Baby Bumps: The Diagnosis and Management of the Pregnancy Dermatoses

Jenny Murase, MD

Palo Alto Foundation Medical Group
University of California, San Francisco
Disclosures

- Disease State Management Speaker
  - Regeneron (Atopic Dermatitis)
  - UCB (Psoriasis in Pregnancy)
- Advisory Board
  - Dermira
  - UCB
  - Genzyme/Sanofi
  - Eli Lilly
- Dermatologic Consulting
  - Ferndale
  - UpToDate
Objectives

- To develop a management algorithm to address pregnancy dermatoses
- To discuss impact of inflammatory dermatoses on pregnancy prognosis and therapeutic choice
# Pregnancy Dermatoses

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Atopic Eruption of Pregnancy

- Atopic diathesis (asthma, hayfever)
- 20% reported as a flare of AD; 80% reported as first manifestation of adult atopic dermatitis
- Most frequent pruritic condition in pregnancy
- Pathogenesis: Triggered by Th1→Th2 shift (estrogen)
Atopic Eruption of Pregnancy

- Presents earlier than PEP
- Classic atopic locations are involved (friction)
- High risk areas: nipple and hands
- Not associated with striae distensae
- Fetal prognosis unaffected
- No cutaneous involvement of the newborn
AEP Therapy

- Emolliation
- Antihistamines (prudent use in last month of pregnancy)
- Topical steroids (stay below 300 grams during pregnancy)
- Narrowband UVB therapy (folic acid supplementation)
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Polymorphic Eruption of Pregnancy

- Why not PUPPP? 50% polymorphous!
  - 17% tiny vesicles (1-2 mm)
  - 22% eczematous change
  - 6% target lesions or erythema
Polymorphic Eruption of Pregnancy

- Self-limited and benign, 3\textsuperscript{rd} trimester
- Associations: primigravidae, multiple gestations, excessive maternal weight gain
- Pathogenesis: abdominal distension?
- Elevated striae: Buttocks, abdomen, and thighs; then generalizes

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Intrahepatic Cholestasis of Pregnancy

- Genetic link: 0.02-2.4% general population
  [Scandinavia and S. America highest rate; 15%-28% Chile]
- Pruritus starts 3rd trimester
- No primary lesions!
- Bile acids may cross placenta!!!
  - Fetus at risk of prematurity (19-60%), stillbirth (1-2%), and fetal distress (22-33%)
Intrahepatic Cholestasis of Pregnancy

- Diagnosis based on lab findings
  - >11 µmol serum bile acid level diagnostic
  - + / - AST/ALT/GGT/bilirubin/AlkP

- Risk for bleeding complications!
  - Vitamin K deficiency in 10% of cases (for those with extrahepatitic cholestasis)
Intrahepatic Cholestasis of Pregnancy

- Ursodeoxycholic acid = naturally occurring, non-toxic bile acid
  - 15 mg/kg/day or 1 g/day
  - Possible side effect: mild diarrhea
  - Off-label use (only approved for PBC)

- Close ob surveillance (CTG monitoring 34 wks)

- Pruritus stops quickly; recurrence 45-70% future pregnancies
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Pemphigoid gestationis

- Vesiculobullous autoimmune disease
- Best studied (but most rare)
  - HLA DR3 & DR4 association
  - Onset 2nd tri/3rd: trophoblastic tumor assoc.
- Autoabs directed against placental matrix antigen (180 kDa BP-AG2 type XVII collagen): both skin and placenta epidermal in origin!
- Inflammation can occur in the placenta!! (this leads to placental insufficiency)
Direct immunofluorescence of perilesional skin: linear deposition of C3 at the DEJ

Indirect immunofluorescence on salt-split skin: deposition of C3 at the epidermal side of the artificial cleft

Ambros-Rudolph CM et al, JDDG 2006
Pemphigoid gestationis

- **Gold standard:** DIF
  - DIF: linear C3 deposition at BMZ (+ IgG 25-30%)
  - IIF: positive (30-100%)

- **Monitoring disease severity**
  - ELISA BP180 NC16a: positive 80-100%

Pemphigoid gestationis

- Risk for small-for-date babies and prematurity; 10% mild skin invol. 3-6 wks
- Pre-partum improve; postpartum flare 75%
- Self-limited; recurrence: menses, OCPs, future pregnancies
PG Treatment

- Prebullous: topical cortisones, antihistamines
- Bullous: 0.5-1 mg/kg/day prednisone
  - 1st trimester: increased risk for cleft palate (forms week 8-11); try to keep prednisone doses to 10-15 mg/day if possible
- Refractory: IV Ig, immunopheresis, azathioprine (preterm/low birth weight risk, halve the dose at 32 wks gestation if mother’s leukocyte count <1 SD below mean)
IV Ig

- IV Ig improves the chance of in vitro fertilization (antibody-mediated disease contributes to 10% of infertility cases)
- IgG crosses placenta around 32 wks
- Consider if requiring more than 20 mg of prednisone

A Case of Pemphigus Vulgaris in Pregnancy

- 1st pregnancy
  - Clobetasol and daily oral prednisone 40-60 mg
  - IV Ig started 26 wks gestation
  - Emergent C-section at 30 wks gestation (2 lbs)
  - HELLP (Hemolysis, Elevated LFTs, Low Platelet count), Gestational diabetes, Intrauterine growth retardation
A Case of Pemphigus Vulgaris in Pregnancy

- 2nd pregnancy
  - IV Ig every 4 weeks (20 g, 0.5 g/kg)
  - Completely discontinued steroid therapy
  - 38 wks gestation (4 lbs 11 oz)
Pruritus in Pregnancy

Algorithm modified from Figure 5
Ambros-Rudolph CM et al, JAAD 2006

Primary lesion?

No

ICP

Yes

Related to pregnancy?

Yes

Onset?

No

Starts on abdomen

First site of involvement?

Early onset

Limbs and trunk

3rd tri onset

PEP

AEP

DIF?

Umbilicus spared

No bullae; DIF negative

Scabies

Allergic contact dermatitis

Irritant contact dermatitis

Psoriasis

etc.

Umbilicus involved

Bullae; DIF positive
Psoriasis in Pregnancy

- Generalized pustular psoriasis (impetigo herpetiformis)
  - “The fifth dermatosis of pregnancy”
  - Often lack previous or family history of psoriasis
Pustular psoriasis of pregnancy

- Generalized pustular psoriasis (impetigo of preg)
- “5th dermatosis of pregnancy,” 3rd trimester, rare
- Often no previous or family history of psoriasis
- Hypocalcemia: seizures and tetany
- Begins in flexural areas, spreads centrifugally
- Can recur in future preg w/ increased severity
- Fetal prognosis less predictable despite therapy

Anti-TNF placental transfer

- Maternal antibodies transported across villi by neonatal Fc receptor to provide immunity to the newborn
- IgG increase from early 2nd tri until delivery; most during the third trimester
- Infant serum up to 7 mo
Biologic placental transfer

- Infliximab, adalimumab, ustekinumab are IgG monoclonal antibodies
  - Large hydrophilic protein, use Fc receptor
- Etanercept is fusion protein
  - Cross placenta by simple diffusion
  - Transferred less in 3rd tri: cord blood 4-7% (vs. IFX 160% and ADA 153% maternal levels)

Mervic L. Acta DermVen (2014)
Fatal case of infant death in mother taking infliximab during pregnancy

- Mother received infliximab every 8 wks (10 mg/kg) for Crohn’s
- Infant healthy until BCG vaccine given at 3 months of age
- Widespread eczematous dermatitis, head lag, poor weight gain
- Died at 4.5 months

Certolizumab is the only PEGylated anti-TNF without an Fc region; study of patients greater than 30 weeks pregnant

CZP levels were below (<0.032 microgram/ml) in 13/14 infant samples at birth; one infant minimal CZP level (infant/mother ratio 0.0009)

No safety signals
Take-home points

- **PG, ICP:** rare but have implications for the pregnancy prognosis (when in doubt, bile acids and DIF!)
- **PEP, AEP:** common, self-limited
- **Pustular psoriasis of pregnancy (5th dermatosis of pregnancy):** check calcium level!
- **Consider IVIG in PG/PV and TNF in PSO/PPP**
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