Update on Hidradenitis

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Nov 3, 2018
CSM 13th Annual Day in Dermatology for Family Physicians
Faculty/Presenter Disclosure

- **Faculty:** Connie Zhang

- **Relationships with financial sponsors:**
  - None to disclose

- No financial support or conflicts of interest to disclose
Disclosure of Financial Support

• This program has received financial support from:
  Abbvie, Actelion, Celgene, Cipher, Galderma,
  Hill Dermaceuticals Inc, InVentiv Health, Janssen, Leo,
  Novartis, Pfizer, Pierre Fabre, Sanofi Genzyme, Valeant
  in the form of unrestricted educational grants

• **Potential for conflict(s) of interest:**
  No conflicts of interest with pharmaceutical companies, pharmaceutical products or pharmaceutical companies providing unrestricted educational grants for this program.
Mitigating Potential Bias

• Whenever possible, generic drugs names will be used. However some trade names will be mentioned.

• Whenever possible, therapeutic suggestions will be evidence based. However, some therapeutics suggestions may be off label.
Pre-quiz

1. In a patient with HS, what systemic co-morbidities are important to monitor for?
2. What is the first-line topical treatment for mild disease?
3. What is the first-line systemic treatment?
4. What is the first drug specifically approved by the US FDA for the treatment of HS?
BACKGROUND
“The word boil provides cultural connotations that play a significant role in the perception of the disease – think of the bubonic plague or the Book of Job. Culturally and in all societies of man, boils are known examples of unclean, contagious signs of divine punishment.” – Gregor Jemec, MD, DMScI
“[HS] has historically been treated by a great number of different specialities, but owned by none: surgeons, emergency physicians, plastic surgeons, infectious disease specialists, general practitioners, and dermatologists.” – Gregor Jemec, MD, DMScI & Alexa Kimball, MD, MPH
Hidradenitis suppurativa – disease burden

- Pruritus
- Pain
- Discharge
- Substantial disability
- Social stigma
- Sexual health

- Depression
- Anxiety
- Diminished QoL
- Decreased work productivity
- Numerous medical co-morbidities
HS Epidemiology

- 0.05-4.10%
- Typically post-pubertal onset
- F:M 2-5:1
- Mean delay of diagnosis – 7.2 years
DIAGNOSIS
Hidradenitis suppurativa

• 3 criteria for diagnosis:
  1. Lesion morphology
  2. Distribution
  3. Chronic recurrent course
Hidradenitis suppurativa

• 3 criteria for diagnosis (modified Dessau def):
  1. Lesion morphology
     – Nodules, abscesses, tunnels, scars
  2. Distribution
     – Intertriginous folds
  3. Chronic recurrent course
     – 2 recurrences within 6 months OR
     – Persistent lesions for 3 months
A few more clues to diagnosis

• Family history
• Absence of pathogenic microbes on culture
• History of pilonidal sinus
• Non-characteristic lesions in typical locations
  – Eg folliculitis, open comedones
• Typical lesions in atypical locations
  – Eg pressure points on belt region of abdomen
1. Perifollicular inflammation

2. Hyperkeratinization of follicular epithelium with occlusion and dilation of the follicle

3. Follicular rupture and release of intrafollicular debris into the dermis with increased inflammation

4. Formation of tunnels (sinus tracts and fistulas) filled with debris and/or fluid that connect to the surface of the skin and to the base of other ruptured follicles.
Newer scoring systems

- mSS – modified Sartorius Score
- HS-PGA – HS-Physician’s Global Assessment
- HSSI – HS severity index
- HiSCR – Hidradenitis Suppurativa Clinical Response
HiSCR

- >50% reduction in inflammatory (transient) lesion count (sum of abscesses and nodules) and no increase in abscesses or draining fistulas (chronic inflamed lesions) when compared with baseline
HiSCR

• Responsive, clinically meaningful
• Test-retest reliability, convergent validity, responsiveness, predictive validity confirmed
• Validated against patient-reported outcomes
  – Pain, DLQI, work/activity impairment
• Correlated with improvements in Hurley stage, mSS, HS-PGA
COMORBIDITIES
The Comorbidity Burden of Hidradenitis Suppurativa in the United States: A Claims Data Analysis

Alexandra B. Kimball · Murali Sundaram · Genevieve Gauthier · Annie Guérin · Irina Pivneva · Rakesh Singh · Arijit Ganguli
US claims data analysis

- Retrospective matched cohort study
- Two severity cohorts (HS-mild and HS-severe) based on treatments received
- 5357 total patients with HS matched to HS-free controls
- Found that comorbidity burden increases with disease severity
Endocrine/metabolic disorders

• Obesity: 11.3% (HS-S) vs 2.6% (control)
• Diabetes: 19.2% (HS-S) vs 6.0% (control)
• PCOS: 2.0% (HS-S) vs 0.6% (control)
• HTN: 33.4% (HS-S) vs 17.4% (control)
• Dyslipidemia: 30.7% (HS-S) vs 18.7% (control)
• Thyroid disease: 12.0% (HS-S) vs 7.8% (control)
Other comorbidities

- Asthma: 9.8% (HS-S) vs 4.8% (control)
- Anemia: 11.1% (HS-S) vs 4.4% (control)
- Depression: 14.4% (HS-S) vs 7.2% (control)
- Anxiety: 9.2% (HS-S) vs 5.9% (control)
- Kidney disease: 3.1% (HS-S) vs 0.5% (control)
- Non-cutaneous cancers: 4.6% (HS-S) vs 2.1%
Yet more comorbidities (at least two-fold increase in prevalence)

- COPD
- Valvular disease
- Psychoses
- Substance abuse
- Sleep-wake disorders
- Fluid and electrolyte disorders
- Congestive heart failure
- Liver disease
- Peripheral vascular disorder
- Weight loss
- Other neurological disorders
Systemic associations of hidradenitis suppurativa

John J. Kohorst, MD, a Alexa B. Kimball, MD, MPH, b and Mark D. P. Davis, MD c

Rochester, Minnesota, and Boston, Massachusetts

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Literature review

• Most convincing association with obesity & the metabolic syndrome

• Other links not reported in US claims analysis:
  – Smoking – 40-92% rate of smoking in HS patients
  – Inflammatory bowel disease
  – Spondyloarthropathy, arthritis (HLA-B27 negative)
  – Pyoderma gangrenosum (PASH, PAPASH, PsAPASH)
  – SCC – 0.5-4.6% rate in HS – aggressive, ++ mets
MEDICAL THERAPY
Therapeutic goals

- Alleviate pain
- Minimize inflammation, scarring
- Prevent disease progression
- Delay the need for surgery
Traditional Framework

**Antibiotics**
- Tetracycline
- Rifampin-Clindamycin
- Dapsone
- Rifampin-Moxifloxacin-Metronidazole

**Retinoids**
- Acitretin
- Alitretinoin

**Anti-androgens**
- OCP
- EE/CPA & CPA
- Metformin
- Finasteride
- Spironolactone

**Immunosuppressants**
- Cyclosporine
- Corticosteroids

**Others**
- Zinc
- Fumarates
Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa

Wayne Gulliver \textsuperscript{1,2} · Christos C. Zouboulis \textsuperscript{1,3} · Errol Prens \textsuperscript{1,4} · Gregor B. E. Jemec \textsuperscript{1,5} · Thrasivoulos Tzellos \textsuperscript{1,6}
1. Diagnosis should be made by dermatologist or other healthcare professional with expert knowledge in HS.


3. Need for surgical intervention should be assessed and evidence-based surgical approach should be implemented.
European guidelines

4. Mild disease: **topical clindamycin 1% solution/gel BID** x 12 weeks **OR tetracycline 500mg PO BID** x 4 months

5. Mod-severe: **clindamycin 300mg PO BID + rifampicin 600mg PO OD** x 10 weeks

6. If no response: **adalimumab 40mg SC inj weekly**

7. If no response after 16 weeks: 2\textsuperscript{nd} or 3\textsuperscript{rd} line therapy
## European guidelines

### 2nd Line
- Zinc Gluconate: III, C
- Resorcinol: III, C
- Intraliesional Corticosteroids: IV, D
- Systemic Corticosteroids: IV, D
- Infliximab: Ib/IIa, B
- Acitretin/Etretinate: III, C

### 3rd Line
- Colchicine: IV, D
- Botulinum Toxin: IV, D
- Isotretinoin: IV, D
- Dapsone: IV, D
- Cyclosporine: IV, D
- Hormones: IV, D
**Hidradenitis Suppurativa**

**Advances in Diagnosis and Treatment**

Ditte Marie Lindhardt Saunte, MD, PhD; Gregor Borut Ernst Jemec, MD, DMSc

<table>
<thead>
<tr>
<th>Medical treatment</th>
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<tr>
<td><strong>First line</strong></td>
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<tr>
<td>Topical treatment</td>
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<tr>
<td>Clindamycin (1%) twice daily for 12 wk (GRADE B) or Resorcinol (15%) once daily; twice daily for flares as needed (GRADE C)</td>
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<td><strong>Second line</strong></td>
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<td>Miscellaneous treatment for individual lesions, such as intralesional triamcinolone (3-5 mg) once, then repeated monthly if necessary (GRADE C)</td>
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<td><strong>Third line</strong></td>
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<td>TNF-α inhibitor</td>
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<tr>
<td>Adalimumab for 12 wk followed by assessment (GRADE A) Loading doses</td>
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<td>Week 0 (160 mg subcutaneous) Week 2 (80 mg subcutaneous) Maintenance (40 mg subcutaneous) weekly or Infliximab (5 mg/kg intravenous) on weeks 0, 2, and 6, and then every 8 weeks thereafter (GRADE B) or Dapsone (25-200 mg) daily (GRADE C) or Acitretin (0.5 mg/kg) daily (GRADE C)</td>
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**Oral treatment**

| Tetracycline (500 mg) twice daily for 12 wk (GRADE B) or Doxycycline and minocycline (50-100 mg) twice daily (GRADE D) |

**Combination**

| Clindamycin (300 mg) twice daily Rifampicin (300 mg) twice daily |

**TNF-α inhibitor**

| Adalimumab for 12 wk followed by assessment (GRADE A) Loading doses |
| Week 0 (160 mg subcutaneous) Week 2 (80 mg subcutaneous) Maintenance (40 mg subcutaneous) weekly or Infliximab (5 mg/kg intravenous) on weeks 0, 2, and 6, and then every 8 weeks thereafter (GRADE B) or Dapsone (25-200 mg) daily (GRADE C) or Acitretin (0.5 mg/kg) daily (GRADE C) |

**Prednisone (40-60 mg) daily**

| for 3-4 days then taper (GRADE C) or Cyclosporine (3-5 mg/kg) daily (GRADE C) |

3rd line: anakinra (IL-1), ustekinumab (p40), dapsone, acitretin
Adalimumab

- Recombinant human IgG1 anti-TNF monoclonal antibody
- Blocks TNF-α
- FDA approval Sept 2015 – mod-severe HS
- PIONEER I, II, OLE
- Dosing: 160mg SC week 0, 80mg week 2, 40mg week 4 and weekly thereafter
PIONEER I & II

- Phase III multicenter, double-blind, randomized placebo-controlled trials
- PIONEER I (n=307), PIONEER II (n=326)
- Primary outcome: HiSCR-50 with no increase in abscess or fistula count from baseline, at week 12
  - 41.8% vs 26.0% in PIONEER I (P=0.003)
  - 58.9% vs 27.6% in PIONEER II (P<0.001)
PIONEER I & II

• Secondary outcomes:
  – Lesions – total abscess/nodule count of 0, 1, or 2
  – Pain – 30% and at least 1-unit reduction in 10-pt scale score
  – Modified Sartorius Score – change from baseline

• Significantly greater improvement in secondary outcomes in PIONEER II only

• Rate of serious adverse events similar between groups
INTEGRATED ANALYSIS

HiSCR Rate During Period 1 of PIONEER I & II Studies (NRI)


*Statistically significant with p-value less or equal to 0.05
A sustained response is seen through week 168 in 52.3% of patients treated with adalimumab, 40 mg weekly, with no additional safety issues identified.
Surgical & light-based therapies

- Incision & drainage
- Wide excision
- Local excision or tissue-saving methods
- Electrosurgery
- Cryosurgery
- Nd:YAG laser
- CO2 laser
- Intense pulsed light
- Photodynamic therapy
Pain management in patients with hidradenitis suppurativa

Barbara Horváth, MD, PhD, a Ineke C. Janse, MD, a and Gary R. Sibbald, MD, PhD b
Groningen, The Netherlands, and Mississauga, Ontario, Canada

1st line

• Topicals
  – Dressings, ice packs, diclofenac gel 1%, xylocaine ung 5%, ketamine 10%, bupivacaine 1%, doxepin 3%, gabapentin 6%
• Acetaminophen
• NSAIDs

2nd line

• Oral opiates
• Anticonvulsants
• SSRIs
• SNRIs
Post-quiz

1. In a patient with HS, what systemic co-morbidities are important to monitor for?
2. What is the first-line topical treatment for mild disease?
3. What is the first-line systemic treatment?
4. What is the first drug specifically approved by the US FDA for the treatment of HS?
Take Home Points

• Consider HS early on in the presentation of recurrent painful nodules and abscesses that scar, in the typical distribution of the intertriginous folds

• Be aware of systemic disease associations particularly the metabolic syndrome, hormonal disorders, and psychosocial sequelae

• In the management of HS, oral antibiotics are first-line among systemic therapies and biologics are supported by the highest-quality evidence; pain management is an important adjunct
References

January 2016

Safety and Efficacy of Anakinra in Severe Hidradenitis Suppurativa
A Randomized Clinical Trial

Vassiliki Tzanetakou, MD¹; Theodora Kanni, MD¹; Sophia Giatrakou, MD²; et al

Author Affiliations  |  Article Information

Anakinra

• Recombinant IL-1R antagonist – inhibits binding of IL-1α and IL-1β to receptors
• RCT of 20 patients – 100mg SC daily achieved HiSCR-50 of 30% of placebo group vs 78% of treatment group at the end of 12 weeks
November 2017

Canakinumab for Severe Hidradenitis Suppurativa Preliminary Experience in 2 Cases

Carine Houriet, MD1; S. Morteza Seyed Jafari, MD1; Rahel Thomi, PhD1; et al

» Author Affiliations  |  Article Information


A Before treatment  B After treatment
Ustekinumab in hidradenitis suppurativa: clinical results and a search for potential biomarkers in serum*

J.L. Blok✉, K. Li, C. Brodmerkel, P. Horvátovich, M.F. Jonkman, B. Horváth

Ustekinumab

• Human IgG1κ monoclonal antibody – binds p40 subunit of IL-12 and IL-23
• Prospective, uncontrolled, open-label study (n=17): 47% achieved HiSCR-50 at week 40, 82% had moderate to marked improvement of the mSS