CLINICAL PATHOLOGICAL CONFERENCE

THREE INTERESTING CASES ON VULVAL PATHOLOGY

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11 JULY 2016
CASE 1
HISTORY

- 44 yo, G0P0, Single, Smoker
- PMH: HT, DM, Acute gangrenous cholecystitis, Left adrenal incidentaloma

- Self noted vulval mass
- Seen private gynaecologist
- PE showed a sessile mass over right labial majora
- Vulval biopsy: condyloma accuminatum and mild to moderate dysplasia
COLPOSCOPY

1 cm x 2 cm warty growth at the right labial majora
Dense acetowhite lesion from 12-1 o’clock with mosaicism and fine punctations; iodine negative
Imp: HG lesion
Cervical smear: negative
Cervical biopsy 12 and 1 o’clock: normal
Vulval biopsy: condyloma acuminatum, low grade VIN

Plan: For excision of vulval mass
MANAGEMENT

- Local excision of vulval mass
- Pathology: HSIL with stromal invasion (depth 0.8mm), margin clear by >5mm
- Diagnosis: CA vulva stage IA
- Plan for observation
CASE 2
HISTORY

- 40yo, G0P0, Single, Smoker
- PMH: autoimmune haemolytic anaemia in remission, Left renal mass with nephrectomy done in private 7 years ago, path: benign angiomyolipoma
- Noted hyperpigmentation at vulval and perianal region since Jan 2014
- Seen private with biopsy done
- Left vulval, left perineal and anal verge biopsy: VIN, no invasive neoplasm
- Progressive increase in size of hyperpigmentation for 2 months
- Referred to KWH
- Colposcopy 11/2015: HPV, VIN1
- Cervical biopsy 11/2015: condyloma
- Vulval biopsy: HSIL
- TVS 11/2015: normal
- Consulted surgery to rule out rectal extension
- Flexible sigmoidoscopy 12/2015: No pigmentation seen in rectum or sigmoid colon
HISTORY

- Noted increase in size of hyperpigmentation on vulval and perianal region, suspected malignant melanoma
- Referred to QMH
- Vulval pruritus
PHYSICAL EXAMINATION

- Small patch of hyperpigmentation over 12 o’clock of vulva
- Another patch of hyperpigmentation 7cm x 5cm over posterior third of vulva
- Hyperpigmentation around anus

Vulval biopsy 3/2016:
- 5 o’clock: condyloma with atypia
- 12 o’clock: VIN II-III
- 2,5,7,9,11 o’clock of vulva / perianal area and posterior fourchette: HSIL (VIN III)

- Cervical smear: HSIL
COLPOSCOPY
COLPOSCOPY
Faint acetowhite lesion at 3 and 9 o’clock with ill-defined border, no mosaicism/punctation, iodine negative
Imp: LG lesion
Cervical biopsy 5/2016
3 o’clock: CIN II-III, HPV
9 o’clock: CIN II, HPV
Consulted surgery:

PR: no definite involvement of sphincter clinically

Endoscopic ultrasound of anal canal: no obvious mass lesions seen in anal canal
OPERATION

- Bilateral skinning vulvectomy, LLETZ, Vaginal stripping
- 1cm x 1cm patch of hyperpigmentation over 12 o’clock of vulva above clitoris
- 7cm x 5cm patch of raised hyperpigmentation over posterior third of vulva involving anus circumferentially
- Cervix no gross lesion
- 0.5cm warty lesion at 9 o’clock of vaginal fornix, iodine negative
- 1cm warty lesion at 1 o’clock of vaginal fornix, iodine negative
- 2cm x 2xm warty lesion at middle of right vaginal wall, iodine negative
- Vulva, vagina, cervix: HSIL
CASE 3
HISTORY

- 51yo, G8P3, Married, Non-smoker
- PMH: Non-toxic nodular goitre with left hemi-thyroidectomy, Angiomyolipoma of kidney, Laparotomy and drainage of perinephric abscess, Ligation and stripping of varicose vein
- Presented to KWH in 7/2012 for 10 year history of right vulval reddish lesion
- Vulval biopsy 8/2012: VIN 3
- Cervical biopsy 3/2013: condyloma
- Cervical smear 3/2013: LSIL
- Referred to QMH for further management of VIN
COLPOSCOPY

Patch of erythema at right vulva

Well demarcated acetowhite lesion with fine punctation at right vulva
Patch of well demarcated acetowhite lesion at right introitus ~1 cm in size with mosaicism

Poor uptake of iodine especially at right introitus
- Vagina, cervix: normal
- Right vulval (12 o’clock) and right lower introitus biopsy 3/2013: VIN 3
MANAGEMENT

- Wide local excision 4/2013
  - G2-3 SCC, 4mm in thickness, arising in the background of VIN, deep margin involved at 3 o’clock

- Radical vulvectomy and bilateral groin node dissection 5/2013
  - Usual VIN with one positive groin lymph node (<2mm with no capsular involvement)

- Diagnosis: CA vulva stage 3A (G2-3 SCC)

- No adjuvant RT is needed
VULVAR INTRAEPITHELIAL NEOPLASIA
CLINICAL PRESENTATIONS

- Often asymptomatic (~40%) and is noted incidentally during pelvic examination
- Vulvar pruritus is most common complaint
- Vulvar pain or burning
- Dysuria
HISTORY

- Symptoms
- Risk factors associated with VIN
  - Majority of cases are associated with HPV infection
  - Risk factors for exposure include sexual contact, including genital, anal, or oral contact to vulva
- Prior history of VIN, genital warts, or vulvar cancer, and of other HPV-associated lower genital tract neoplasia, most commonly cervical neoplasia
- Smoking
- Conditions associated with immunosuppression
PHYSICAL EXAMINATION

- Inspection and palpation of vulva and groin for lesions, color changes, masses, or ulceration
- Most (49%) VIN lesions are multifocal and located in non-hairy part of the vulva
- Lesions are often raised or verrucous and white, but the color may be red, pink, gray or brown
- Macular lesions mostly occur on adjacent mucosal surfaces
- NO pathognomonic clinical appearance, and more than one of these patterns may be seen in the same patient
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Holschneider C. UpToDate. 2014
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PHYSICAL EXAMINATION

- Condylomata acuminata may be difficult to differentiate from VIN
- VIN may be difficult to distinguish from invasive vulvar squamous carcinoma and both may coexist
- Other lesions may mimic VIN
  - Lichen sclerosus
  - Lichen planus
  - Condyloma lata
DIAGNOSIS - BIOPSY

- Visible vulvar lesion
  - Woman who fails to respond to treatment
  - Clinical suspicion of VIN or cancer
  - Most pigmented lesion
  - Presumed genital warts in postmenopausal women and failed topical therapies

- Vulva with multiple areas of abnormalities warrants multiple biopsies

- Infrequently, a biopsy is appropriate in the absence of a visible lesion
COLPOSCOPY

- Identify subclinical lesions not appreciated on gross visual examination
- Define extent of disease and guide biopsy

- Persistent symptoms consistent with VIN, but no gross visible lesions
- Remain symptomatic despite treatment for other conditions (eg. candidiasis, dermatitis, vulvodynia)
- Persistent abnormal cervical cytology with no CIN on biopsy

- If no lesion at colposcopy and symptoms cannot be explained by another diagnosis ➔ biopsy
- Evaluate entire lower genital tract (cervix, vagina, vulva) and perianal area - high prevalence of multicentric synchronous intraepithelial lesions
- RCOG: Women who have been treated for VIN are at risk of intraepithelial neoplasia at other sites. Colposcopy examination should be available at follow-up (C)

RCOG Green-top Guideline No. 58: The management of vulval skin disorders. 2011
Treatment is indicated for all cases of VIN

Goals of treatment

- Relieve symptoms
- Exclude invasive cancer
- Reduce risk of invasive cancer
- Preserve normal vulvar anatomy and function
TREATMENT

- Choice of treatment depends primarily on risk of invasive disease based upon histology and risk factors
- Other factors are location and extent of disease and symptoms

- Wide local excision is recommended when cancer if suspected, despite a biopsy diagnosis of only VIN, to identify occult invasion
  - 19-22% of women undergoing excision of VIN have clinically unrecognised invasion diagnosed on histology
  - When occult invasion is not a concern, surgical therapy, laser ablation or topical imiquimod is an option

- RCOG: The gold standard for the treatment of VIN is local surgical excision (C).
SURGICAL THERAPY

- Wide local excision
  - Preferred initial intervention in women whom clinical or pathologic findings suggest invasive cancer

- Skinning vulvectomy (removes all vulvar skin)
  - Rarely needed, may be useful for cases of confluent multifocal lesions (immunocompromised women)

- Pathologic clear margins – lower but still significant risk of recurrence

- Gross margins 0.5-1cm around tissue with visible disease appear optimal – may alter to avoid injury to clitoris, urethra or anus

ACOG Committee Opinion No. 509: Management of vulvar intraepithelial neoplasia. 2011
LASER ABLATION

- Acceptable when cancer is not suspected
- Can be used for single, multiple or confluent lesions
- Requires destruction of cells through entire thickness of epithelium
- Hair-free areas: ablate through dermis (up to 2mm)
- Hair-bearing areas: must ablate hair follicles, which can contain VIN and extend into subcutaneous fat for ≥3mm
  - Large VIN lesions over hair-bearing areas may be preferentially treated with other modalities
- Offer cosmetic advantages over skinning vulvectomy
- Limitations
  - Special training is required
  - Another method may be preferred for lesions in hair-bearing areas because laser treatment destroys hair follicle

ACOG Committee Opinion No. 509: Management of vulvar intraepithelial neoplasia. 2011
SURGICAL THERAPY VS LASER ABLATION

- Systematic review: 1905 surgically treated patients
- FU 12 to 75 months (mean, 39 months)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Recurrence rates</th>
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<tbody>
<tr>
<td>Vulvectomy</td>
<td>19%</td>
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<tr>
<td>Partial vulvectomy</td>
<td>18%</td>
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<tr>
<td>Local excision</td>
<td>22%</td>
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<tr>
<td>Laser ablation</td>
<td>23%</td>
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</tbody>
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- Risk of VIN recurrence or vulval cancer did not differ significantly between surgical excision and laser ablation

van Seters M et al. Gynecol Oncol. 2005
MEDICAL THERAPY - IMIQUIMOD (ALDARA)

- Topical immune response modifier: its antiviral and antitumor effects are mediated through the stimulation of local cytokine production and cell-mediated immunity
- Off-label use (not approved by US FDA for this purpose)
- Systematic review: included 2 RCT and 8 observational studies (total n = 162)
  - Complete response rate – 51%
  - Partial response rate 25%
  - Recurrence rate 16%
- Regimens: 3x/wk application to affected areas for 12-20wk with colposcopic assessment at 4-6wk intervals
- Adverse effects: pain, erythema, swelling ➔ non-compliance
  - Common: up to 2/3 of women reduce number of applications, mostly from 3x to 2x/wk
  - To reduce incidence of local inflammation: consider escalating dose regimen, starting 1x/wk for 2 wk, then 2x/wk for 2 wk, then, if tolerated well, 3x/wk

Mahto M et al. Int J STD AIDS. 2010
MEDICAL THERAPY - OTHERS

- Topical cidofovir (used in treatment of genital warts)
- Photodynamic therapy
- Interferon
- Therapeutic HPV vaccine
PREVENTION

- Quadrivalent HPV vaccine
- Smoking cessation
- Treatment of vulvar dermatoses
- No screening strategies
SURVEILLANCE

- Post treatment recurrence rates 30-50% with all treatment regimens
- Higher recurrence rates
  - Positive excision margins: BUT the risk of residual or recurrent disease is not sufficient to recommend re-excision in the absence of clinical disease
  - Multifocal lesions vs unifocal lesions (66% vs 34%)
- Women with VIN should be considered to be at risk of recurrent VIN and vulvar cancer (~4%) throughout their lifetimes
- Value of vulvae self-examination and serial FU has not been proved prospectively, but both appear prudent
- Given slow rate of progression, women with complete response to therapy should be monitored at 6 and 12 months and annually thereafter
- RCOG: Women with VIN need to be seen on a regular basis for vulvoscopy or careful clinical assessment and biopsy of any suspicious area (C)
SUMMARY

- NO pathognomonic clinical appearance
- Diagnosis by biopsy +/- colposcopy
- Treatment by surgical excision (esp if cancer suspected), laser ablation or topical imiquimod
- Risk of recurrence
- Risk of multicentric synchronous intraepithelial lesions
THANK YOU