

Cutaneous manifestations in pregnant women

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Abstract

During pregnancy, various cutaneous manifestations of physiological or pathological nature can develop from hormonal, metabolic or immunologic changes which occur during this period. The physiological manifestations can include pigmentation, vascular manifestations, hair, nail modifications and structural modifications of the skin. Pathological manifestations can include dermatoses which occur for the first time during pregnancy and pre-existing dermatoses which worsen or improve during pregnancy.

Keywords: pregnancy dermatoses, physiologic changes, pigmentary features, hormonal changes

I. Physiological cutaneous modifications

I.1. Pigmented lesions which can occur physiologically during pregnancy are: melasma gravidarum, hyperpigmentation of the linea alba, hyperpigmentation of the areolae and nipples, pigmentation of existing melanocitary structures⁽¹⁾. The pigmentation of the linea alba, the nipples and areolae, and sometimes of the inguinal and axillary regions occurs early in pregnancy. The linea alba thus becomes the linea nigra and secondary areolae can appear. These modifications disappear slowly after birth, but in some cases the color does not completely return to the original⁽²⁾. The melasma is a pregnancy-specific pigmentation, caused by estrogen excess. Also known as the 'mask of pregnancy', it can also occur during the use of oral contraceptives. More obvious in women with darker skin tones, on topographical areas such as the forehead, cheeks or upper lip, this hyperpigmentation is worsened by exposure to ultraviolet radiations. This unpleasant hyperpigmentation occurs in the second trimester of pregnancy, and it disappears within approximately one year postpartum. If it persists, there are numerous efficient treatments (i.e. depigmentation with topical solutions, chemical peelings, and laser therapy)⁽³⁾.

I.2. Vascular lesions: palmar erythema, spider angiomas, tumours (i.e. pyogenic granuloma, glomeric tumours), varicose veins, and cutis marmorata. Palmar erythema occurs in the first trimester and disappears after birth, being caused by estrogen excess. Spider angiomas occur especially in the first part of the pregnancy, in the upper body regions (i.e. face, and upper limbs) and usually disappear postpartum. The persistent angiomas can be successfully eliminated by non-ablative laser therapy. Modifications of naevic lesions which refers to the darkening of these lesions, the growth of new naevi or the increase of the size of pre-existing ones. Such modifications can also occur in case of ephelides. The role of estrogen in the occurrence of melanoma is not yet known precisely, thus such pigmented lesions should be closely monitored⁽⁴⁾. Varicose veins affect over one third of pregnant women, being an extremely unpleasant problem. Varicose vein dilations can occur on the lower limbs, rectum or vagina and are caused by increased intra-abdominal pressure and hormonal changes. They rarely persist after birth, the persisting ones requiring sclerotherapy. In

most cases, they disappear after birth, but can recur in future pregnancies. Cutis marmorata is a temporary coloring which can occur in certain cases, in cold weather, due to the vasomotor imbalance caused by estrogen excess. It affects lower limbs. Pyogenic granuloma is a red to purple tumour formation occurring frequently after traumas and is located on the face, mucosae and extremities (i.e. calf and fingers). The formation, consisting of vascular tissue, is smooth at palpation and sometimes covered by crusts⁽⁵⁾.

I.3. Skin and nail modifications: hirsutism, telogen effluvium, nail modifications. Hirsutism is described as the presence of hair follicles in anatomical regions where they do not occur normally. It can occur on the face and arms, developing early in pregnancy and disappearing about 6 months postpartum. Telogen effluvium is also a result of pregnancy, consisting of heavy and unabated hair loss, which is, however, reversible and temporary (telogen phase)⁽⁶⁾. Nail modifications during this period involve increased fragility, with the presence of distal onycholysis and sub-ungual hyperkeratosis. On the other hand, an accelerated growth of the nails is observed.

I.4. Structural modifications of the skin: striae gravidarum, molluscum fibrosum gravidarum. Molluscum fibrosum occurs frequently during pregnancy and is a fibroma of the soft tissue, hyperpigmented or of skin colour, measuring up to several centimetres in diameter. Treatment consists in ablative laser therapy, cryotherapy or electric cauterisation⁽⁷⁾. Pregnancy stretch marks (i.e. striae gravidarum) occur very frequently during pregnancy on the abdomen, breasts, buttocks, thighs, upper limbs⁽⁸⁾. Apparently, they are related mostly to genetic factors than to weight gain (Figure 1).

II. Specific pregnancy dermatoses

These are conditions which appear de novo during pregnancy and can be categorized as follows: atopic eruption of pregnancy, intrahepatic cholestasis of pregnancy, pemphigoid gestationis, polymorphic eruption of pregnancy, and pruritic folliculitis of pregnancy.

II.1. Atopic eruption of pregnancy or prurigo gestationis Besnier, is by far the most frequent skin condition of pregnancy. This is a rash formed of erythematous, pruritic papules, laid out symmetrically on the torso and limb

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Figure 1. Structural modifications of the skin by genetic factors (personal collection)

extension areas. The skin is extremely dry. It occurs in the second trimester of pregnancy, sometimes even in the first trimester, and is often mistaken for scabies. However, it does not respond to specific antiparasitic treatment. It is believed to be associated with atopy, as in many pregnant women, an increased number of immunoglobulins G can be noted. In 20% of the cases, the patients have pre-existing atopic dermatitis which worsens during pregnancy, sometimes even suffering from erythrodermia. Treatment consists of systemic antihistamines and topical dermatocorticoids⁽⁹⁾.

II.2. Intrahepatic cholestasis of pregnancy has unclear aetiology, but genetic predisposition to cholestasis, as well as hormonal changes during pregnancy seem to be important. It occurs in the second or third trimester and is manifested by intense pruritus and jaundice. No cutaneous manifestations occur initially, but secondary manifestations can develop, such as excoriations caused by scratching and nodules. Pruritus occurs first on the palms and soles. It disappears after birth, but it can recur if using oral contraceptives. Haemorrhages can occur due to vitamin K deficit. It can affect the foetus and can lead to premature birth or foetal death. Lab tests show increased levels of bile acids, bilirubin and AST. Treatment can be symptomatic cholestyramine, and pathogenic ursodeoxycholic acid⁽¹⁰⁾.

II.3. Pemphigoid gestationis, also known as herpes gestationis, usually it is not related to the herpes virus. It is a bullous condition which occurs late in pregnancy, being associated with the productions of IgG autoantibodies. It shows high genetic determinism. Also, the placenta seems to play an important role. It is clinically characterized by a highly pruritic rash formed of vesicles, bullae and erythematous-papular lesions similar to urticarial ones, located on the abdomen, palms and soles. It can also be associated with other autoimmune disorders: Hashimoto's thyroiditis, Graves' disease, pernicious anaemia. Diagnosis is made by direct immunofluorescence or by serum detection of auto-

antibodies by indirect immunofluorescence. This disorder is risky, because it predisposes to premature birth and the development of a product of conception with a small weight as compared to the gestational age. Treatment is aimed at diminishing pruritus and preventing the formation of new bullae. Small dose glucocorticoids are used: prednisone 20-60 mg/day⁽³⁾.

II.4. Polymorphic eruption of pregnancy occurs mostly in primiparous women, in the third trimester. Sometimes it occurs right in the last days of pregnancy. Etiology is unknown, but it seems that it involves the destruction of conjunctive tissue through abdominal distention or due to foetal antigens. It is clinically manifested through an eruption formed of erythematous papules which evolve into urticarial plaques of pregnancy located on the buttocks, abdomen, and thighs and rarely on the breasts, face and palms. It includes longitudinal striae, which are characteristic for this condition. The umbilical area is usually not affected. The eruption can become generalized. Immune tolerance during the following pregnancies prevents recurrences. This condition is self-limiting, only very rarely requiring treatment to alleviate pruritus, high-potency topical corticosteroids⁽⁵⁾.

II.5. Pruritic folliculitis of pregnancy develops usually during the second half of the pregnancy. It is characterized by a histopathological aspect which shows follicular impact. Clinically, it develops as a papular-follicular eruption. This condition resolves spontaneously, after several weeks from birth. The treatment is the same as for mild cases of acne (requiring no antibiotics): benzoyl peroxide 10% and hydrocortisone acetate 1%⁽⁵⁾.

III. Dermatoses which modify during pregnancy

Many dermatological conditions are modified during pregnancy, either improving or worsening. The best example of a condition which improves during pregnancy is

psoriasis. On the other hand, lupus erythematosus can worsen.

III.1. Psoriasis is the typical example of a condition whose evolution is improved during pregnancy and worsened after birth. Psoriasis is a cutaneous inflammatory disease clinically characterised by the development of erythematous-squamous papules and plaques, with pearled squames, with various locations. The factors involved in the physiopathology of psoriasis are genetic predisposition, environmental factors, central nervous system and immunological factors (natural and acquired immunity). Dendritic cells lose tolerance and activate T cells, which will produce cytokines and pro-inflammatory molecules (i.e. eicosanoids). In the development of psoriasis, it seems that the succession of the events is as follows: in a person with genetic predisposition, at a given time, an aggressive factor such as stress, infections or certain medications can trigger the eruption. The evolution is characterised by remissions and recurrences of the lesions. About 40% of the psoriasis cases also cause articular problems like arthropathic psoriasis, characterised by enthesitis, involvement of distal interphalangeal articulations, spondylarthritis, sacroiliitis⁽¹¹⁾. Psoriasis usually improves during pregnancy in a large number of cases. Worsening or lack of improvement is seen in all other cases. Treatment is made with topical preparations, attempting to avoid systemic therapy. Topical dermatocorticoids are usually used. In severe cases, a short cycle of cyclosporins can be attempted.

III.2. Erythema nodosum is a condition which can be worsened by pregnancy. Clinical aspect involves erythematous nodules occurring on the front of the shins. Evolution lasts several months. Nodules are painful spontaneously and at palpation. The incriminating factors triggering this disease are infections and various medications, also including oral contraceptives. It was thus concluded that hormonal factors are important in triggering the disease. It can occur in the first or second trimester of pregnancy, and can be treated with non-steroidal anti-inflammatories. In the third trimester of pregnancy, these drugs can no longer be used safely⁽⁶⁾.

III.3. Lupus erythematosus is usually worsened during pregnancy and in the weeks or month following birth. The disease can also occur at that time. This is one of the most frequent inflammatory conditions affecting women of reproductive age. There is a 10% risk of miscarriage due to this disease⁽¹²⁾. If the disease debuts in the first trimester of pregnancy, the reason for miscarriage are the active disease; if the disease is triggered later in pregnancy, it will impact on the pregnancy due to the antiphospholipid antibody syndrome, despite heparin or aspirin treatment. Another risk is that of premature birth due to preeclampsia, premature rupture of membranes, high doses of prednisone, kidney disease. All pregnant women suffering from lupus should be tested for antiphospholipid syndrome. For the mother, the highest risk is that of kidney or hematologic anomalies and lupus arthritis. 3% of children born to mothers suffering from lupus will develop neonatal lupus^(6,12). This form of lupus is manifested through temporary eruption and hematologic anomalies. Most times, this condition resolves by the time the child is 3-6 months old and will not recur. It is characterised by the presence of anti-Ro antibodies. A major risk

for these children is atrioventricular block or other heart anomalies, which occur in half of the children with neonatal lupus. This heart anomaly is permanent, and if occurring, it requires the insertion of a pace-maker. Lupus treatment in pregnant women can be performed with prednisone, hydroxychloroquine, azathioprine⁽¹²⁾.

III.4. Systemic scleroderma is an inflammatory condition which can interfere with pregnancy. The major risk is that of cardiovascular or renal complications which can occur early in the disease's development. If the condition develops in a woman who wishes to get pregnant, it is recommended to postpone the pregnancy as much as possible until the disease is stabilised. A pregnancy occurred during the most aggressive period of the disease requires very careful monitoring, especially regarding kidney function. The most severe complication is acute renal failure with signs of preeclampsia in the third trimester. Treatment must be fast, aggressive, with angiotensin converting enzyme inhibitors. There is a major risk for the mother's death or miscarriage, premature birth or birth of a small for date infant.

III.5. Dermatomyositis is rare during pregnancy. However, two types of this disease were described associated with pregnancy. The first type is characterised by worsening during pregnancy and improvement after birth. The second type debuts in the postpartum period. The risk given by this condition is foetal death or prematurity. Clinical aspect in pregnant women is non-specific, usually producing fatigue and peri-ungual erythema. Treatment is recommended to be performed with immunoglobulins, evolution being favourable (both mother and foetus). Corticotherapy can also be administered, but side effects can be strong, especially during pregnancy⁽¹³⁾.

III.6. Acne during pregnancy can improve or worsen. It can be mild, moderate or severe, the main incriminating factor being hormonal, androgenic hormones. A high androgen level is responsible for the acne outbreaks developing at any time during pregnancy. Most times, pregnancy acne resolves spontaneously several months before or after birth. The treatment considered safe in pregnancy includes azelaic acid, salicylic acid in low concentrations, benzoyl peroxide, erythromycin. Other treatments effective against acne have teratogenic effects and should be avoided: isotretinoin, topical retinoids, tetracycline and its derivatives, doxycycline and minocycline.

III.7. Pemphigus vulgaris is an autoimmune condition characterised by the presence of autoantibodies against desmoglein-1 and 3. It is clinically manifested by the development of bullae on the skin and mucosae. This condition can worsen during pregnancy, and treatment is difficult to administer due to the high corticoid doses required and to the severe side effects. A better and safer treatment includes immunoglobulins⁽¹⁴⁾.

III.8. Infections with herpes simplex virus are usually more severe during pregnancy. This is not usually the first infection, but it can be the first time when clinical manifestations occur, as the virus is in an asymptomatic, latent stage. There is a 30% risk for transmission to the new-born during birth, therefore C-section is recommended for pregnant women infected with herpes virus.



Figure 2. Infection of the skin with HPV in pregnant women (personal collection)

Treatment is performed with acyclovir, considered safe during pregnancy⁽¹⁵⁾.

III.9. Infections with HPV during pregnancy can produce condylomata acuminata which grow rapidly, particularly during weeks 12 to 24 (Figure 2). They bleed very easily. Most of the times, they require delivery by C-section. Treatment can be performed with trichloroacetic acid, cryotherapy, cauterisation, vaporisation with ablative laser or pulsed dye laser^(15,16).

III.10. Yeast infections are a common type of vaginal infection that is particularly common in pregnant women. These infections are produced most frequently by *Candida albicans*. During pregnancy, the higher level of estrogen causes vagina to produce more glycogen, making it even easier for yeast to grow there. Some researchers consider that estrogen may also have a direct effect on yeast, causing it to grow faster and stick more easily to the walls of the vagina. As a general rule, during pregnancy it is best to use drugs as less as possible or none at all. Drugs strictly prohibited during

pregnancy are, among others: retinoids, estrogens, danazol, finasteride, thalidomide, methotrexate. Other drugs which can have adverse effects and should be avoided: non-steroidal anti-inflammatories, azathioprine, cyclophosphamide, colchicine. If they are necessary, however, topical versions are preferred rather than systemic ones. If systemic versions are required, oral administration is advisable.

Conclusions

In this present paper we showed the most important physiologic changes that appear during pregnancy and some of the pathological aspects. In pregnancy period may develop many immunologic, hormonal and metabolic reactions and some of these can lead to cutaneous disorders named the dermatoses of pregnancy. We tried to reveal the most significant aspects of these disorders and the available therapeutic options accessible at this moment all around. Unfortunately, their precise pathogenesis is still unknown, but we are very optimistic about the power of modern treatment options. ■

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