Management of Severe Pediatric Psoriasis

Kelly M. Cordoro, M.D.
Associate Professor of Dermatology and Pediatrics
University of California, San Francisco

cordorok@derm.ucsf.edu
Disclosure

Consultant for Pfizer and Valeant Pharmaceuticals.

I will discuss off-label use of drugs to treat psoriasis in children.
Clinical images have been removed from this handout.

• Cases will be discussed in detail to emphasize the main learning points.

• The handout will not reflect the totality of those discussions.
Severe Psoriasis Patient Management

Assess for triggers
Evaluate for comorbidities
Choose therapy
Case Discussions.

12 year old male, severe guttate

18 year old female, severe guttate and plaque

9 year old male, erythrodermic
Severe Psoriasis Patient Management

- Assess for triggers
- Evaluate for comorbidities
- Choose therapy
Identifiable disease triggers are common in children.

- Infections: bacterial & viral
- Drugs: (steroid withdrawal)
- Stress: Social Stigma
Look for pharyngeal and peri-anal streptococcus. Treat with oral antibiotics if positive.

4 year-old boy with new onset guttate psoriasis.

- Family history (-)
- Throat culture (+)

Cleared with topical steroids and oral antibiotics. Still clear 4 years later.
12 y/o boy with waxing/waning guttate psoriasis since age 4.

Family history (+)  Throat culture (-)

Required systemic therapy.
Strep as a trigger may impart favorable prognosis.
(especially if negative FHx of psoriasis)

Preceding strep pharyngitis predicted guttate morphology and eventual resolution.
Ko et al. J Dermatol 2010

Preceding strep pharyngitis predicted guttate morphology but not severity.

Initial guttate morphology in absence of strep predicted progression to severe psor.
Mercy et al. Ped Derm 2013
Consider more aggressive monitoring and management of guttate psoriasis

-especially strep negative cases-

given risk of progression to severe disease.

Severe Psoriasis Patient Management

Assess for triggers

Evaluate for comorbidities

Choose therapy
Assessments

- QOL and CBI
- H&P ROS
- BMI
- Behaviors
- Joint Exam
- Bowel Symptoms

Pediatric Psoriasis
All Psoriasis Patients Aged 2-21

Annual

• Blood pressure
• BMI (body mass index)
• Arthritis screen
  – Joint pain / swelling / inflammation
  – Joint stiffness after rest or sleep
  – Limp
• Mood disorders screen
  – Anxiety, depression

Additional screening for DM, lipids, NAFLD as indicated based on weight, other risk factors.

Courtesy Emily Osier, MD on behalf of CSI.
Adolescent Psoriasis Patients

Every Visit

• Update history, exam, ROS

• Ask about QOL, social activities
  – Patient and caregiver

• Elicit high risk behaviors
  – Substance abuse
  – School truancy, etc

• Offer support/resources

Important to validate a teen’s cutaneous body image as a medical concern and not vanity.

Gupta MA and AK. Clin Dermat 2013

Tollefson MM et al. JAAD 2017
Identify patients at risk for metabolic syndrome.

* Severe psoriasis, overweight

Weight loss significantly reduces modifiable CV risk factors except microvascular endothelial function.

- Diastolic blood pressure
- Resting heart rate
- Total cholesterol
- Triglycerides and VLDL
- Plasma glucose
- HbA1c
- Tissue plasminogen activator inhibitor

Opportunity for early intervention/prevention.

Jensen Acta Derm-Ven 2014
Severe Psoriasis Patient Management

Assess for triggers
Evaluate for comorbidities
Choose therapy
Non-immunosuppressive

Phototherapy
Oral Retinoids

Immunosuppressive

Methotrexate*
Cyclosporine
Apremilast (PDE-4)

Biologics

TNF inhibitors**
IL12/23 inhibitors
IL-17 inhibitors

*MTX: most commonly used drug worldwide. (Bronkers et al. ‘17)

** TNF inhibitors: Most efficacy and safety data for pediatric psoriasis.

Paller et al. NEJM 2008
Paller et al. JAAD 2016
Papp et al. Lancet in press, 2017
Drug Approvals for Moderate-Severe Pediatric Plaque Psoriasis

Enbrel 2009: age 8 and above (EU), now reduced to age 6
- age 4 and above (US as of Nov 2016)

Humira 2015: age 4 and above (EU)

Stelara 2015: age 12 and above (EU)

Apremilast in US trials for pediatric patients age 6 and older.

Upcoming trials: Ustekinumab 6-12 years; Ixekizumab 12 and older.
Newer Biologic Therapy for Severe Pediatric Psoriasis

**IL12/23: ustekinumab**

- CADMUS- safe/effective in adolescents
  
  *(Landells et al. JAAD 2015)*

- Approved in 2015 in EU for patients 12 and older

**IL17: secukinumab**

- Case reports for GPP
  
  *(Böhner et al. JAMA Derm 2015)*

- Case report for DITRA
  
  *(Cordoro et al. JAMA Derm 2016)*
Case 1: 12 y/o male with waxing/waning guttate psoriasis since age 4.

**Evaluation:**
No strep. BMI healthy. BP normal. No arthritis or other comorbidities. Labs NL.
Rx Choices: NB-UVB, Retinoids, CSA, MTX, Biologic

Acitretin 0.3mg/kg/d + NB-UVB = Synergistic

Psoriasis cleared.

Taper acitretin 1st, then NB-UVB.

Kopp, Br J Dermatol. 2004
Key Points: Oral Retinoids for Severe Psoriasis

Guttate. Best combined with NB-UVB.

Teratogen- males. Non-immunosuppressive.

Dose-limiting SE: xerosis, cheilitis, PG.

LFT, lipids- reversible. HCG in females.

Potential bone toxicity if high dose/duration.

Dose: $< 1 \text{mg/kg/d}$.

Brecher and Orlow JAAD 2003.
Charbit et al. BJD 2015.
2 years later...

Severe flare, cleared on etanercept.

No strep -> bad prognosis?
Case 2: 18 y/o female with plaque psoriasis and recent guttate flare.

Evaluation: pharyngeal strep culture positive. BMI slightly elevated; BP and baseline labs normal.

Ideally: fast acting, gain control, taper off. Refused injections.

Rx: Cephalexin for strep. Cyclosporine 3mg/kg/day

On OCP.
Improvement pre and post 1 month s/p CSA 3mg/kg/day
Escalated dose to 5mg/kg/d. Clear and off drug 1 year later.
Key Points: Cyclosporine Therapy for Severe Psoriasis

Rapid onset of action. Used in all ages.

Rescue drug: control, taper to lowest effective dose.

AE: Kidney function, lipids, lytes, BP. Monitor closely.

Dose: 2-5mg/kg/day.

Total exposure < 1 year. 25% relapse after d/c.
She relapsed 1 year after discontinuing cyclosporine.

Shared decision making.

Prescribed apremilast; insurance denied.

Started adalimumab 2/17/17.
Case 3: 9 year old male with plaque -> erythrodermic psoriasis

Labs: ALT high initially then NL. PPD negative. No strep.
Choices: TNF-inhibitor due to severity, need for speed.

Adalimumab denied by insurance.

Rx: Methotrexate

5mg test dose, CBC in 6 days, escalate.
Moderate improvement
3 weeks later s/p 3 doses of MTX: 5mg test dose then 12.5mg/week
Key Points: Methotrexate for Severe Psoriasis

- Slower onset but sustained remission.
- #1 Rx in kids internationally.
- Baseline TB, vaccines. CBC, LFT- ongoing.
- 0.2-0.7mg/kg/wk po or SQ. Max 25/wk.
- Folate supplementation 1mg daily.

TNF-Inhibitors

Etanercept SQ: QW or BIW

Adalimumab SQ: every two weeks.

Infliximab IV: 0, 2, 6 then every 8 weeks.

Some continue MTX (5mg/week) to block antibody formation.

Key Points: Anti-TNF Therapy for Severe Psoriasis
Most Data Among All Biologics / Primary Place in Rx

Rapid onset. Less lab monitoring though little consensus.
Only required lab per PI is TB test.

AE: TB risk, injection site reaction, no lymphoma in ped pso to date.

Efficacy may wane over time: MTX to prevent HAHA and HACA.

Etanercept PI: 2016.
Key Messages: Comorbidities and W/U

**Best available evidence**: ped psoriasis associated with obesity, metabolic syndrome and psychosocial impairment.

**In absence of specific signs/sx**, evidence does not support lab screening beyond standardized age-based pediatric guidelines.

**Goal**: Identify at-risk patients, optimize physical and mental health to halt progression/prevent downstream effects.
Rx of guttate psoriasis: NB-UVB #1, + acitretin is synergistic. Look for strep to risk stratify and optimize treatment.

Severe Plaque: Treatment is individualized. No “one right answer”. Biologics becoming 1\textsuperscript{st} line. Shared decision making.
The Dermatology Foundation has supported & advanced my career.

www.pedraresearch.org