Optimising management of lichen sclerosus and chronic thrush

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No conflict of interest

Golden Rules

- Lichen sclerosus is best diagnosed early
- Treatment with potent topical steroids
- works!
- Long-term treatment and follow-up probably decreases cancer risk
- Chronic thrush is due to hypersensitivity to candida albicans
- Long-term oral treatment gives best results

CASE 1

- Mrs VF 48 year-old woman, farmer’s wife
- Presented with sore lesion on vulva
- 10 years before had had itchy rash there treated by dermatologist, got better
- Busy on farm, two young children
- Eventually mentioned it to GP, embarrassed

Squamous cell carcinoma with lichen sclerosus

- Surgery and lymph node dissection
- Nodes involved
- Radiotherapy but died 2 years later
- SCC associated with HPV less now
- Lichen sclerosus: 5% SCC
- Does treatment change prognosis?
Case 2: Mrs JK, 60 year-old lady

- Itchy vulva for 8 years, waking her at night now
- Treated as thrush: clotrimazole cream, fluconazole
- Treated as atrophic vaginitis: Vagifem
- Intercourse uncomfortable; has stopped last few years.
- Post menopausal, not on HRT

Loss of normal architecture
- White thickened skin over labia majora, perianal area “figure of eight”
- Diagnosis: Lichen sclerosus

Variations
Vitiligo

- Erosions
- Severe architectural change
- Post surgery and laser Rx

Perianal LS

- Erosions
- Severe architectural change
- Post surgery and laser Rx

Extra genital lichen sclerosus

- Usually not itchy
- White patches
- Overlap with morphea

Extragenital lichen sclerosus
Mrs. JK: Management

- Biopsy: 3-4mm punch, dissolving suture
- Good skin care
- Diprosone OV or Clobetasol ointment bd for a month, daily for a month then at least 2x/week
- Explanation: need strong cream as it needs to penetrate to thick area.
- Review in 3/12
- May change to weaker steroid then
- Long term follow up: 2-5% cancer, probably more if untreated.

Mrs. JK

Lichen Sclerosus

- Uncommon disease of genital skin
- Prevalence: 3% of female population
- Significant risk (scarring 50%, SCC 5%)
- Autoimmune association: thyroiditis
- Large impact on quality of life
- All age groups including children: mean is 55

Previous treatment guidelines for Lichen Sclerosus (BAD 2010)

- Initial treatment with clobetasol 0.05%
- Then treatment with clobetasol 0.05% to control flares
- 3 visits: presentation, 3/12 and 9/12 then primary care
- Most cases are uncomplicated = <60g clobetasol yearly
- There are no randomised trials to compare treatments
- Risk of SCC is 5% and this is considered "rare".
- It is not known if treatment lessens risk
- Follow up in specialized clinic

Key questions about Lichen Sclerosus

- Can treatment with topical corticosteroids long-term
  - Reduce CANCER risk?
  - Preserve vulvar ARCHITECTURE?
  - Improve FUNCTION as well as suppress symptoms?
  - Do so without SIDE EFFECTS?
Scarring and loss of vulval architecture

Vulval cancer

Cancer: Untreated 5%

Problems in long-term management

Latest research

Study aims and Protocol
- Prospective longitudinal cohort study
- 2008-2014
- Intervention: TCS used regularly with follow up
- Induce remission with potent TCS
- Maintain remission with moderate regular TCS
- Titrate to normal skin colour and texture long-term
- Determine outcomes of compliers vs non-compliers

Patient Data

- Patients n = 507 with biopsy proven lichen sclerosus
- Age >18, F/U >2 years
- Compliance: 357 compliant, 150 partially compliant
- Mean age at presentation = 55.4 years (18-86)
- Mean duration of follow up 4.7 years (2.0-6.8)
- Mean duration to onset of neoplasia: 4.2 years
Grading of VLS severity

- **Very severe (4+)**
  - TCS strength: Ultra-potent

- **Severe (3+)**
  - TCS strength: Super-potent

- **Moderate (2+)**
  - TCS strength: Moderate

- **Mild (1+)**
  - TCS strength: Mild

Choice of induction treatment based on degree of hyperkeratosis

TCS strength used in initial management of VLS

<table>
<thead>
<tr>
<th>TCS Strength</th>
<th>Symptom resolution</th>
<th>Dyspareunia resolution</th>
<th>Scar progression</th>
<th>SCC or VIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultra-potent</td>
<td>93.3%</td>
<td>93.7%</td>
<td>3.4%</td>
<td>0%</td>
</tr>
<tr>
<td>Super-Potent</td>
<td>14.8%</td>
<td>65.5%</td>
<td>40.0%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Moderate</td>
<td>67.1%</td>
<td>65.7%</td>
<td>11.7%</td>
<td>8%</td>
</tr>
<tr>
<td>Mild</td>
<td>8.5%</td>
<td>55.5%</td>
<td>18.7%</td>
<td>12.7%</td>
</tr>
<tr>
<td>None / Remission</td>
<td>0.8%</td>
<td>64.1%</td>
<td>30.8%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

Summary of outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Compliant %</th>
<th>Partially compliant %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 357 (70.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom resolution</td>
<td>93.3%</td>
<td>14.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyspareunia resolution</td>
<td>93.7%</td>
<td>65.5%</td>
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Is this going to be too expensive?

- Cost of one patient with vulvar cancer
- Cost of regular follow up to prevent cancer and prevention of morbidity from scarring

NNT to prevent 1 cancer = 21
NNT to prevent scarring = 2.7

Significance of this research

- This is the first study adequately powered to demonstrate that cancer and scarring can be prevented by regular treatment
- This is now the recommendation in the latest version of Therapeutic Guidelines: Dermatology
Summary: How to treat Lichen Sclerosus

- Start with a confirmatory biopsy and check thyroid
- Induce remission with potent TCS (4-6 months)
- Use preventative treatment to maintain normal skin
- No "as needed" treatment.
- Follow up patients: adjust treatment, encourage compliance
- Titrate TCS to disease severity, response
- Target outcome: normal skin colour and texture.
- Long-term management with TCS is safe, effective
- The course of the disease can be modified by treatment

Karen, 21 Student

- Itchy, sore, swelling, splitting, discharge, dysuria
- Started after first sexual activity at 19
- Dyspareunia
- Worse before periods and with antibiotics
- Swabs sometimes positive for C. Albicans but not consistently
- Partner gets itchy after sex
- Gets almost better with topical and oral antifungals but rapidly recurs

Chronic candidiasis

- For last year itch, dyspareunia, erythema
- No discharge
- Swab +ve for C. Albicans
- No response to antifungals
- Continues to take Livial and not keen to stop

Jen 52. Menopause at 48. HRT for last 4 years

- Itchy, sore, swelling, splitting, discharge, dysuria
- Started after first sexual activity at 19
- Dyspareunia
- Worse before periods and with antibiotics
- Swabs sometimes positive for C. Albicans but not consistently
- Partner gets itchy after sex
- Gets almost better with topical and oral antifungals but rapidly recurs
- Candida is a normal commensal of gut and vagina
- Vulvovaginitis from this normal organism is host dependent
- Candidiasis is oestrogen dependent: not seen before menarche and after menopause unless on HRT
- It behaves like a hypersensitivity response to something that is a normal part of the human body
- The threshold for that response is genetic
- In order to suppress the response you need to suppress the antigen for as long as the patient remains hypersensitive

Diagnosis of chronic thrush

- Clinically a non erosive vulvovaginitis
- Biopsy shows spongiosis
- A low vaginal swab is only +ve in 75% of cases
- pH is normal 4.5
- Office microscopy is time consuming, requires skill that many of us don’t have and sensitivity is low
- Take a careful history

History taking in chronic thrush

- Have you ever had a +ve swab for Candida?
- Do your symptoms cycle?
- Do you experience pain with sex?
- Do you get thrush from antibiotics
- Do you experience soreness (itch is non-specific although common)
- Do you have a discharge?
- Do you get better with antifungals?
- Do you experience swelling?

Hong et al Vulvovaginal candidiasis as a chronic disease: Diagnostic criteria and definition J Lower Genital Tract Disease 2013

Differential diagnosis of chronic thrush

- Psoriasis
- Oestrogen hypersensitivity vulvovaginitis

Who gets CVVC?

- Healthy pre-menopausal women mostly
- Majority onset is in late teens – 20’s
- Atopic
- Post menopause on HRT who had it before menopause
- Immunosuppressed
- Long term antibiotics
- Mirena
- Diabetics
- Not HIV
- Not children
Impact on quality of life

- CVVC is one of the most devastating vulvovaginal conditions
- Mean DLQI in a cohort of 82 patients was 15 (high impact)
- It affects young, sexually active women
- Major impact on sexuality and activities
- Major impact on clothes

Managing Candida

- Acute candida is easy: topical or stat dose of Diflucan
- Recurrent candida = 4 confirmed attacks per year +ve swabs
- Chronic candida = symptomatic all the time, swabs may be -ve
- Recurrent or chronic candida is very difficult: need prolonged oral antifungal therapy, good skin care and attention to any underlying disease.
- If not better after two courses of antifungals or comes right back: think CVVC

Management of CVVC

- Long term low-dose oral antifungal
  - Itraconazole or fluconazole 50-100mg/day for 3 months
  - In a group of 82 women mean DLQI went from 15 to 3.4
  - Reduce gradually to maintenance dose
  - Titrate dose to symptoms
  - Treat secondary dermatitis with weak steroid only
  - If secondary to HRT, stop it temporarily until recovered then restart under antifungal cover
  - ?Depot provera

Long term prognosis of CVVC

- Group of 201 women: 98% still using antifungal treatment, mainly fluconazole, up to 8 years later
- Vulva may always look red even when asymptomatic
- Doses vary from prn to daily
- Most are on 50mg twice a week
- Increase to daily if relapse, antibiotics or travel
- Long-term fluconazole is as safe as long-term valacyclovir
- Fluconazole does not cause drug induced hepatitis
- 95% can tolerate fluconazole long term
- Cost is $30 a month on continuous therapy

Summary CVVC

- CVVC is a recent concept
- RVVC and CVVC are probably on a spectrum
- This is NOT an infection
- It has a huge impact
- The prognosis is good with long-term suppressive therapy
- Treatment is safe and cost-effective
- This treatment recommendation is now in Therapeutic Guidelines
Golden Rules

- Lichen sclerosus is best diagnosed early
- Treatment with potent topical steroids works!
- Long-term treatment and follow-up probably decreases cancer risk
- Chronic thrush is due to hypersensitivity to candida albicans
- Long-term oral treatment gives the best outcome