GENITAL HPV

Most common sexually transmitted infection in the US
More than 50% of adults infected with at least one type
>50% of new infections occur in ages 15-21
More than 40 types transmitted through sexual contact and known to infect the anogenital region
Causes genital warts, cervical cancer, oropharyngeal cancer, anogenital SCC
Treatments include cryotherapy, CO2 laser ablation, surgical excision, imiquimod, podophyllin

Gardasil 9

FDA approved December 10, 2014
5 additional HPV types covered
16, 18, 31, 33, 45, 52, 58, 6, 11
Has potential to prevent 90% of vulvar, vaginal, cervical and anal cancers
The 5 new types prevent 20% of the above cancers
Inclusion of 6 and 11 protects against genital warts
Approved for females aged 9-26 and males 9-15 (age 11-12 ideal)
A series of 3 shots, initial, 2 and 6 months later.
GENITAL HPV

VEREGEN
Sinecatechin
Partially purified water extract from green tea leaves Camilla sinensis
Applied TID for up to 16 weeks
53.6% complete clearance, 47.2% men, 60.4% women. Median time to clearance 16 weeks
Side effects: erythema, pruritis, burning, pain, ulceration, edema, induration, and vesicular rash
$1000 for a 30 gram tube

(VEREGEN prescribing information, Fougera)

GENITAL LICHEN SCLEROSUS: NEW UNDERSTANDING OF PATHOPHYSIOLOGY

Hypoxia and ischemia may precipitate GLS in susceptible individuals
Supported by the finding of increased glut-1 and decreased VEGF expression in affected skin (Clin Exp Dermatol. Dec 2009;34(8):e531-6)
PCR–based studies: no increased incidence of borrelial infection (J Cutan Pathol. Dec 10 2009)
Local irritation, trauma plays a role (incontinence in women, uncircumsized men, poor hygiene)

GENITAL LICHEN SCLEROSUS: NEW UNDERSTANDING OF PATHOPHYSIOLOGY

Oral contraceptives in premenopausal women increases risk (RR 2.5)
40% of vulvar LS and LP patients have reactive T cells to the NC16A domain of bullous pemphigoid antigen 180 (J Eur Acad Dermatol Venereol Feb 2010;24(2):186-90)
Autoantibodies to ECM 1 reported now by several independent investigators
Circulating autoantibodies 28% in LS, as high as in bullous LP (Arch Dermatol Nov 2008;144(11):1432-5)
LICHEN SCLEROSUS IN CHILDREN

Does not appear to go into sustainable remission with puberty onset
Elizabeth Ellis and Gayle Fischer published a retrospective series of 46 prepubescent girls with lichen sclerosus: Permanent remission does not occur with puberty
Long term treatment with ultrapotent topical steroids required to prevent disease progression

LICHEN SCLEROSUS: TREATMENT UPDATE

Clobetasol 0.05% superior to tacrolimus 0.1%; both effective
Double blind RCT, 58 women, 12 week trial
Both treatments resulted in improvement of signs and sx
55% of patients in the clobetasol group had absence of signs and symptoms of lichen sclerosus vs 32% of patients in the tacrolimus group
More rapid response seen with clobetasol
Burning sensation common, but mild. 78% of tacrolimus group, 48% of clobetasol group. No individual discontinued trial due to SEs.
(Funaro, L.A. JAAD, 71 (1), 84-91; 2014)

LICHEN SCLEROSUS: TREATMENT UPDATE

Pimecrolimus 1%; compared to clobetasol, both equally effective at controlling sx of itch; clobetasol superior at controlling visible signs of disease
No role for topical testosterone, dihydrotestosterone, or progesterone (JAAD, 67(2), 305-312; 2012)
Fig 3 Patient 12 with lichen sclerosis before (A) and after (B) 3-month treatment with topical tacrolimus 0.1%.

Deana Funaro, Audrey Lovett, Nathalie Leroux, Julie Powell

A double-blind, randomized prospective study evaluating topical clobetasol propionate 0.05% versus topical tacrolimus 0.1% in patients with vulvar lichen sclerosis

Journal of the American Academy of Dermatology, Volume 71, Issue 1, 2014, 84 - 91

http://dx.doi.org/10.1016/j.jaad.2014.02.019

LICHEN SCLEROSUS: PLATELET RICH PLASMA

Autologous concentration of platelets and plasma
Blood sample collected, added to ACD-A tubes, centrifuged, plasma extracted
Injected, or applied after non-ablative fractional resurfacing (1540 nm) or microneedling
EGF, PDGF, TGF-beta, VEGF in high concentrations

Number of fibroblasts
Dermal thickness
Elasticity
Volume of collagen in papillary dermis


LICHEN SCLEROSUS: PRP

Multiple clinics in US and Europe performing procedures they call “cell therapy” or “stem cell lift”, combining injection of PRP and adipose stem cells
Claiming remissions and overall improvement of lichen sclerosus
No studies in lichen sclerosus or vulvar skin in Medline search 6/2015
Centers for Vulvovaginal Disorders currently enrolling 10 women with LS for a study of injection of PRP into areas of LS
(www.cvvd.org/research_studies)
LS: ALTERNATIVE TREATMENTS

Avocado and soybean extracts
Topical and oral treatment; oral also contained vitamin E and PABA
23 patients with mild-to-moderate vulvar lichen sclerosus
24 weeks, no placebo
Primary endpoint: >75% improvement of GSS and GOS
Subjective parameters: itch, burning, dyspareunia
Objective parameters: erythema, leukoderma, hyperkeratosis, lichenification
70.5% achieved GSS75, 72.2% GOS75
100% GSS50, 88.9% GOS50
Claims of anti-inflammatory, anti-fibrotic, and emollient effects
Soybean oil contains genistein, with claims of potent antioxidant and anti-inflammatory activity and collagen stimulation

POSTMENOPAUSAL ATROPHY

OSPHEMA
Oral treatment for dyspareunia due to postmenopausal vulvar and vaginal atrophy
Approved 2013
Ospemifene 60 mg daily
Tissue-specific estrogen receptor agonist/antagonist (SERM)
Binds ERα and ERβ with approximately equal affinities
Increased risk of VTE, hemorrhagic stroke
Estrogen-like effects on the vaginal epithelium, neutral endometrial profile, antiproliferative effects in breast, and estrogenic effects in bone

ACUTE GENITAL ULCERS IN NON-SEXUALLY ACTIVE GIRLS

Rare, painful and distressing condition, cause unknown.
9-19 year old girls
Deep ulcers on the inner aspect of the labia minora.
Black, necrotic, shallow ulcers with “labial swelling” and “purulent exudate”; exquisitely tender.
71% with systemic symptoms (flu-like), 46.8% prior history of oral ulcers, 32.2% recurrent episodes
ACUTE GENITAL ULCERS IN NON-SEXUALLY ACTIVE GIRLS

70% ultimately idiopathic (6 patients with EBV, 1 patient with CMV, 1 with mycoplasma)

Fairly consistent picture across the series:
- Most have mild prodromal symptoms (flu-like)
- Biopsies unhelpful (nonspecific ulceration and necrosis)
- Infectious work-up largely negative, doesn’t change management

Best understanding is idiopathic vulvar aphthosis, with some cases having infectious agent precipitating

ACUTE GENITAL ULCERS IN NONSEXUALLY ACTIVE GIRLS

Recommendations:
- Limited workup for infection, directed.
- Exposure
- Severe systemic symptoms
- Rheumatologic or ophthalmologic evaluation if clinical suspicion
- Rule out HSV with lesional PCR
- Avoid biopsy unless a specific dermatologic condition is suspected

Treatment:
- Pain relief paramount
- Lidocaine gel, Sitz baths, acetaminophen, narcotics
- Monitor for acute urinary retention due to pain and edema, hospitalize if needed
- Topical clobetasol ointment, intralesional with new lesions
- Insufficient data to determine benefit of systemic steroids

HIDRADENITIS SUPPURATIVA (ACNE INVERSA)

Chronic disorder of the folliculopilosebaceous units (FPSU)
Weakeness in the support structure of the follicular portion of the FPSU likely predisposes to follicular rupture caused by local trauma

Comedones, cysts, inflammatory nodules, scarring and sinus tracts in intertriginous areas

Chronic, disabling, disfiguring, treatment resistant

Average age of onset 23
1.4% prevalence, women:men 3.3:1
HIDRADENITIS SUPPURATIVA (ACNE INVERSA): ANDROGENS

In women, HS begins with menarche, flares premenstrually, worse with androgenic OCPs, better in pregnancy and after menopause. No difference in serum levels of androgens between HS and controls; likely end-organ sensitivity higher.

Increased insulin/IGF-1 signaling (IIS) of Western diet superimposed on the increased IIS of puberty inhibit FoxO1. "Access" to androgen receptors increased.

POTENTIAL ROLE OF FOXO1 AND MTORC1 IN THE PATHOGENESIS OF WESTERN DIET-INDUCED ACNE

HIDRADENITIS SUPPURATIVA: TREATMENT

Oral contraceptives (drospironone)

Spironolactone (50-200 mg/d)

Diet (no dairy, low GI) and weight loss

Finasteride

• Inhibitor of type II isomer of 5α-reductase, reducing levels of dihydrotestosterone in hair follicles

• Improved HS of 6/7 adults and 3 children

• Dose 5-10 mg/day

• Combine with OC in women (non-androgenic)

• Category X

TNFα inhibitors and ustekinumab

J Dermatolog Treat. 2006;16(2):75-78

HIDRADENITIS SUPPURATIVA: TREATMENT

Adalimumab:
Weekly dosing more effective than every 2 weeks

Infliximab:
5 mg/kg at 0, 2, 6, then every 8 weeks (psoriasis dosing)
5 mg/kg every 4 weeks (small series of 11 patients Hurley 3, failed 3 prior to, 9/11 well controlled on 0, 2, 4 then every 4; medial follow up 60 months; 4 patients secondary skin infections, 3 resp infections, 1 tonsillitis, 1 Hodgkin's lymphoma). Consider dosing used in IBD.

Acitretin: prospective series of 17 patients
0.56 +/- 0.8 mg/kg/d
47% improved more than 50%; 47% dropout rate


COSMETIC TREATMENTS
ThermiVa: Temperature controlled radio frequency treatment for vulvovaginal laxity
Same technology as ThermiTight, ThermiSmooth
3 treatments over 3 months
Cosmetic and functional outcomes improved
Pending approval in US