Pregnancy Dermatoses

Basic Dermatology Curriculum

Updated August 4, 2016
Goals and Objectives

- The purpose of this module is to help medical students develop a clinical approach to the evaluation and initial management of patients presenting with specific dermatoses of pregnancy.

- By completing this module, the learner will be able to:
  - Identify and describe the morphology of specific dermatoses of pregnancy
  - Know which dermatoses of pregnancy carry risks for the mother and the fetus
  - Explain basic principles in the diagnosis and treatment of specific pregnancy dermatoses
Pregnancy Dermatoses

There are four specific dermatoses of pregnancy, according to the most recent proposed classification:

1. Pemphigoid gestationis
2. Pruritic urticarial papules and plaques of pregnancy (PUPPP)
3. Atopic eruption of pregnancy
4. Intrahepatic cholestasis of pregnancy
Pregnancy Dermatoses

Each pregnancy dermatosis is distinct and carries different risks for the mother and the fetus.

A distinction must be made between dermatological diseases that happen to occur while the patient is pregnant versus specific dermatoses that occur only during pregnancy.

Pregnant patients with dermatologic conditions requiring treatment should be co-managed with their obstetrician.
Case One

Mrs. Smith
Case One: History

- Mrs. Smith is a 34-year-old woman who presents with a one-month history of a skin eruption.
- She is 23 weeks pregnant with her first child.
- She says that she first noticed the eruption after she swam in a lake. The rash started on her abdomen, appearing urticarial, and rapidly spread to her arms and legs. Her umbilical area is involved. No one else in her family who swam in the lake has this rash.
- The eruption is very pruritic and sometimes forms blisters.
- Treating with calamine lotion did not bring relief. The lesions continue to progress.
- She is otherwise healthy and is on prenatal multivitamins.
Case One: Skin Exam

![Image of skin rash]
Case One, Question 1

What is the most important piece of information in Mrs. Smith’s history?

a. She describes blisters
b. She is in her third trimester of pregnancy
c. The eruption started on her abdomen
d. The rash appeared after swimming in a lake
e. No one else has this rash
Case One, Question 1

Answer: a

What is the most important piece of information in Mrs. Smith’s history?

a. She describes blisters (this suggests a diagnosis of pemphigoid gestationis)

b. She is in her third trimester of pregnancy (actually she is in her second)

c. The eruption started on her abdomen (not a specific finding)

d. The rash appeared after swimming in a lake (not related)

e. No one else has this rash (true, but not diagnostic)
**Diagnosis: Pemphigoid gestationis**

- Autoimmune blistering disease
- Incidence: 1 in 10,000-50,000 pregnancies
- Starts in 2nd or 3rd trimester (mean onset = 21 weeks)
- Presents as pruritic urticarial papules and plaques/vesicles/bullae
- Involves the umbilicus in 50% of cases
- Also known as herpes gestationis
- May also occur in presence of choriocarcinoma and with hydatidiform mole
Case One, Question 2

What would be the next best step(s) in making a diagnosis?

a. Order serum IgE level
b. Skin biopsy for H&E
c. Skin biopsy for immunofluorescence (IF)
d. Skin biopsy for H&E and IF
e. Treatment trial of topical steroids
Answer: d

What would be the next best step(s) in making a diagnosis?

a. Order serum IgE level (not useful in this condition)
b. Skin biopsy for H&E
c. Skin biopsy for immunofluorescence (IF)
d. Skin biopsy for H&E and IF
e. Treatment trial of potent topical steroid cream (not diagnostic)
Pemphigoid gestationis

- Histopathology often helps with the diagnosis. H&E findings include a subepidermal blister containing predominantly eosinophils.
- Direct immunofluorescence provides a definitive diagnosis with findings of a linear band of C3 with +/- IgG at the basement membrane zone.
Mrs. Smith was diagnosed with pemphigoid gestationis based on her clinical picture, histopathology and immunofluorescence. Which of the following is the most appropriate treatment option?

a. Methotrexate
b. Mycophenolate mofetil
c. Oral steroid
d. Topical steroid
e. Minocycline
Answer: c

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a. Methotrexate
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c. Oral steroid
d. Topical steroid
e. Minocycline
Pemphigoid gestationis: Treatment

- Topical steroids can be helpful in mild disease.
- Patients with widespread disease should be referred to a dermatologist.
- With widespread disease, patients will often benefit from oral steroids.
- Patients with widespread disease should be co-managed with their OB physician.
Case One, Question 4

Mrs. Smith is worried about the implications for her child. Which of the following is a complication of pemphigoid gestationis?

a. Cleft lip and palate
b. Hydrops fetalis
c. Patent ductus arteriosus
d. Preterm delivery
e. There are no complications known
Answer: d

Which of the following is a complication of pemphigoid gestationis?

a. Cleft lip and palate
b. Hydrops fetalis
c. Patent ductus arteriosus
d. Preterm delivery
e. There are no complications known
Pemphigoid gestationis: Complications

- Risks include premature delivery, small-for-gestational age (SGA) infants, and a 5-10% risk of blisters in the neonate secondary to maternal transfer of antibodies.

- Pemphigoid gestationis carries a small risk of autoimmune thyroiditis for the mother.
Topical Steroid Use in Pregnancy

- Evidence-based: first choice for topical anti-inflammatory
- Well-tolerated in embryonic, fetal, and peripartal stages
- Mild to moderate strength cortisones should be preferentially used
- Always treat the smallest area indicated
- Chronic potent topical corticosteroids should be avoided if possible due to potential third trimester growth inhibition for fetus; use only short term if needed
- Topical steroid use has no increased risk of cleft lip/palate or preterm delivery
Oral Steroid Use in Pregnancy

- Avoid if possible
- If needed, always co-manage with OB
- Prednisone, a nonfluorinated form, is drug of choice.
- Keep dosing as low as possible
- Many potential complications:
  - increased cleft lip/palate incidence if given in first trimester
  - premature delivery
  - premature membrane rupture
  - small for gestational age (SGA)
  - gestational diabetes
  - hypertension, preeclampsia, and eclampsia
Pemphigoid gestationis: Prognosis

- There is often a flare at the time of delivery (75% of cases).
- Recurrence with later pregnancies is common.
- Pemphigoid gestationis can start postpartum (20% of cases).
- Recurrence with menses or OCP use has been reported but is rare.
Case Two

Mrs. Richards
Case Two: History

- Mrs. Richards is a healthy 28-year-old primigravid.
- She is in her 34th week of gestation.
- Two weeks ago, she developed an “itchy rash” on her abdomen; she feels that her striae are “bumpy.”
- She takes prenatal vitamins. She has not used any new topical products. She has not had weed or grass exposure. Her husband farms. No history of atopy.
Case Two: Skin Exam
Case Two, Question 1

What is the most likely diagnosis?

a. Allergic contact dermatitis
b. Atopic dermatitis
c. Pemphigoid gestationis
d. PUPPP (Pruritic urticarial papules and plaques of pregnancy)
e. Intrahepatic cholestasis of pregnancy
Case Two, Question 1

Answer: d

What is the most likely diagnosis?

a. Allergic contact dermatitis
b. Atopic dermatitis
c. Pemphigoid gestationis
d. PUPPP (Pruritic urticarial papules and plaques of pregnancy)
e. Intrahepatic cholestasis of pregnancy
Pruritic Urticarial Papules and Plaques of Pregnancy: PUPPP

- This is a case of pruritic urticarial papules and plaques of pregnancy (PUPPP)
- Common dermatosis of pregnancy
- Incidence: 1 in 300 pregnancies
- Onset during 3\textsuperscript{rd} trimester (mean = 35 weeks)
- Predominantly affects primigravids
PUPPP: Pathogenesis

The pathogenesis is unclear.

- One leading theory is abdominal wall distention, especially since PUPPP is more common in primigravids and multiple gestation pregnancies.
- Hormonal, immunological, and paternal factors may also play a role.
Case Two, Question 2

Which of the following is the most important physical exam finding?

a. Absence of blisters
b. Limited to the abdomen
c. Involvement of striae
d. Sparing of the umbilicus
e. Non-involvement of face
Case Two, Question 2

Answer: c

Which of the following is the most important physical exam finding?

a. Absence of blisters (helps to distinguish from pemphigoid gestationis, but in PUPPP blisters can occur)

b. Limited to the abdomen (PUPPP may spread beyond the abdomen)

c. **Involvement of striae** (unique to PUPPP)

d. Sparing of the umbilicus (Both PG and PUPPP can involve the umbilicus)

e. Non-involvement of face (not specific for PUPPP)
Typical lesions are erythematous urticarial papules surrounded by a pale halo.

In the vast majority of cases, the eruption starts within the abdominal striae (with periumbilical sparing) and progresses from there.

Less commonly, PUPPP can present with blisters and the umbilicus may be involved.
PUPPP: Evaluation

- The diagnosis is made based on the history and the clinical picture.
- A biopsy is rarely helpful in diagnosing PUPPP. It does, however, rule out pemphigoid gestationis, which is an important differential diagnosis.
  - If the patient has an atypical presentation or if you are concerned about pemphigoid gestationis, refer to a dermatologist.
  - A skin biopsy of PUPPP would reveal non-specific findings
Mrs. Richards heard of a friend who had PUPPP as well. Her friend’s baby was born prematurely. She asks you if you think there was a connection. What if any associations have been shown?

a. Low birth weight
b. Premature birth
c. Failure to thrive
d. Decreased Apgar score
e. No known associations
Case Two, Question 2

Answer: e
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a. Low birth weight
b. Premature birth
c. Failure to thrive
d. Low Apgar score
e. No known associations
PUPPP: Prognosis

- Has not been shown to have increased maternal or fetal risks
- Excellent prognosis
- Generally resolves within days postpartum
- No reports of recurrence postpartum, with menses, or with use of oral contraceptives
PUPPP: Treatment

- Therapeutic options are aimed at symptomatic relief:
  - Topical steroids
  - Oral prednisone
  - Non-sedating oral antihistamines
- If symptoms persist or worsen, refer to a dermatologist
- Treatment by or in conjunction with OB physician; communicate with newborn’s physician if mother is on or has been on oral steroids
# Pemphigoid gestationis vs PUPPP

<table>
<thead>
<tr>
<th></th>
<th>Pemphigoid gestationis</th>
<th>PUPPP: Pruritic urticarial papules and plaques of pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ONSET</td>
<td>Usually 2\textsuperscript{nd} trimester but can be 3\textsuperscript{rd} trimester or postpartum</td>
<td>Usually late 3\textsuperscript{rd} trimester</td>
</tr>
<tr>
<td>BLISTERS</td>
<td>common</td>
<td>rare</td>
</tr>
<tr>
<td>BIOPSY/IF</td>
<td>diagnostic</td>
<td>non-diagnostic</td>
</tr>
<tr>
<td>FETAL RISKS</td>
<td>SGA, preterm, blisters</td>
<td>none</td>
</tr>
<tr>
<td>RECURRENCE</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
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**American Academy of Dermatology**
Case Three

Ms. Wilson
Case Three: History

- Ms. Wilson presents with intense, non-remitting pruritus without primary skin lesions.
- States that the itching is worse at night
- She is G3P2. Both previous pregnancies were uncomplicated. She is in her 32nd week of gestation.
- She is healthy, except for a history of eczema as a child and well-controlled hypothyroidism.
Case Three, Question 1

Which of the following is the most likely cause of her pruritus?

a. Aquagenic pruritus
b. Atopic dermatitis
c. Hypothyroidism
d. Intrahepatic cholestasis of pregnancy
e. Scabies
Case Three, Question 1

Answer: d

Which of the following is the most likely cause of her pruritus?

a. Aquagenic pruritus
b. Atopic dermatitis
c. Hypothyroidism
d. Intrahepatic cholestasis of pregnancy
e. Scabies
Intrahepatic Cholestasis of Pregnancy: ICP

- Accounts for 20% of obstetric jaundice
- Presents with
  - Generalized pruritus +/- jaundice; less likely only palms and soles
  - Absence of primary lesions; may have secondary excoriations
  - Biochemical abnormalities consistent with cholestasis
  - No history of hepatitis or hepatotoxic drugs
Intrahepatic Cholestasis of Pregnancy: ICP Factors

• Increased levels of estrogen which inhibit reuptake of bile acids into hepatocytes and inhibit bile transport proteins
• Altered metabolism of progesterone
• Genetic factors
Case Three, Question 2

Which of the following is the most important abnormal finding in intrahepatic cholestasis of pregnancy?

a. Abnormal hepatobiliary ultrasound
b. Elevated bile acids
c. Elevated bilirubin
d. Elevated transaminases
e. Decreased transaminases
Case Three, Question 2

Answer: b

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a. Abnormal hepatobiliary ultrasound
b. Elevated bile acids
c. Elevated bilirubin
d. Elevated transaminases
e. Decreased transaminases
Intrahepatic cholestasis of pregnancy (ICP): Evaluation

• Although bilirubin, transaminases, and alkaline phosphatase may be elevated, the hallmark of ICP is elevation of serum bile acids.

• In late pregnancy, serum bile acids can be slightly elevated and not be problematic.
Which of the following is true?

a. ICP is a benign disorder and is self-limited in nature.
b. Patients with ICP need a liver biopsy.
c. The standard of care for ICP is Vitamin K supplementation.
d. Untreated ICP can lead to fetal distress and death.
e. Untreated ICP can lead to maternal death at delivery but has no increased risk for the fetus.
Case Three, Question 3

Answer: d

Which of the following is true?

a. ICP is a benign disorder and is self-limited in nature.

b. Patients with ICP need a liver biopsy.

c. The standard of care for ICP is Vitamin K supplementation.

d. **Untreated ICP can lead to fetal distress and death.**

e. Untreated ICP can lead to maternal death at delivery but has no increased risk for the fetus.
Intrahepatic Cholestasis of Pregnancy (ICP): Complications

- For the mother, risks associated with ICP include bleeding, intestinal malabsorption, and cholelithiasis.
- For the fetus, risks include prematurity, fetal distress, and death.
Intrahepatic Cholestasis of Pregnancy (ICP): Treatment

- Although ICP resolves after delivery, treatment should be started when the diagnosis is made.
- The intent of treatment is to decrease circulating bile acids.
- Vitamin K supplementation plays a role in management if bleeding parameters become abnormal.
The goal of treatment of ICP is to reduce symptoms and to prevent maternal and fetal complications.

- Most publications recommend early induction of labor, commonly at 37 to 38 weeks.
  - When cholestasis is severe, delivery is considered earlier if fetal lung maturity is established.
- Ursodeoxycholic acid
  - Considered 1st-line treatment
  - Randomized controlled trials (RCTs) demonstrate decreased pruritus and decreased serum bile acids
  - May decrease fetal mortality
Case Four

Ms. Campbell
Ms. Campbell is a 25-year-old woman who comes in for an itchy eruption that began three weeks ago.

Her lesions are lichenified papules, many of which are excoriated.

She is 22 weeks pregnant with her second child. Her previous pregnancy was unremarkable.

She is healthy and has no history of atopy.
Case Four: Skin Exam

[Image of skin examination]
Atopic eruption of pregnancy is a term that encompasses other pruritic inflammatory dermatoses which appear or worsen during pregnancy:

- Atopic dermatitis in pregnancy
- Prurigo of pregnancy (Besnier)
  - Prurigo = intensely itchy papules
- Pruritic folliculitis of pregnancy
  - Pruritic folliculitis = itchy inflammation around the hair follicle
Diagnosis: Atopic Eruption of Pregnancy (AEP)

- This is an example of an atopic eruption of pregnancy (prurigo type).
- Atopic eruption of pregnancy (AEP):
  - Eczematous in 2/3 and prurigo type in 1/3
  - Starts earlier in pregnancy (mean=18 weeks)
  - 80% of patients have a previous history of atopic dermatitis while 20% do not.
Atopic eruption of pregnancy

Journal of the American Academy of Dermatology 2006 54, 395-404
DOI: (10.1016/j.jaad.2005.12.012)
Atopic Eruption of Pregnancy (AEP)

- AEP is a clinical diagnosis.
- Histopathology is non-specific.
- Immunofluorescence is negative.
Ms. Campbell is worried that her baby will be affected by her condition of atopic eruption of pregnancy (AEP). What do you tell her?

a. She will need to be monitored as a high-risk pregnancy.

b. There have been reports of fetal distress in patients with AEP.

c. There is increased risk of small-for-gestational age births in AEP.

d. There is increased risk for birth defects in AEP.

e. There is no need to worry. Fetal distress is not increased in patients with AEP.
Case Four, Question 2

**Answer: e**

Ms. Campbell is worried that her baby will be affected by her condition of atopic eruption of pregnancy (AEP). What do you tell her?

a. She will need to be monitored as a high-risk pregnancy.
b. There have been reports of fetal distress in patients with AEP.
c. There is a risk of small-for-gestational age births in AEP.
d. There is increased risk of birth defects in AEP.
e. **There is no need to worry. Fetal distress is not increased in patients with AEP.**
Atopic Eruption of Pregnancy (AEP): Treatment

- AEP is a benign disease and does not carry increased maternal or fetal risks.
- Treatment is largely dependent on controlling the eruption with topical steroids.
- Oral steroids can be used in recalcitrant cases.
- If the eruption does not respond to topical steroids, referral to dermatology is recommended.
- Contact the patient’s OB if oral steroids are used.
- The eruption may persist after pregnancy as a chronic dermatitis.
Going back to our cases:
Review Question 1

Which disease is caused by specific antibodies?

a. Atopic eruption of pregnancy
b. Intrahepatic cholestasis of pregnancy
c. Pemphigoid gestationis
d. Pruritic urticarial papules and plaques of pregnancy
e. None of the above
Review Question 1

Answer: c

Which disease is caused by specific antibodies?

a. Atopic eruption of pregnancy
b. Intrahepatic cholestasis of pregnancy
c. **Pemphigoid gestationis**
d. Pruritic urticarial papules and plaques of pregnancy
e. None of the above
Review Question 2

Which of the following is true?

a. Atopic eruption of pregnancy only occurs in patients with a history of atopic dermatitis.

b. Intrahepatic cholestasis of pregnancy can have serious complications for both mother and child.

c. PUPPP and pemphigoid gestationis have identical findings on immunofluorescence.

d. There is a high risk of blisters in the neonate in pemphigoid gestationis.

e. None of the above are true
Answer: b

Which of the following is true?

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c. PUPPP and pemphigoid gestationis have identical findings on immunofluorescence.

d. There is a high risk of blisters in the neonate in pemphigoid gestationis.

e. None of the above
In Summary

- There are specific dermatoses that occur during pregnancy.
- While most dermatoses of pregnancy that occur are benign, there are instances when serious complications can arise.
- It is important to have a working knowledge of these pregnancy dermatoses to make a proper diagnosis to prevent maternal and fetal morbidity and mortality.
- Intrahepatic cholestasis of pregnancy does not have primary skin findings but carries great risk for mother and fetus.
- With topical steroid use, use the lowest potency and smallest amount which adequately treats the condition.
- Use oral steroid only if topical has failed or widespread involvement dictates for control.
- Refer to a dermatologist as indicated and always co-manage with the patient’s obstetrician.
Acknowledgements

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- Revisions and editing August 2016: Susan K. Ailor, MD, FAAD
End of the Module

To take the quiz, click on the following link:

https://www.aad.org/quiz/dermatoses-of-pregnancy-learners