

## ANAL CANCER

### **Epidemiology:**

Incidence: (a)1.2/100,000 (b)80/100,000 MSM HIV+ive (c)5/100,000 MSM HIV-ive (d)cervical/vulval/penile Ca prevalence areas

Gender: female 1.8x

Age: median 60 at presentation

### **Aetiology:**

**HPV (90%):** 16<sub>(81%)</sub> & 18<sub>(4%)</sub> (less commonly 31&33) → condylomata → AIN → anal SCC

Other risk factors: receptive anal sex/HIV/genital warts (*Daley et al*)

### **Pathology:**

Types: (a)SCC (b)Other: basaloid (TZ)/muco-epidermoid

Site: (i)Anal canal: poorly diff'd (cf margin cancers) (ii)Anal margin: hair-bearing skin distal to verge, within 5cm radius of orifice

Spread: *Locoregional*= cephalad/outwards to sphincters, RV septum, perineum, scrotum, vagina

*Nodes*= perirectal→inguinal→haemorrhoidal→lateral pelvic; depends on T stage and invasion depth

*Mets*= liver/lung/bone

### **Presentation:**

Symptoms: pain/bleeding/discharge/mass/tenesmus/anopelvic sepsis and fistula

Signs: (i)**mass**: size/relationship to verge/circumferential involvement

(ii)**inguinal nodes**: T3 2x T2; 14% at presentation, 50% normal biopsy

\*VE mandated in women

### **Investigations:**

**MRI**: better than CT for mesorectal nodes

**CTTAP**: routine staging

**18F-FDT PET/CT**: if negative CT/MRI or high risk of mets (T2+)

**ERUS**: small T1's for amenability to local excision

\*Pre-treatment (i)HIV test/CD4<sup>+</sup>/viral load (ii)Cervical PAP smear → optimise both conditions

T1 ≤2cm	N0	M0
T2 2-5cm	N1 mesorectal nodes	M1
T3 >5cm	N2 unilateral ilioinguinal/int iliac	
T4 organ invasion	N3 bilateral ilioinguinal/in iliac OR mesorectal + inguinal	

## MANAGEMENT

### **(1)CHEMORADIOTHERAPY:**

Synchronous **Mitomycin** + **5FU/capecitabine** + **low-dose DXT** (30Gy)

*RCTs: UKCCR ACT I/EORTC 22861: combo CRT improved local control/fewer stomas than DXT alone*

*ROG 87-04: combo CRT has fewer stomas than 5FU alone*

*UK ACT II/ROG-98: failed to establish cisplatin over MMC; induction therapy → worse outcomes (all)*

\*IMRT: reduces acute/late toxicity → use in all in whom definitive CRT intended

\*Induction/adjuvant therapy not routinely recommended

\*Uninvolved nodes: treat in all T2-4s; can omit in small T1s

\*Avoid treatment gaps (pre-treatment stoma/seton)

### **Treatment response:**

(i)Complete response (ACT-II Protocol): 8wkly Yr1, 3mthly Yr2, 6mthly Yr3-5 →perineum/DRE/ing nodes→EUA-Bx

(ii)Slow regression: can take 6mths post-CRT → assess @6-8wks then 4-8wkly until clinical+radiological cure  
→ MRI 3-6mthly (not earlier) if locally advanced/palpable abnormality

### **Treatment failure:**

1(a)Persistent Disease: biopsy-proven disease up to 6mths post-cessation of CRT (10%)

1(b)Local Relapse:...beyond 6 mths (54% yr1, 26% yr2, 13% Yr3) \*usually site of 1<sup>o</sup> tumour\*

Investigations: EUA+Bx/MRI/CT/18F-FDG PET

Treatment: Salvage Surgery for all local relapses(<50% 5yr survival) → radical APE/exenteration +/-perineal recon  
(wide IR fossa fat excision if breached EAS/puborectalis) (delayed wound healing 40%)

2. Regional disease: inguinal nodes → US-FNA + CTCAP + MRI +/- 18F-FDG PET

→ LN dissection if previous CRT/salvage CRT if no previous DXT (rare scenario)

3. Distant Metastases: incurable → palliative chemo (cisplatin + 5FU/capecitabine); 10% in absence of local relapse

## **(2)SURGERY:**

1. **WLE:** T1s – excise w/ margin of perianal skin/deeper tissue/distal IAS (often just generous biopsy; complete excision compromises IAS function)
2. **APE: (i)**Unresectables if DXT contraindicated/unfit for CRT/declines CRT  
(ii)Treatment failure

Inguinal node dissection: (i)DXT contraindicated (ii)prophylactically at APE w/ NO (iii)nodal recurrence  
Surgery for complications: fistula/incontinence as IAS/EAS damaged by treatment  
Pre-treatment stoma: advanced tumours T3+/obstruction/vaginal inversion/severe tenesmus or pain  
Fistula: long-term seton before CRT

### ANAL INTRAEPITHELIAL NEOPLASIA

Precursor for SCC due to HPV (70% sexually-active adults have had occult/overt genital HPV)  
HIV increases transformation rates (50% estimated; much lower rate in immunocompetents)  
Clinical features: Asymptomatic or Symptomatic (Pain/pruritis/bleeding/discharge)  
Investigations: Biopsies mandated in high-risk groups with AIN (highres anoscopy + 3% acetic acid)  
Treatment: induce regression/eradicate AIN to prevent malignant transformation  
(a)Topical: imiquimod/trichloroacetic acid/5FU  
(b)Ablation: electrocautery better than (a) in HIV+ MSMs but high recurrence in Dutch trial  
Surveillance: AIN I – observe alone  
AIN II/III – 6mthly for 5 yrs w/ photography and repeat biopsies if too large an area to excise; otherwise excise

### Persons Living With HIV

AIN/anal SCC 40x commoner but managed as per general population  
Late diagnosis if misdiagnosed → low threshold to EUA-Bx  
CRT: safe with similar outcomes to general population  
(i)cART started before CRT (reduces CRT toxicity)  
(ii)Treat opportunistic infections before CRT (persistent CD4<sup>+</sup> reduction)

### SISSCA (Superficially Invasive SCC of Anus)

Definition: Invasive SCC (i)invasive depth ≤3mm from basement membrane of point of origin  
(ii)horizontal spread ≤7mm in maximal extent  
(iii)has been completely excised  
Management: observation

### Other

True adenocarcinoma : arises from anal glands; 4% of anal cancer? → CRT  
Malignant melanoma: mimics thrombosed external pile; 1% of anal cancer; dismal prognosis w/ 8mth median survival