

ANAL CANCER

Incidence

- 1.5% of all digestive system malignancies in the US
- increasing incidence over the last 30 years from 10 to 20 million cases
 - female gender
 - HPV infection
 - # of sex partners
 - cigarette smoking
 - receptive anal intercourse
 - HIV
- Carefully conducted epidemiologic studies showed that cure of anal CA can be possible in majority of patients with preservation of the anal sphincter

Epidemiology

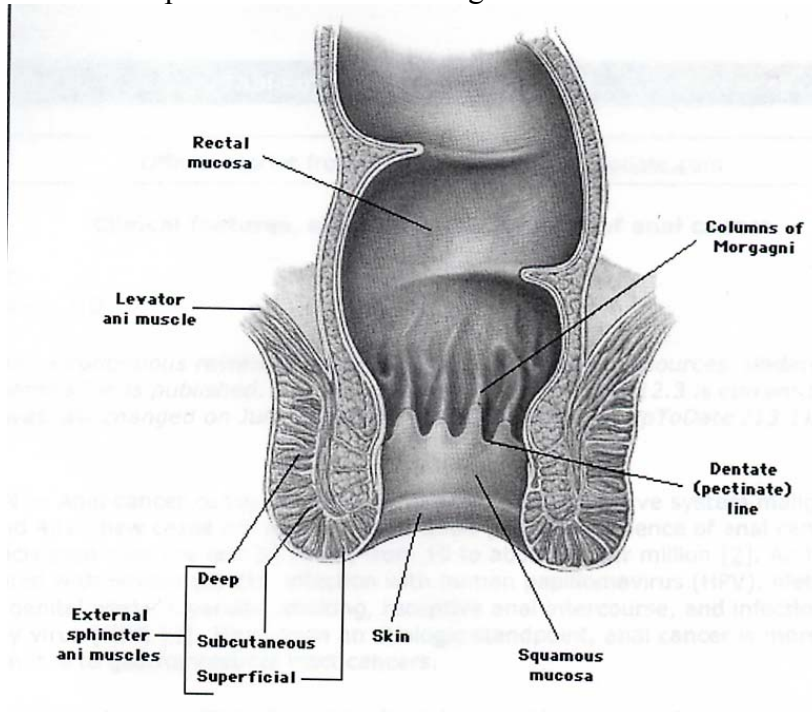
- annual incidence among men & women
 - 1994 and 2000 (2.04 and 2.06)
 - 1973 and 1979 (1.06 and 1.39)

Risk factors

- thought to develop in areas of chronic local inflammation
 - hemorrhoids, fissures, fistulae
 - case reports of anal CA in patients with IBD led to conclusion that it was result of chronic inflammation in setting of IBD
 - subsequent case control studies found little to no impact of a history of hemorrhoids, fissures, fistulae on development of CA
 - large Danish series none of the 1160 patients with IBD developed anal CA
 - another Danish study followed 9602 patients with IBD for development of anal CA over 18 years: 2 cases occurred vs. 1.3 (expected) during the 99,299 person years of observation
- sexual activity
 - population based case controlled studies have shown a confirmed relationship between anal cancer and receptive anal intercourse in men & significantly elevated risks with 10 or more lifetime partners
- HPV infection
 - HPV DNA has been isolated in 46-100% of in situ and invasive SCC of anal CA
 - HPV 16 is the most frequently isolated type in anal malignancy
 - ASIL particularly HSIL is considered precursor to anal CA
- HIV infection
 - increase in the incidence of ASIL in HIV + homosexual males
 - HSIL and anal CA higher in HPV infected individuals who are HIV +
- cigarette smoking
 - several case control studies have shown a statistically significant risk of anal CA in smokers

Anatomy

- 2 regions:
 - mucosa lined anal canal
 - epidermis lined anal margin



Histology

- 74% Squamous cell carcinoma
- 19% Adenocarcinoma
- 4% Melanoma
- 3% Neuroendocrine/carcinoid/Kaposi's sarcoma/leiomyosarcoma/lymphoma

Location

- Anal canal tumors
 - Pathologic classification of tumors in this area is difficult
 - no easily identifiable landmarks between rectum and anus & transition zone has widely variable histologic appearance
 - some have abrupt transition from glandular rectal tissue to anal squamous tissue
 - others have intervening segment of junctional mucosa (basaloid or cloacogenic mucosa)
 - ❖ pseudostratified epithelium with cuboidal or polygonal surface cells (resembling urothelium)
 - thus, tumor classification MUST be executed by histologic means
 - ❖ SCC arising in transition zone share the same biology, natural history, and treatment outcomes
 - ❖ adenocarcinomas in this area share same natural history as rectal adenocarcinoma and are treated similarly

- Anal margin tumors
 - most often SCC but can also be basal cell carcinoma/Bowen's disease/melanoma/Paget's disease
 - SCC of anal margin treated similarly to SCC of the anal canal
 - tumors of perianal hair-bearing skin are treated like skin cancers

Lymphatic drainage

- dependent on location of tumor (dentate line)
 - above dentate line drains to the perirectal & perivertebral nodes
 - below dentate line drains to inguinal & femoral nodes

Clinical presentation

- 45% rectal bleeding
- 30% pain/sensation of rectal mass
- 20% no symptoms

Treatment of localized SCC

- Anal margin tumors
 - Local surgery
 - wide local excision with 1 cm margins of normal tissue & primary closure
 - if tumor encompasses > ½ of anal circumference → APR
 - 5 year survival rate > 80% for tumors < 2cm in greatest dimension
- Anal canal tumors
 - APR (with permanent colostomy)
 - 5 year survival rate 40-70% with 3% perioperative mortality rate
 - Combined modality therapy
 - Wayne State devised protocol:
 - 5-FU, mitomycin, and intermediate dose radiation
 - follow up series: preop chemoradiation therapy and subsequent APR if residual tumor in postradiation biopsy
 - combined chemoradiation therapy results in local failure 14-37%, 5 year survival rates 72-89%, and 5 year colostomy free survival rates of 70-86%
 - after confirmation through multiple investigators, this has become the **standard of care**
 - Radiation therapy alone
 - Anal Cancer Trial Working Party of the United Kingdom Coordination Committee on Cancer Research (UKCCCR)
 - 585 patients to radiation therapy alone vs. radiation therapy + 5-FU & mitomycin
 - chemoradiation associated with significant reduction in local failure (61 vs. 39%)
 - European Organization for the Research and Treatment of Cancer (EORTC)
 - 110 patients with locally advanced anal CA to radiation vs. radiation & chemo
 - combined modality treatment vs. radiation alone complete pathologic remission rate (80 vs. 54%), 18% higher 5 year locoregional control rate, and 32% higher colostomy-free rate

- Role of mitomycin
 - joint trial by Radiation Therapy Oncology Group (RTOG) & Eastern Cooperative Oncology Group (ECOG)
 - 310 patients randomly assigned to groups receiving combined therapy with & without mitomycin
 - ❖ mitomycin addition led to improved 4 year colostomy-free survival rate (71 vs. 59%), disease free survival (73 vs. 51%)
 - ❖ no improvement in pathologic response rate or in overall survival
 - alternative to mitomycin is Cisplatin
 - US intergroup study now studying cisplatin vs. mitomycin

Treatment of anal adenocarcinoma

- Principles same as those for rectal CA
 - APR is the primary treatment
 - adjuvant therapy may include chemoradiation

Harshpal Singh, M.D.
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