The Itching Vulva: Lichen Sclerosus and Vulvovaginal Atrophy

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March 2, 2019
Forum F044: The Vulva: What do you know?
DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Miriam Keltz Pomeranz

Forum F044: Vulvar Disease: What do you know? The Itching Vulvar: Lichen Sclerosus and Vulvovaginal Atrophy

March 2, 2019

DISCLOSURES

Proctor and Gamble: member of Scientific Advisory Board
UpToDate: Royalties
Vulvar Lichen Sclerosus

Nomenclature

• Kraurosis Vulvae
• Vulvar Dystrophy
• White spot disease
• Guttate scleroderma
• Lichen sclerosus et atrophicus

Vulvar Lichen Sclerosus epidemiology

- Prevalence unknown – asymptomatic
- Margesson – 1/300 to 1/1000
- Age onset: girls mean 5.4yrs; women mean 55.1 yrs; Margesson women 30-40
- In women: 78% post menopausal

Vulvar Lichen Sclerosus: epidemiology

- 28% of pts with other autoimmune dz:
  - Alopecia areata
  - Vitiligo
  - Thyroid dz (most common)
  - Pernicious anemia
  - Morphea
- Family hx: 12% (likely underreported)
- ? Asst HLA DQ7, DQ8, DQ9


Vulvar Lichen Sclerosus - clinical

• Signs – porcelain white papules/plaques; echymoses/purpura; “cigarette paper”; hyperkeratosis; ulceration; fusion of labia minora to majora; “phimosis” of clitoral hood (“burying of the clitoris”); “Closures of the commissures” (vestibule smaller – like zip closed from under clitoris);

Vulvar Lichen Sclerosus - clinical

- 70% of women with some scarring
- Symptoms – pruritus, irritation, burning, dyspareunia, tearing; constipation in girls; can be asymptomatic

Vulvar Lichen Sclerosis: clinical

• Distribution – 59% vulvar and perianal (figure of eight); vagina spared
• Extragenital 11-13% (exclusively extragenital: 6%)
• Rate of malignancy (SCCa) about 2-5% as high as 6.7% (Bleeker)

Vulvar Lichen Sclerosus: clinical

Hyperpigmentation:

• vulvar lentiginosis:
  • can be dark and irregular
  • on bx clearly not melanoma

• nevi in LS:
  • clinically suspicious for melanoma
  • histologically suspicious for melanoma
  • tell pathologist in setting of LS
Lichen Sclerosus: pathology

- Pathognomonic changes: in papillary dermis homogenization & sclerosis with atrophy of epidermis (not always present, esp in early lesions); bx center of white lesion

Lichen Sclerosus: pathology

- Lymphocytic, lichenoid interface dermatitis in LP and LS
- Elastic stain – marked decrease in papillary dermal elastic fibers in LS c/w LP

Vulvar Lichen Sclerosus: etiology

- Unknown – thought to be autoimmune
- Sera of pts with auto antibodies:
  - 67% with antibody to extracellular matrix 1 protein
  - 30% with antibody to BP180 and BP 230
  - Another study: 4/149 had BP180 antibody (not significant)
- Expert opinion – antibodies secondary; likely T cell mediated disease

Vulvar Lichen Sclerosus: diagnosis

- Biopsy (except in prepubertal child) vs clinical
- Biopsy may not be diagnostic
  - McCarthy et al 13/39 bx in clinically certain LS not diagnostic
- Rebiopsy
- Response to treatment
- Look for other diseases

Vulvar Lichen Sclerosus Treatment

• Ultra potent topical steroids:
  • 96% partial-complete relief; (65% women sx free)
  • 23% return to normal skin exam
  • If not responding, consider other diagnosis

Vulvar LS: Treatment

- Tacrolimus/pimecrolimus
  - 50-94% at least partial improvement
- Pts failed topical steroids
- Burning/itching week(s); ?increase risk of SCCa

Marren P, Walkden V, Mallon E, Wojnarowski F. Vulval cicatricial pemphigoid may mimic lichen sclerosus.
Vulvar LS: Treatment

- Intrallesional steroids (esp. very hyperkeratotic)
- Other: retinoids, MTX, cyclosporin, cryotherapy, autologous platelet rich plasma – not helpful

Vulvar LS: Treatment

- Lasers
  - fractionated erbium yag – for hyperkeratotic areas; adjunctive
  - fractionated/ablative CO2 – hyperkeratotic; adjunctive
- PDT – may be helpful but not proven


Vulvar LS: Treatment

- Follow up q 6-12 months screening exam
- Never totally stop treatment

Vulvar Lichen Sclerosus: treatment

- Lee et al:
  - suggest treatment 3 times/week
  - lower strength of topical steroid if improved
  - 0/357 compliant patients with SCCa/VIN
  - 7/150 partially compliant patients SCCa/VIN

Atrophic Vaginitis = Vulvovaginal Atrophy (VVA) = Genitourinary Syndrome of Menopause

- Symptoms:
  - Dyspareunia
  - Vulvovaginal dryness/itching/pain
  - Urinary complaints
  - After 4 years of menopause, > 60% have sxns

Vulvovaginal Atrophy

Consequences of low estrogen:
- Reduce mucosal elasticity
- Reduce mucosal hydration
- Vagina loses rugae; shorter; narrower
- Vagina, introitus, labia minora mucosa thin and pale
- Loss of vasculature
- Decreased vaginal secretions (transudate from vasculature)

Vulvovaginal Atrophy

- Post-menopausal vulva:
  - Labia majora - less fat and hair; gray
  - Labia minora – smaller to absent
  - Introitus (vestibule) – pale, shiny, dry
  - +/- petechiae; fissures of post. forchette
  - Urethral caruncle (PG-like); urethral prolapse

## Topical Estrogens

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Trade name</th>
<th>Vehicle</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogens 0.625 mg/g</td>
<td>Premarin Vaginal Cream</td>
<td>Cream</td>
<td>0.5-1gm PV 7 days then BIW; 0.5gm 21 days off 7 days</td>
</tr>
<tr>
<td>Estradiol 0.1mg/g</td>
<td>Estrace Vaginal Cream</td>
<td>Cream</td>
<td>2-4 g cream PV 1-2 wks; taper to 1g 1-3/wk</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td>Estradiol 10 or 25 mcg</td>
<td>Vagifem/Yuvifem (generic)</td>
<td>Tablets</td>
<td>1 tab PV q day for 14 then 1 tab BIWk</td>
</tr>
<tr>
<td>Estradiol 4 or 10 mcg</td>
<td>Imvexxy</td>
<td>Insert tear shaped</td>
<td>1 insert PV q day for 14 then 1 insert BIWk</td>
</tr>
</tbody>
</table>

The Medical Letter on Drugs and Therapeutics. Imvexxy – another estradiol vaginal insert for dyspareunia. 2018; 60: 147-8
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<tr>
<td>Estradiol 7.5mcg/24 hr</td>
<td>Estrings</td>
<td>Vaginal ring</td>
<td>Place in upper vagina for 90 days</td>
</tr>
<tr>
<td>Estradiol 50mcg/24 hr or 100mcg/24 hr</td>
<td>Femring</td>
<td>Vaginal ring</td>
<td>Place in upper vagina for 90 days; designed to get systemic levels</td>
</tr>
</tbody>
</table>

Topical Estrogens: Use

- Most studies show no increase serum level estrogens above menopausal norms
- Use lowest effective dose
- Safety data only up to 1 year
- Vaginal ring lowest systemic absorption and highest pt satisfaction
- Screen endometrium with pelvic ultrasound or endometrial biopsies

Topical Estrogens: Use

• No increased risk of breast cancer, endometrial cancer, stroke, venous thromboembolism with intra vaginal estrogen in the women’s health initiative observation study

• contraindicated in pts with genital bleeding, “estrogen dependent neoplasm”, hx of VTE, active arterial thromboembolic dz, thrombophilic dz, liver dz, breast

CJ Crandall et al. Breast cancer, endometrial cancer and cardiovascular events in participants who used vaginal estrogen In the Women’s Health Initiative Observational Study. Menopause 2018; 25: 11.

**Topical Estrogens: Use**

- Suggest “clinician vigilance” varying depending on patient
- “Data are insufficient to mandate endometrial surveillance or dictate frequency or means of surveillance.”
- “Data are insufficient to recommend annual endometrial surveillance in asymptomatic women using vaginal ET.”


Topical Estrogens: Use

“Although these products generally appear safe, a precise estimate of risk to the endometrium with sustained vaginal estrogen use is not clear, and additional long-term study with more consistent assessment of the endometrium and more sensitive assessment for changes in serum estradiol is needed.”

Topical Estrogens: Alternatives

- Selective estrogen receptor modulators: ospemifene; PO med; helpful in studies for vulvovaginal atrophy; FDA approved
- Topical DHEA (prasterone) – improves sexual dysfunction due to vaginal atrophy; FDA approved
- Vitamin D – one study vit D improved sx s VVA

Topical Estrogens: Alternatives

- lasers:
  - fractional CO2 laser (MonaLisa Touch™ (DEKA, Florence, Italy))
  - others being studies

Topical Estrogens: Alternatives

- Vaginal moisturizer as alternative for dryness:
  - Replens (active ingredient polycarbophil carries water and stays for 2-3 days)
  - Summer’s Eve (based on pectin)
  - RepHresh
  - Emerita
  - Yes (from UK)
- Hyaluronic acid-based:
  - Hyalo GY (US)
  - Hyalofemme (UK)
  - Repadina (UK) - ovules

Topical Estrogens: Alternatives

• Use in patients with a history of breast or endometrial cancer
• Equally effective as estrogens in patients with just one symptom

Topical Estrogens: Alternatives

- Vaginal lubricants: for use prior to sex
- No long term therapeutic effect

Topical Estrogens: Alternatives Lubricants

- **Water based:**
  - Astroglide liquid
  - Astoglide gel liquid
  - Astroglide
  - Just like me
  - K-Y jelly
  - Pre-Seed
  - Slippery Stuff
  - Liquid Silk

- **Silicone based**
  - Astroglide X
  - ID Millenium
  - K-Y Intrigue
  - Pink
  - Pjur Eros

- **Oil Based**
  - Elegance Women’s Lubricants
  - Olive oil

Topical Estrogens: Alternatives

- Regular vaginal coital activity
  - fewer sxs
  - less shrinkage/stenosis of vagina
  - thought because increase blood flow, maintain vaginal elasticity/pluckiness