Treatment Strategies for Anal Cancer

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Disclosure

- I have no disclosures.
Lower GI Tract Cancers

- Lower GI cancers are very common
- Colorectal cancer is the 2nd leading cause of cancer-related deaths
- Well-defined screening modalities
  - Adenoma/Carcinoma sequence
- Treatment strategies: surgery, chemotx, radiation tx
Lower GI Tract Cancers

- Cancers of the anal canal and anal margin are uncommon
- However, HPV is strongly related to anal canal cancer
- HPV is the most common STI
  - Epidemic
- Anal cancer incidence is increasing at an alarming rate especially in certain population of patients
Case Presentation

Case #1

- 47 y/o male with constipation for 6 months, small caliber stool and occasional blood w/ BM for 8 months
- PMH: HIV +, herpes, smoker, MSM with anal intercourse; HAART tx
- Treated for hemorrhoids, had a colonoscopy 2 yrs previously
- When patient didn’t improve DRE and flex sig demonstrated a 5 cm mass in anal canal covering ~ 60% of circumference
Case Presentation

- **Case # 2**
  - 56 y/o male constipation and blood with BM on and off for 2 years
  - PMH: AIDS, anal fissure/fistula, Crohn Disease, HAART tx; MSM with anal intercourse
  - Colonoscopy in 2013 demonstrated abnormality at 6cm, bx negative
  - 5/2014: DRE – large anal canal mass 4 x 3 cm
Case Presentation

- **Case # 3**
  - 56 y/o paraplegic male with rectal bleeding for 1 year
  - PMH: HIV +, Hep C tx for hemorrhoids for 1 year, HAART tx
  - Colonoscopy in 2008 and 2012 (reported as normal)
  - DRE in 2014 revealed a 5 x 5 cm mass in the anal canal extending as an ulcerated lesion on to perianal skin
Anal cancer

- Uncommon cancer: ~2.4% of digestive system cancers
- New cases: 1.8/100,000 men and women per year
- 7060 new cases (2630 men and 4430 women) in 2013
- 880 deaths in 2013
- Incidence is increasing (1.9X for men, 1.5X for women)
Risk Factors

- Infection with HPV (16/18)
- HIV +
- Hx of HPV-related genital malignancies
- Previous sexually acquired diseases
- Cigarette smoking
- Anoreceptive intercourse
- Multiple sexual partners
- History of solid organ transplant
- Other forms of immunosuppression
Risk factors

- High index of suspicion with pts presenting with anorectal complaints
  - Men who have sex with men (MSM)
  - HIV +
- Detailed sexual history important (potentially sensitive and difficult)
- Must determine the presence or absence of these risk factors
Risk Factors

- Association between anal cancer and HPV infection is strong

- Systematic review of 35 peer-reviewed anal cancer studies showed prevalence of HPV-16/18 to be 72% (Hoots, Palefsky, et al. Int J Ca 2009)

- Population/registry studies have reported similar rates (Steinau, Unger, et al. J Low Genit Tract Dis 2013)

- CDC estimates that 86% - 97% of anal cancers are attributable to HPV infection (MMWR Morb Mortal Wkly Rep 2012)
Risk factors

- Suppression of the immune system
  - Facilitates persistence of HPV infection in the anal region

- HIV-infected population
  - Incidence: increased from 19/100,000 to 78.2/100,000 (1992-1995 → 2000-2003)
  - Reflects both the survival benefits of HAART and the lack of an impact of HAART on the progression of anal cancer precursors
  - Recent reports: Incidence is 131/100,000 in HIV + MSM

NCCN.org, 2/2014
Risk Reduction: Vaccination against HPV 16/18

- HPV 16 and 18
- Targeted vaccination in high-risk cohorts
- Recommendation for the use of quadrivalent vaccine immunization
  - Boys and girls aged 11 and 12
  - Females aged 13 to 26
  - Males aged 13 to 21
  - MSM up to age 26

MMWR 2010, 2011; NCCN 2 2014
Risk Reduction

- HGAIN (high-grade anal intraepithelial neoplasia) can be a precursor to anal cancer
- Estimates from a recent systematic review and meta-analysis of studies in MSM
- Progression rates of HGAIN to cancer might be quite low, prospective data are lacking
- Spontaneous regression rate of HGAIN is not known
HGAIN

- Can be found incidentally during surgery for unrelated anal pathology
- High-risk populations
  - MSM
  - HIV-negative women w/ hx of anoreceptive intercourse; or other HPV-related anogenital neoplasia
  - Immunosuppression ie transplantation
  - HIV positivity (60% have HGAIN)
Risk Reduction

- Routine screening for AIN in high-risk individuals is controversial
  - MSM
  - HIV + patients
- Randomized controlled trials of efficacy at reducing anal cancer incidence and mortality are lacking
Risk Reduction: Anal Pap

- Anal Pap may be useful in the detection and follow-up of LGAIN/HGAIN

- Screening procedures for LGAIN/HGAIN
  - Anal cytology, colposcopy, biopsy, high-resolution anoscopy (HRA)

- Screen high-risk patients
  - Sensitivity: 69% to 93%
  - Specificity: 32% to 59%

- Surveillance after treatment for LGAIN/HGAIN

Guidelines for the Tx of HGAIN

- Considerable debate regarding the optimal treatment strategy for LGAIN/HGAIN
- High rate of recurrence: maybe expectant management with surveillance every 4 to 6 months is preferred “watch and wait” (2C)
- Comprehensive approach: cytology, HRA, targeted biopsies and directed therapy (1C)
  - Reported clearance of HGAIN in up to 80%
  - < 5% progression to higher-grade or invasive CA
  - Close long-term clinical follow-up (1C)

Guidelines for the Tx of HGAIN

- RC trial in 246 HIV + MSM found that Electrocautery was superior to both topical imiquimod and topical fluorouracil in the treatment of intra-anal HGAIN.
- Subgroup of perianal HGAIN appeared to respond better to imiquimod.
- Regardless of tx: recurrence rates are high.
- Careful follow-up is needed.

Anal Cancer: Anatomy/Histology

- Rectum
- Anal Columns of Morgagni
- Pectinate or Dentate Line
- Internal Sphincter Muscle
- Anal Crypt
- Anal Gland
- Sweat Glands and Hairs in Perianal Skin
- Anal Verge
- Anoderm
- External Sphincter Muscle
Anal Cancer: Pathology

- **Histology: Epidermoid**
  - Squamous cell carcinoma
  - Cloacogenic
  - Transitional
  - Basaloid
  - Mucoepidermoid
  - Round cell
- **Adenocarcinoma**
- **Melanoma**
Clinical Presentation

- Slow growing mass located in the intra-anal or perianal position
- Pain and bleeding are common; 20% asymptomatic
- Delay in diagnosis: 70% to 80% of patients !!!
  - Non-specific symptoms attributed to benign anorectal pathology
  - Poor rectal exam or none at the time of eval for symptoms
Physical examination

- Anorectal exam
- Evaluation of the inguinal nodes
- DRE identify lesion location, fixation and presence of sphincter invasion
- Anoscopy/Proctosig with Bx
  - Establish size, determine location, confirm dx
- Presence of palpable inguinal LN – FNA/Core Bx
Radiologic/endoscopic evaluation

- Biopsy under direct vision
- Colonoscopy recommended
  - Even though anal ca is not a risk faction for colorectal cancer, colorectal neoplasia have been demonstrated in up to 15% of patients with anal cancer
- Chest, abdomen, and pelvic CT
- MRI/ EAUS
- FDG-PET/CT

Staging

- **AJCC**
- **Size of primary tumor**
  - Based on PE
- **Involvement of regional lymphatics**
  - Based on PE initially and then by imaging
  - LN > 1 cm are considered +
- **Presence or absence of distant metastatic disease**
  - Lymphovascular drainage is systemic
Staging

- **pT1**: ≤ 2cm
- **pT2**: 2 - 5cm
- **pT3**: > 5cm

- **N1**: Perirectal, Internal iliac, Inguinal

- **N2**: Perirectal, Internal iliac, Inguinal

[www.oncolex.no](http://www.oncolex.no)
Primary treatment for most SCCs of the anal canal should be combined modality chemotherapy/radiotherapy (1A)
- Primary tumor bed and inguinal nodal basin
- Higher disease-free survival

Primary radiation tx may be considered in patients who cannot tolerate the addition of chemo

Local excision: for small lesions only

Anal Canal Cancers: Treatment

- Chemoradiation Protocol
  - 4500cGy over 5 weeks to perineum and inguinal areas
  - 5-FU 1000mg/m² - Continuous infusion day 1 - 4 and repeat day 29 - 32
  - Mitomycin C 10mg/m² bolus on day 1 and 29
  - Evaluate the anal canal in 8 -12 weeks
  - If positive – wait additional 4 wks; if negative – observation

- Metastatic Disease (Stage 4): Cisplatin-based chemotx + RT
Anal Canal Cancer: Treatment

- Salvage APR for progressive, persistent or recurrent

- N = 63
- Male - 64%
- AA – 92%
- Mean age at diagnosis: 53
- Pathology: epidermoid
- HIV + in 21%
- Stage at diagnosis: 2 and 3
- APR salvage: 7%
Prognosis

- SEER database
- Localized in 50% at initial diagnosis
  - 80% 5-year survival
- LN involvement: 34%
  - 60% 5-year survival
- Distant mets: 15%
  - 30.5% 5-year survival

Thank you

Questions