follow up from an ED visit for mouth pain.

HPI:

- Lesion on the left buccal mucosa that is painful for 2 months
- History “little lump” being removed from oral cavity at outside oral surgeon with no pathology performed
- Pain is constant requiring narcotics
- White area in center of lesion is new and lesion appears to be growing

Pre Visit Treatment

- ED gave patient oral Augmentin (amoxicillin/clavulanate), Percocet (oxycodone/acetaminophen) and Magic Mouthwash (diphenhydramine/aluminum hydroxide, magnesium hydroxide, simethicone/viscous lidocaine)
- Patient reports area 30% better but not resolved

History

- Past Medical History
  - HIV + with stable CD4 count
  - HTN
  - No known exposure to HPV
- Surgical History
  - Removal of oral lesion
- Medications
  - Enalapril
  - Atripla
  - Percocet
- Allergies
  - NKDA
- FH
  - HTN
- SH
  - Lives with his partner
  - 10pack year history of tobacco use
  - Past use of alcohol, none currently
  - In nursing school and working full time in group home

Physical Exam

- 2cm intraoral left buccal mucosal ulceration with cheesy white debris
- Submucosal firmness surrounding ulcer for total area 2.5cm
- Exquisitely tender to palpation
- Remainder of intraoral and head and neck exam negative

Differential Diagnosis

- Infectious
- HIV related oral ulcers
- Aphthous ulcers
- Oral Crohn's disease
- Lichen planus
- Bullous pemphigoid
- Mucous Membrane pemphigoid
- Pemphigus vulgaris
- Burning Mouth
- Epidermolysis bullosa acquisita
- Behcet's disease
- Erythema multiforme
- Stevens-Johnson syndrome
- Systemic lupus
- Contact stomatitis
- Malignancy

Burning Mouth Syndrome

- Characterized by a burning sensation in the mouth and/or tongue that is present most or all of the day
- Normal intraoral exam
- All other disorders that may cause this have been ruled out

Burning Mouth Syndrome

Underlying Conditions that Need to be Ruled Out

- Xerostomia
- Vitamin Deficiencies
  - B 12
  - B6
  - Iron
  - Folate
  - Zinc
- Contact Stomatitis
- Benign Migratory Glossitis***
- Thyroid abnormalities
- Psychogenic
- Reflux
- Fungal Infection

*** this has physical findings on exam

Benign Migratory Glossitis

- Can be associated with atopy, psoriasis, and reactive arthritis
- Biopsy not indicated

Burning Mouth Syndrome

- Thought to be a sensory neuropathy
- Can consider traditional medications used for neuropathies

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Behcet's Disease

- Neutrophilic inflammatory disorder causing oral and genital ulceration
- Must have 3 oral ulcer episodes per year with two of the following
  - Recurrent genital ulcers
  - Eye lesions
  - Skin lesions
  - Positive pathergy test

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Erythema Multiforme

- Acute, immune-mediated hypersensitivity reaction that causes oral, genital, and target skin lesions
- Usually self-limited
  - Rarely recurs frequently over the course of years
- Associated with
  - Herpes
  - Mycoplasma
  - Medications
  - Idiopathic
- Erythema and edema of the lips with intraoral bullae is common
- Skin biopsy for diagnosis

Stevens-Johnson Syndrome

- Severe mucocutaneous hypersensitivity reaction often associated with medications
- Mucous membranes are affected in over 90 percent of patients
  - Usually at two or more distinct sites (ocular, oral, and genital)
- Erythematous purpuric macules characterized by extensive necrosis and detachment of the epidermis
  - Nikolsky sign and/or the Asboe-Hansen sign may be present
- Lab abnormalities
  - Anemia, lymphopenia, hypoalbuminemia, electrolyte imbalance, increased blood urea nitrogen, increased glucose, elevated aminotransferase

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Systemic Lupus

- Mucous membranes are involved about 50% of the time
- Patients often have other systemic symptoms
- Oral Lesions
  - Discoid lesions
    - Keratotic plaques with altered pigmentation
    - Irregular raised plaques with punched out ulcerations
    - Usually present on the hard or soft palate

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Contact Stomatitis

- Caused by allergic reaction to topical items such as
  - Flavoring in toothpaste/ mouthwash/ candy/ gum etc.
  - Dental restoration materials
  - Dental procedure exposures
  - Acrylic
- Wide variety of appearances

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Infectious

- Fungal
- Viral
- Bacterial

- Other Infections
  - Syphilis
  - Mycobacterium Avium
  - H. Pylori
  - Amoeba
  - Leishmaniasis

Fungal Infection

- Typically Candidiasis
  - Typically white patches on buccal mucosa and tongue
  - Can cause “cheesy” debris
  - Also may cause atrophic changes or red beefy tongue
- Can be more invasive fungal infection especially in the immunosuppressed patient

Viral Infection

- Herpes Simplex
  - Vesicles bordered with inflammatory base
  - Can cause many ulcerations on bucal mucosa in immunocompromised patients
- Varicella Zoster
  - Unilateral grouped vesicles
  - History of chicken pox infection in past
- Coxsackie Virus
  - Intraoral and palmar/plantar lesions
  - Oval papules on skin Apthus ulcers on oral mucosa
- Human Papilloma Virus
  - Some types predispose for oral cancers

Bacterial Infection

- Oral flora can become opportunistic infections when ulceration occurs
  - Streptococcus
  - Lactobacillus
  - Staphylococci
  - Cornybacterium
  - Anaerobic bacteria
- Other bacteria
  - Diphtheria

Syphilis

- Caused by spirochetes
- Not present at initial infection- secondary
- Split fissured papules of the oral commissure and ulceration of buccal mucosa

HIV Related Ulceration

- Multiple ulcerations on oral mucosa with generalized mucositis
- Occur in up to approximately 14% of patients
- Happen with CD4 count below 100

Aphthous Ulcers

- Painful shallow round ulcers with white base
- Heal within 10-14 days without scaring
- Causes
  - Familial
  - Trauma
  - Stress
  - Associated with Celiac Disease
  - Medications
  - ?B12 deficiency

Oral Crohn's Disease

- Uncommon manifestation of Crohn's Disease
  - Occurs in less than 0.5% of patients
- Most patients present with aphthous type ulcerations that are more numerous or last longer
  - Can also be linear ulcers, pseudopolyps or induration of the lips and buccal mucosa
- About half of the oral ulcerations were noted before or at the time of diagnosis

Lichen Planus

- Chronic inflammatory disorder of the skin and/or mucous membranes
- Oral appearance
  - Reticular white plaques
  - Erosions
  - Ulcerations
  - Hyperkeratotic plaques
- Cause – not fully understood but may be associated with
  - Medications
  - Trauma
  - Autoimmune disorder

Malignancy

- Squamous cell cancer
  - Most common oral cavity cancer
  - Ulcerative appearance most common
  - Usually painless
- Melanoma
  - Typically pigmented macules
- Other malignancies
  - Lymphoma
  - Mucoepidermoid Carcinoma
  - Adenoid Cystic Carcinoma

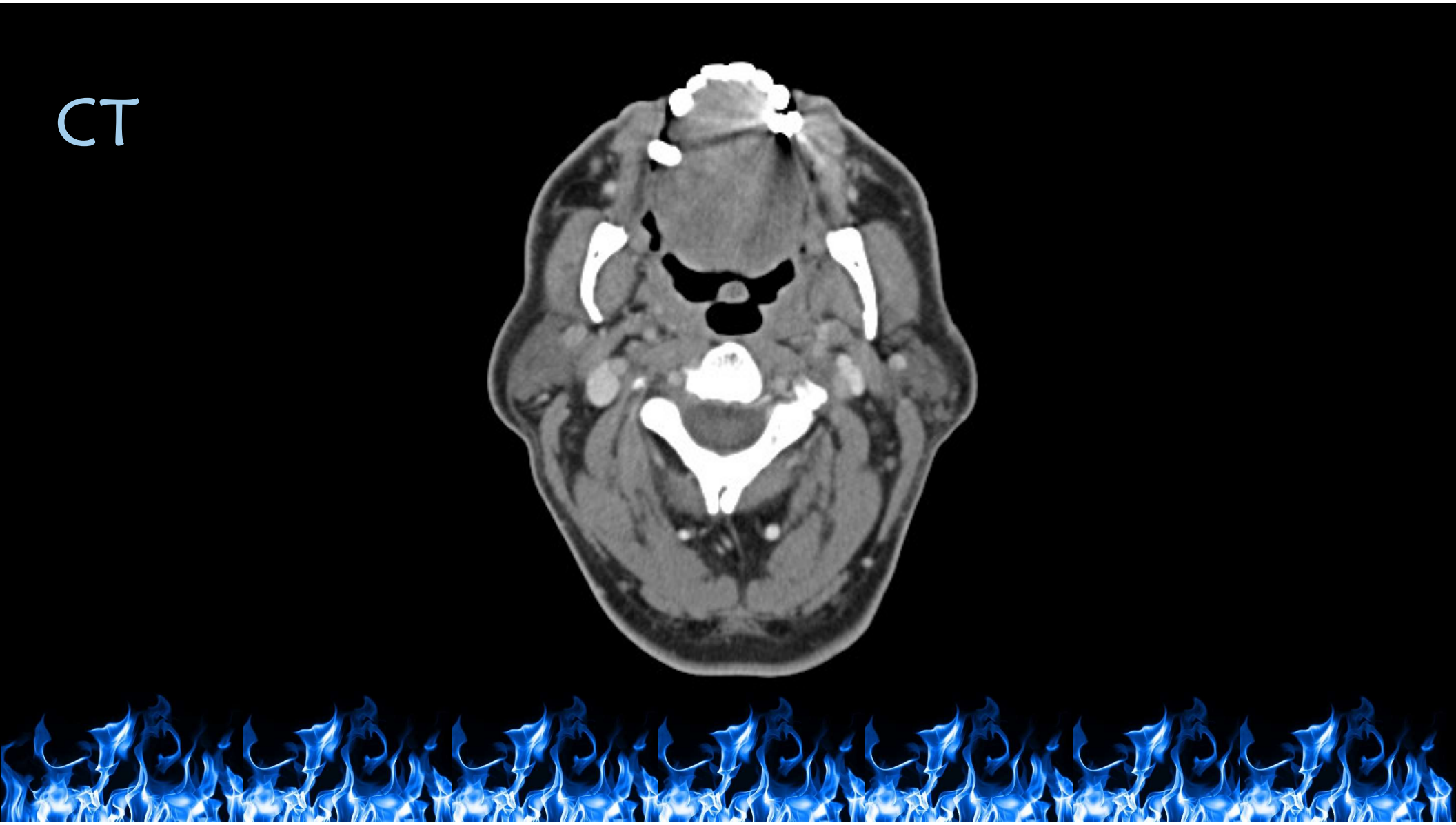
Features Concerning for Malignancy

- Lesion of more than 3 weeks duration
  - Or recurrent lesion in the same location
- Red or red and white lesion
- Ulcerative
- Lump
- Especially when in combination or if indurated

Treatment

- Patient started on Cleocin (clindamycin) for broad coverage of superinfected ulceration
- CT ordered to rule out mass

CT



10 Day Follow Up

- After treatment the ulcerative area had gotten significantly smaller and less painful

4 Week Follow Up

- The pain returned as did the debris in the ulcer and the ulcer had returned to pre-treatment size
- Phil was treated with Diflucan (fluconazole)

7 Week Follow Up

- Pain and debris had improved but returned when completed fluconazole
- Biopsy was performed of the ulcer to rule out malignancy

Biopsy

- Punch biopsy usually sufficient size for oral cavity lesions
- Use lidocaine with epinephrine to control bleeding
- Sample should include the margin between normal mucosa and the lesion
  - Take 2 biopsies if needed
  - Avoid the temptation to take the center if ulcerated
    - May only show necrosis

Results

- Hyperkeratosis
- Acanthosis
- Acute inflammation
- Bacterial colonies and fungal elements consistent with Candida

Treatment

- Longer course of fluconazole - 3 weeks
- Appointment with Infectious Disease Clinic to evaluate for possible resistant fungal infection related to HIV
  - They were unsure of the cause and suggested prolonged course of antifungal

12 Week Follow Up

- Ulcer much smaller, approximately 7mm x 4mm ulceration
- Still with pain requiring narcotics
- Treatment
  - Continue oral antifungals and reassess in 1 month

16 Week Follow Up

- Patient still with very small ulcer 5x3mm
- Discussed need to rule out other diagnosis and decided to repeat biopsy due to clinical inconsistencies
  - If biopsy still negative, referral to another center for second opinion

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Bullous Pemphigoid

- Autoimmune blistering disease
- Tense, fluid-filled bullae on skin
- Oral cavity involvement
  - Occurs in approximately 1/3 of patients
  - Presents as blisters or erosions on the buccal mucosa
  - Is uncommon as the presenting location

Mucous Membrane Pemphigoid

- Blistering autoimmune disorder of the mucous membranes only
- Affects oral and pharyngeal areas most commonly
  - Can also include ocular, laryngeal, genital, and anal mucosa
- Appears as desquamated areas that tend to scar

Pemphigus Vulgaris

- Autoimmune blistering disease
- Flaccid bullae that usually begin in the oropharynx and can evolve to include the skin
- Bullae burst easily so patient can present only with painful erosions

Epidermolysis Bullosa Acquisita

- Rare autoimmune blistering disease
- Blisters form at the site of trauma
- Heal as scars

Treatment

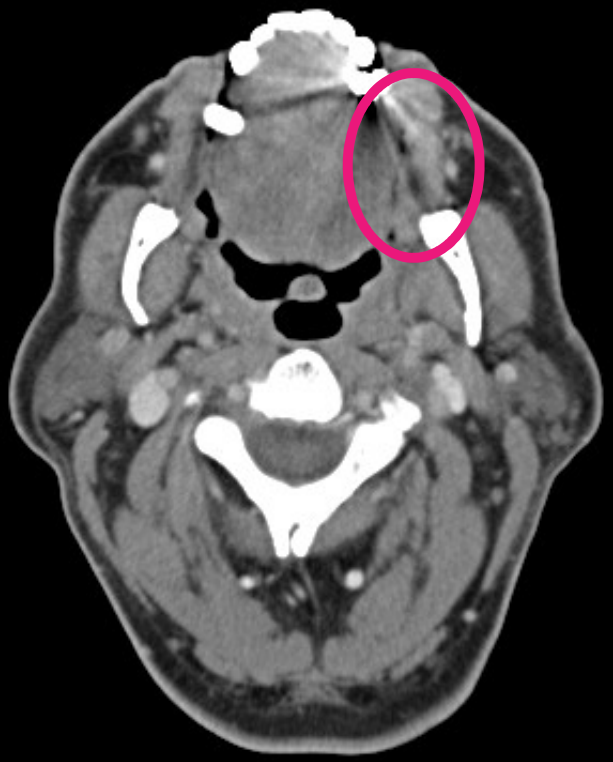
- Repeat biopsy with tissue sent in both Michel's medium to allow for immunofluorescence testing to rule out blistering diseases and formalin

Pathology Results

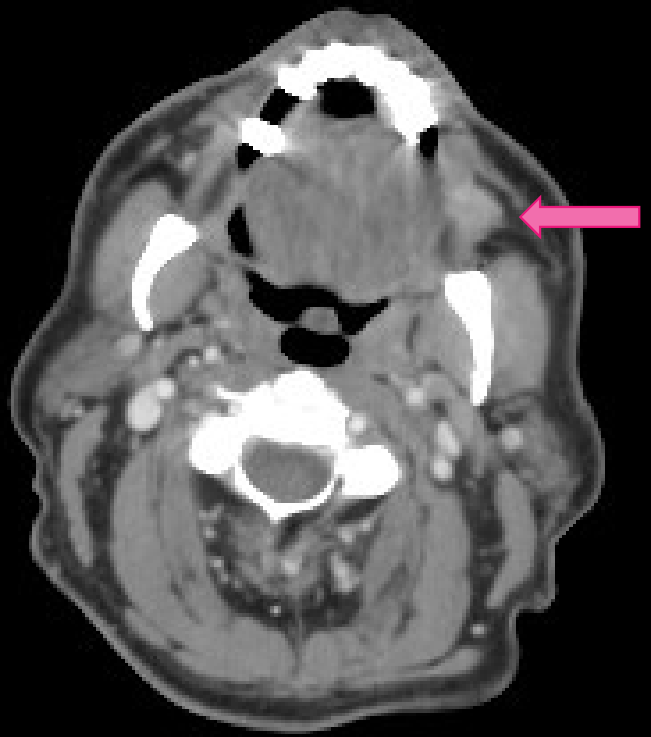
- Invasive keratinizing well-differentiated squamous cell carcinoma, positive for p16 immunohistochemical stain
- p16 immunohistochemical stain is a marker for HPV

CT

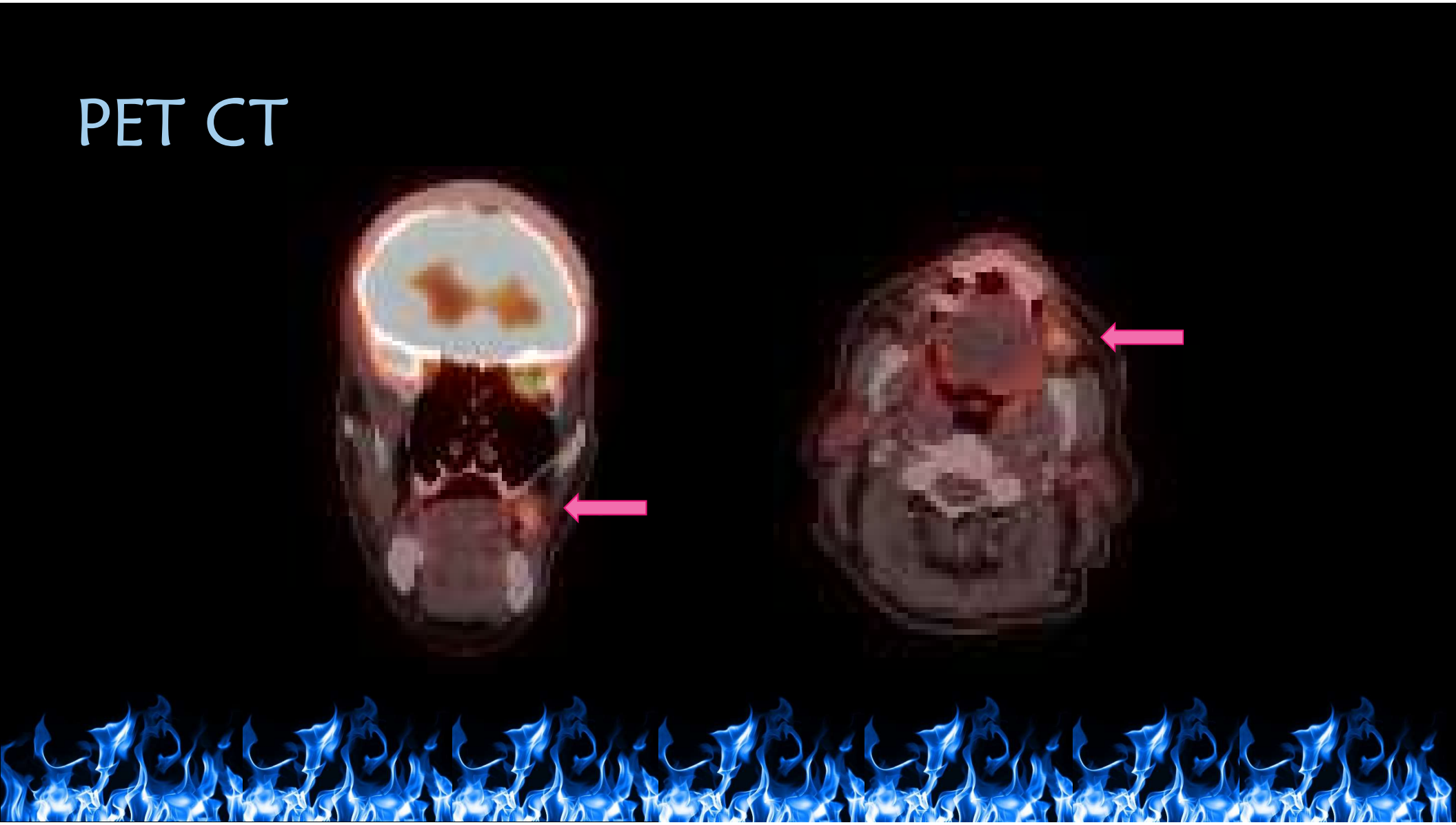
First CT



Second CT



PET CT



Treatment

- Phil went to the OR for a wide local excision of his SCC of left buccal mucosa
- Final Staging T1N0M0

HPV Positive Squamous Cell Cancer

- Despite the decrease in tobacco use, the incidence of oropharyngeal cancer initially remained constant and then began to rise
- Evidence linked the increase in oropharyngeal cancer to HPV-related cancers arising in the base of the tongue and the tonsillar region
- Human papillomavirus (HPV) infection is the most commonly diagnosed sexually transmitted disease in the United States
- HPV 16 genotype of HPV as a causative agent
  - 18, 31, and 33 also causative but much less common
- Timing between exposure to HPV and the development of oropharyngeal cancer probably exceeds 10 years
- Overall prognosis and survival is better

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