Itchy rashes in pregnancy

An approach to diagnosis and management

Itch is a common symptom in pregnancy, affecting at least 17% of gravid women. Although many cases are due to common skin conditions coincidental to the pregnancy, the specific pregnancy-related dermatoses should always be considered.

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The skin undergoes many changes during pregnancy with the altered hormonal milieu. Increased pigmentation, increased hair growth, vascular instability and stretch marks are a few of the common physiological changes. In addition, a range of troublesome cutaneous eruptions may develop. Itch is a common symptom, affecting at least 17% of gravid women.[1]

This article reviews the main causes of itch and itchy rashes that occur in pregnancy (Table 1), and provides an approach to their diagnosis and management.

Itchy disorders coincidental to the pregnancy

Pregnant women are obviously susceptible to the same range of itchy rashes as nonpregnant women. Atopic eczema, scabies, pediculosis, pityriasis rosea, psoriasis, contact dermatitis, insect bites, urticaria, viral rashes, drug eruptions and iron deficiency are all causes of widespread itch. Candidiasis and trichomonal vaginitis are common causes of localised vaginal and perineal itch. There are a few important points to note about some of these conditions.

Scabies

The best treatment option for scabies in pregnancy is permethrin 5% cream (Lyclear, Quellada Scabies Treatment). A single eight-hour application has a 91% cure rate; this can be improved by a second application seven days later. Systemic absorption is minimal and there appears to be no increase in the fetal malformation rate.

Treatment of household members and other contacts of the patient is important to manage scabies effectively in pregnancy. This action will prevent re-infection of the pregnant woman and also protect the newborn child from contracting the infection.

IN SUMMARY

- **Atopic eruptions, including dermatitis, folliculitis and prurigo, are the most common itchy rashes in pregnancy.**
- **Polymorphic eruption of pregnancy is most common in primigravidas, women pregnant with twins, and women who gain excessive weight during pregnancy.**
- **Polymorphic eruption of pregnancy starts on the abdomen, in or near stretch marks.**
- **Intrahepatic cholestasis of pregnancy is strongly associated with an adverse fetal outcome.**
- **The hallmark of pemphigoid gestationis is a band of the complement component C3 along the dermoepidermal junction.**
- **Pemphigoid gestationis, intrahepatic cholestasis and generalised pustular psoriasis of pregnancy can all recur with subsequent pregnancies and with use of the oral contraceptive pill.**

continued

Table 1. Causes of itching in pregnancy

Itching coincidental to pregnancy

Atopic eczema
Psoriasis
Insect bites
Scabies
Pediculosis
Pityriasis rosea
Contact dermatitis
Urticaria
Viral rashes
Drug eruptions

Pregnancy-related itches

Atopic eruption of pregnancy
Polymorphic eruption of pregnancy
Pemphigoid gestationis
Intrahepatic cholestasis of pregnancy
Generalised pustular psoriasis

Table 2. Sedating antihistamines safe for use in pregnancy

Pheniramine (Avil)
Dexchlorpheniramine (Polaramine)
Cyproheptadine (Periactin)
Diphenhydramine (Snuzaid, Unisom Sleepgels)

Urticaria

Urticaria may be triggered in pregnancy by a viral infection, bacterial infection (such as a streptococcal throat infection or urinary tract infection) or drug or food allergy. It needs to be distinguished from some of the specific pregnancy-related dermatoses, which can have an urticarial component. Antihistamines are the mainstay of treatment for urticaria, with some of the older sedating antihistamines having a well established safety profile in pregnancy (Table 2). While there is less experience with the newer nonsedating antihistamines in pregnancy, a recent study has failed to show any increase in fetal malformation rate with loratadine (Alledine, Allereze, Claratyne, Lorapaed, Lorastyne).[2]

Viral rashes

Varicella is one of the itchiest viral infections and has potentially serious sequelae in pregnancy. Early in the first trimester varicella can cause severe fetal damage, including CNS defects, ocular defects and limb hypoplasia. The other dangerous period for a pregnant woman to develop varicella is from four days before to two days after delivery. From birth the neonate is no longer protected by maternal antibodies and would be at risk of developing severe varicella. Severe varicella has a 30% mortality rate in neonates, and prompt administration of aciclovir may be life saving.

Nonspecific rashes that are thought to be due to viral infections should be investigated with viral serology. Potential fetal complications of viral infections need to be kept in mind.

Iron deficiency

Iron deficiency is a cause of generalised pruritus without a rash. As iron requirements increase significantly in pregnancy, symptomatic iron deficiency can readily develop in patients with marginal iron stores.

Specific pregnancy-related itch disorders

Atopic eruption of pregnancy

Atopic eruption of pregnancy (AEP) is a term recently introduced to cover atopic dermatitis, prurigo of pregnancy and pruritic folliculitis of pregnancy.[3] Atopic dermatitis is the most frequent skin disorder in pregnancy, accounting for nearly 50% of all pregnancy-induced rashes. Its development is thought to be due to immunological changes that occur during pregnancy, which favour T-helper cell type 2 (Th2) driven diseases. The onset of AEP can occur at any stage of pregnancy: 36% of pregnant women develop skin lesions in the first trimester and 40% in the second trimester. Approximately 20% of patients have a history of atopic dermatitis prior to pregnancy that is exacerbated by pregnancy. The remaining patients have an atopic background but develop their first skin lesion during pregnancy.

Clinical features

Eczematous changes can affect all parts of the body, including the face, hands and feet. The appearance varies from typical flexural eczema to follicular and nonfollicular papules and prurigo lesions (excoriated papules and nodules).

Investigations

An elevated immunoglobulin E is noted in 71% of patients with AEP; however, for most patients AEP is a clinical diagnosis and laboratory investigations are not necessary.

Course

The development of AEP is unpredictable but prompt treatment may help prevent widespread dissemination.

Complications

There is no significant maternal or fetal risk associated with AEP. However, secondary staphylococcal infection should be recognised and treated prior to delivery to prevent spread of the bacterium to the neonate.

Treatment

Moisturisers and topical corticosteroids are the mainstay of treatment. Topical corticosteroids are generally thought to be safe in pregnancy, although one retrospective review claimed a slightly increased risk of cleft lip/palate.[4] It may, therefore, be prudent to minimise topical corticosteroid use in the first trimester.

Polymorphic eruption of pregnancy

Polymorphic eruption of pregnancy

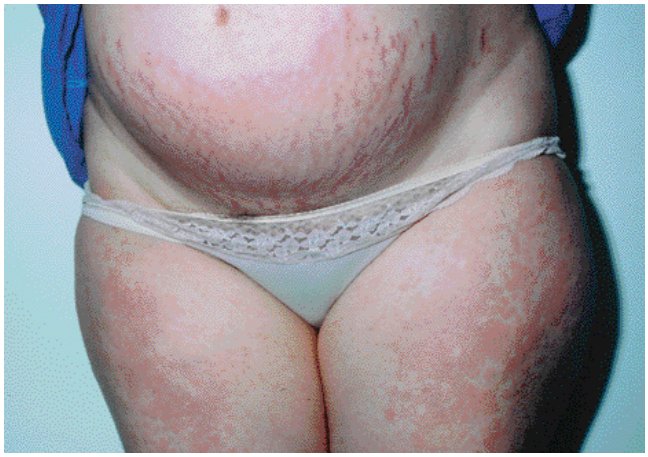

Figure 1. Polymorphic eruption of pregnancy (also called pruritic urticarial papules and plaques of pregnancy). Note the inflamed stretch marks.

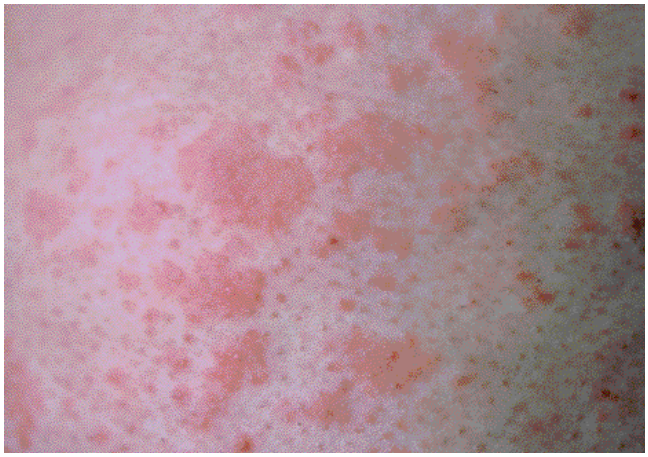

Figure 2. Erythematous papules coalesce to form urticarial plaques in polymorphic eruption of pregnancy.

(PEP), also called pruritic urticarial papules and plaques of pregnancy (PUPPP), is the second most common pregnancy-induced rash, occurring in approximately one in 160 pregnancies. It is an intensely itchy eruption that develops late in the third trimester (83%) or in the immediate postpartum period (15%).[5] Polymorphic eruption of pregnancy typically affects primigravidas and is more common in women with excessive weight gain or in those pregnant with twins. The precise cause is unknown, but rapid late abdominal wall distension with damage to connective tissue may be an important factor. Fetal DNA has also been isolated from cutaneous lesions of PEP, suggesting that fetal cells can migrate to the mother's skin during gestation and possibly induce inflammation.[6]

Clinical features

In nearly all cases, the itchy rash begins on the abdomen, sparing the immediate periumbilical area. There is a propensity for the rash to start within, or adjacent to, stretch marks (Figure 1). As the rash progresses, it spreads to the inner thighs, buttocks and arms, and rarely to the face, palms of the hand and soles of the feet. Erythematous papules of 1 to 2 mm diameter coalesce to form urticarial plaques (Figure 2). As the rash develops it becomes more polymorphic, with macular erythema, and targetoid and eczematous lesions. Vesicles are exceptionally rare, which distinguishes PEP from pemphigoid gestationis. Other differential diagnoses to consider include scabies, contact dermatitis, drug eruptions and viral exanthema.

Investigations

No investigations are required in classical cases of PEP. If necessary, a skin biopsy can be taken to exclude other diagnoses. The histopathology is fairly nonspecific, showing a superficial and mid-dermal perivascular lymphohistiocytic infiltrate with dermal oedema and scattered eosinophils. Direct immunofluorescence is always negative for linear C3 (third component of the complement system) and IgG along the dermoepidermal junction.

Course

The mean duration of PEP is four weeks. It resolves spontaneously within a few days of delivery and tends not to recur in subsequent pregnancies or with future use of hormonal preparations.

Complications

There are no fetal or maternal complications of PEP.

Treatment

Emollients, topical corticosteroids and oral antihistamines are the mainstays of treatment. Bland antipruritic preparations such as 0.5% menthol/0.5% phenol in aqueous cream are also helpful.

Pemphigoid gestationis

Pemphigoid gestationis, also called herpes gestationis, is a rare immunologically mediated bullous dermatosis that occurs in approximately one in 50,000 pregnancies. The aetiology is poorly understood, but IgG antibodies (the HG factor) are initiated in response to an antigenic stimulus that is peculiar to pregnancy. The antibodies are directed toward the 180 kDa bullous pemphigoid antigen present in the hemidesmosomes of the basement membrane zone. Once deposited at this site, these antibodies activate the complement cascade, which generates an inflammatory response and results in subepidermal blister formation.

Pemphigoid gestationis can also occur with trophoblastic tumours, hydatidiform moles and choriocarcinoma.

Clinical features

Pemphigoid gestationis is an extremely itchy disorder that usually begins in the third trimester but develops in the second

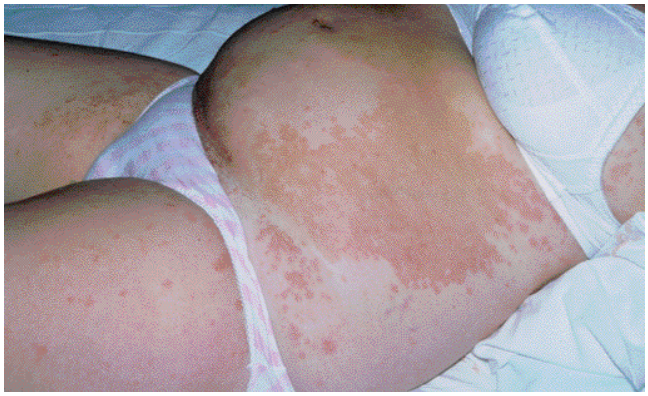

Figure 3. Pemphigoid gestationis starts in the periumbilical area and eventually spreads to involve the chest, back, extremities, palms of the hand and soles of the feet.

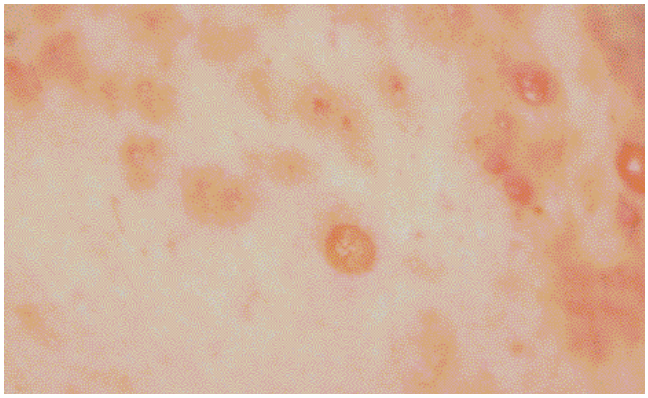

Figure 4. Tense bullae arising from urticarial plaques in pemphigoid gestationis. Grouped papulovesicles develop within erythematous or urticarial plaques and coalesce to form these large bullae.

trimester in just under one-third of cases.[3] The condition starts in the periumbilical area (Figure 3) and spreads to involve the chest, back, extremities, palms of the hand and soles of the feet. Grouped papulovesicles develop within erythematous or urticarial plaques, coalescing to form large bullae (Figure 4).

The main clinical differential diagnoses include bullous pemphigoid (very rare in women of childbearing age), PEP, erythema multiforme and dermatitis herpetiformis.

Investigations

A diagnosis of pemphigoid gestationis is confirmed with a perilesional skin biopsy taken for histopathology and direct immunofluorescence. The histopathology shows marked dermal papillary oedema with an inflammatory infiltrate consisting of eosinophils, lymphocytes and a few neutrophils. Direct immunofluorescence shows linear C3 (100%) and linear IgG (40%) along the basement membrane zone. Circulating IgG antibasement membrane zone antibodies can be detected in 25% of patients using indirect immunofluorescence.

Course

Pemphigoid gestationis often flares up at the time of delivery or immediately postpartum. The condition settles a few days or weeks after delivery but recurs in subsequent pregnancies. It may also be triggered by hormonal preparations such as the oral contraceptive pill.

Complications

There has been some controversy about the potential risks to the fetus of pemphigoid gestationis. The most recent studies show there is a tendency for premature delivery and a trend for small neonates (based on their gestational age), but there is no increase in spontaneous abortions or stillbirths.[7] Transient blistering may occur in the neonate due to the transplacental passage of antibodies; this settles spontaneously.

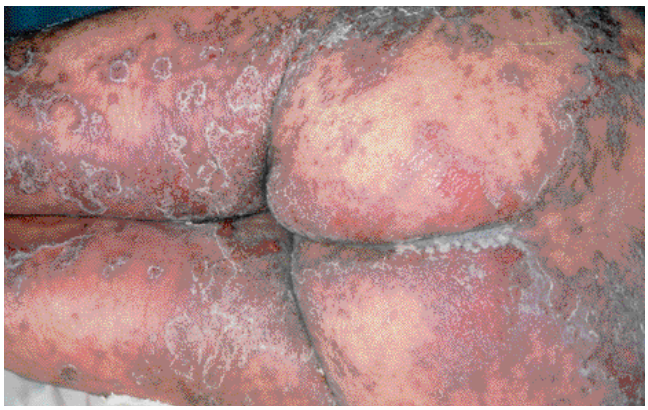

Figure 5. Severe generalised pustular psoriasis of pregnancy that has progressed to total body involvement.

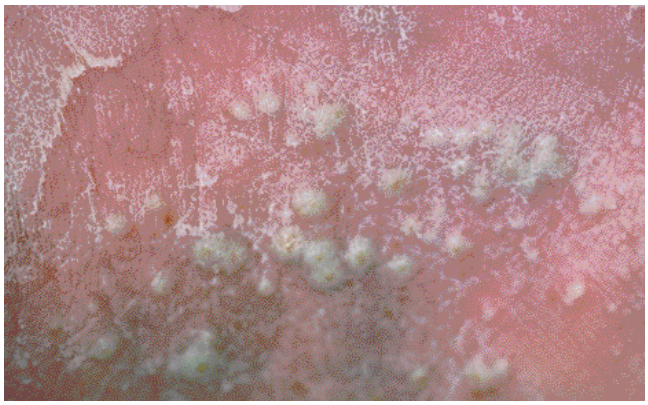

Figure 6. Sterile pustules are a clinical feature of generalised pustular psoriasis of pregnancy.

Treatment

In mild cases, topical corticosteroids and antihistamines may be enough to settle symptoms of pemphigoid gestationis. In more severe cases, 20 to 40 mg/day of prednisolone (Panafcortelone, Solone, Predsolone) may be required.

Intrahepatic cholestasis of pregnancy

Intrahepatic cholestasis of pregnancy (ICP) is a genetically linked, hormonally induced, reversible cholestasis that occurs in 0.02 to 2.4% of pregnancies.

Clinical features

Pruritus is the main symptom and usually develops in the third trimester of pregnancy. It may be localised at first, but gradually becomes more generalised, severe and persistent, resulting in widespread excoriations.

After two to four weeks jaundice develops, although patients with low grade cholestasis may remain anicteric. Accompanying symptoms include anorexia, fatigue, nausea, vomiting and right upper quadrant discomfort. Pale stools and dark urine may also be noted. The main differential diagnoses to consider are acute fatty liver of pregnancy and infectious hepatitis.

Investigations

Liver function tests may be normal at first, but eventually they reveal elevated bilirubin, alkaline phosphatase and gamma-glutamyl transferase levels. Transaminase levels are normal or slightly elevated. Elevated total serum bile acid levels are diagnostic.

Course

The pruritus subsides within a few days of delivery. It tends to recur in subsequent pregnancies and may also be precipitated by oral contraceptives.

Complications

There is an increased incidence of premature births (20 to 60%), intrapartal fetal distress (20 to 30%), stillbirths (1 to 2%) and low birthweight in the neonates of women with ICP, particularly when the pruritus and jaundice have been severe. These adverse effects on the baby are due to placental anoxia that is caused by decreased fetal elimination of toxic bile acids.[8]

Treatment

The treatment of choice is ursodeoxycholic acid (Ursofalk).

Generalised pustular psoriasis of pregnancy

Generalised pustular psoriasis of pregnancy (GPPP), also called impetigo herpetiformis, is a rare explosive form of pustular psoriasis that generally develops in women with no personal or family history of psoriasis. Some cases appear to be related to the development of hypocalcaemia in women who have mild hypoparathyroidism.

Clinical features

GPPP is a mildly pruritic disorder that usually develops during the third trimester of pregnancy (Figure 5). Erythematous patches develop in flexural areas, notably the groin, axillae and neck. At the margins of these peripherally expanding patches are tiny sterile pustules (Figure 6). Gradually, large areas of the body may become involved and secondary bacterial infection may occur. Most patients are systemically unwell and may develop fever, rigors, nausea, vomiting, dehydration and renal failure.

Investigations

A skin biopsy from women with GPPP shows features of pustular psoriasis with collections of neutrophils in spongiotic foci in the epidermis and subcorneal region.

Course

GPPP remits promptly after delivery but may recur in subsequent pregnancies.

An approach to the pregnant woman with itch

History

Note the following:

- duration of itch and gestational period when itch began
- distribution and nature of any rash present
- associated systemic symptoms
- previous skin, medical and obstetrical problems (e.g. atopic patient, history of rashes during previous pregnancies)
- family history (e.g. atopy, liver problems, other family members with itch)
- medications and allergies.

Skin examination

Determine:

- whether the patient has a rash or just excoriations
- the location of the rash (trunk, limbs)
- the appearance of the rash (i.e. eczematous, papular, urticarial, blistering or pustular).

Refer to the flowchart on page 40.

Investigations

Consider:

- skin biopsy with direct immunofluorescence
- liver function tests
- iron studies
- microscopy and culture of any pustules present.

Treatment

Remember:

- always consider the potential effects of prescribed topical or systemic medications on the fetus
- if the diagnosis indicates the fetus is at increased risk, institute antenatal monitoring
- counsel the patient about the risk of recurrence of the rash in future pregnancies or with the use of the oral contraceptive pill.

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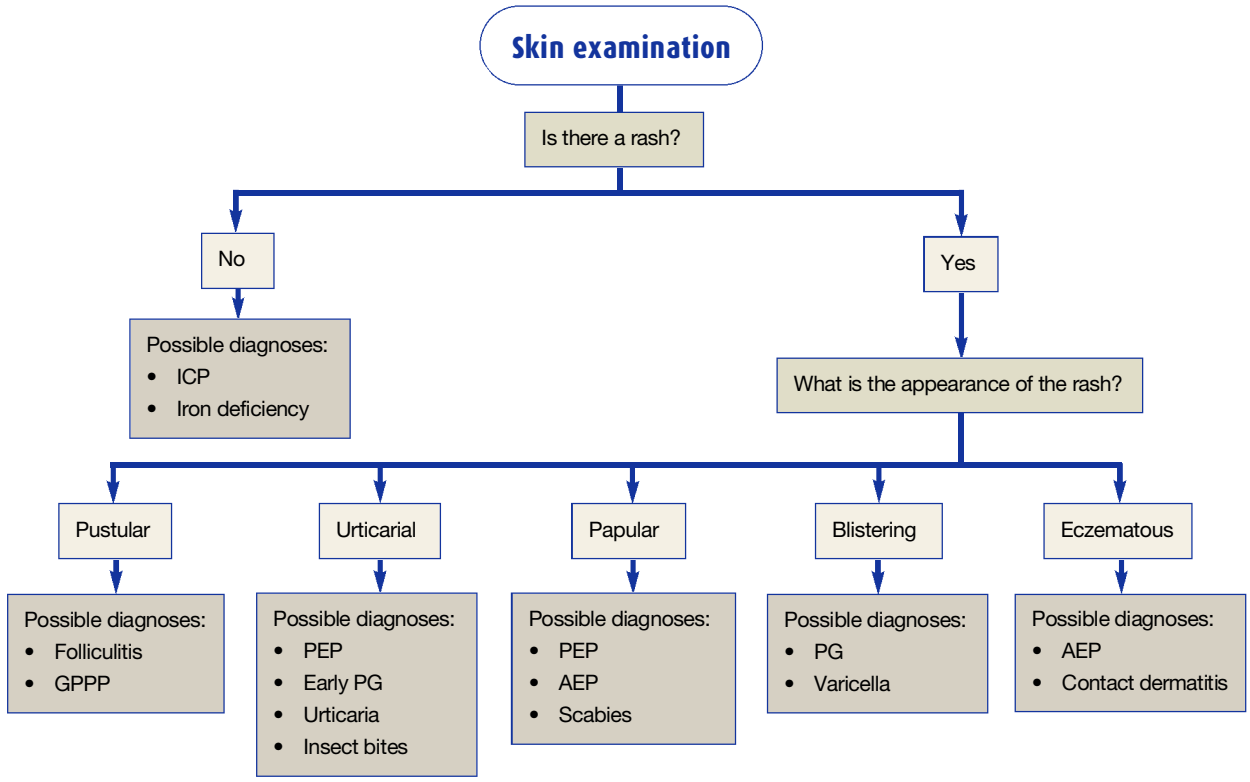
Skin examination in a pregnant woman with itch



Abbreviations: ICP = intrahepatic cholestasis of pregnancy; GPPP = generalised pustular psoriasis of pregnancy; PEP = polymorphic eruption of pregnancy; PG = pemphigoid gestationis; AEP = atopic eruption of pregnancy.

Complications

In severe cases of GPPP fetal morbidity and mortality are increased, but this should be ameliorated by good general medical care.

Treatment

Admission to hospital is nearly always warranted for women with GPPP. Prednisolone (40 to 60 mg/ day) is the treatment of choice but must be accompanied by good supportive care and antenatal monitoring. Calcium supplements may be required in hypocalcaemic patients.

Summary

When a pregnant woman presents with itch, the approach outlined in the box on page 39 and in the flowchart on this page is suggested. MT

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