MANAGEMENT OF PSORIASIS DURING PREGNANCY

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1. INTRODUCTION

Psoriasis is considered a chronic inflammatory condition characterized by well-defined red papules and plaques covered with thick, easily shed white scales, primarily appearing in the hairline and pressure areas. The disease is associated with several conditions, including cardiovascular diseases, inflammatory bowel disease, depression, and metabolic syndrome. The physical and mental burden negatively impacts the quality of life of patients.

The pathogenesis of psoriasis is believed to be mediated by the immune system, while also influenced by environmental and genetic factors. Th1 and Th17 cells, along with a variety of cytokines such as Interleukin (IL) -1, IL-2, IL-6, IL-8, IL-12, IL-13, IL-17, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-36, interferon (IFN) -γ, IFN-α, and tumor necrosis factor (TNF) -α, have been shown to play significant roles in the disease mechanism. Notably, the IL-23/IL-17 immune axis is the main immune pathway in the pathogenesis of psoriasis (Figure 1)[1].

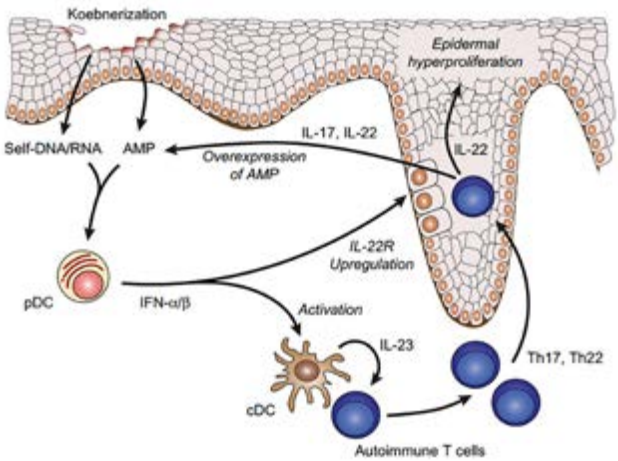

Figure 1. Pathogenesis of psoriasis. Source: Flatz et al.[1]

Additionally, sex hormones play an important role in regulating biological and immune responses in the skin, contributing to changes in psoriasis activity during menstrual cycles, menopause, and pregnancy in women. Pregnancy is associated with significant hormonal changes and substantial adjustments in immune response to create a state of tolerance for the fetus. Managing the disease during this period is indeed a challenge to ensure safety for both the mother and the fetus[2].

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2. THE CORRELATION BETWEEN PSORIASIS AND PREGNANCY[2]

Effects of pregnancy on psoriasis

Most studies indicate that pregnancy has a positive effect on psoriasis, with symptoms generally tending to improve. However, psoriasis symptoms may flare up during the postpartum period if not well-controlled and managed. The most noticeable changes occur in the first trimester, with some signs evident in the second trimester, and this change tends to persist in subsequent pregnancies. Pustular psoriasis shows less change during pregnancy compared to other forms of psoriasis. Breastfeeding does not seem to have a significant impact on psoriasis[2].

Boyd and colleagues observed that the improvement of the condition during pregnancy is associated with immune system suppression due to hormonal effects, with progesterone playing the most crucial role. Hormonal changes during pregnancy may directly affect keratinocytes, as they metabolize steroid hormones such as estrogen and progesterone. High levels of IL-10 during pregnancy may also positively influence psoriasis. Additional theories regarding the positive effects of pregnancy on psoriasis include the immunosuppression of the fetus and the roles of human placental lactogen and chorionic gonadotropin.

Effects of psoriasis on the pregnancy process

Some studies suggest that female patients with psoriasis, particularly severe cases, often give birth to low-birth-weight infants. Among mothers with severe psoriasis, a study by Yang and colleagues found that 20 women treated systemically during pregnancy did not have an increased risk of low-birth-weight babies, indicating that this risk may arise from the psoriasis itself. Cytokine imbalances can lead to endothelial dysfunction, vascular and placental abnormalities. Additionally, inflammation and the increase of cytokines in psoriasis can also affect fetal development.

3. TREATMENT OF PSORIASIS DURING PREGNANCY[3,4]

Treatment for psoriasis generally includes three main therapies: topical therapy, systemic therapy, and phototherapy. The choice of treatment for each patient will depend on the severity of the disease, comorbid conditions, treatment efficacy, and individual patient needs. Overall, the treatment of psoriasis in pregnant and non-pregnant patients is relatively similar, except for certain medications that should be avoided during pregnancy due to the risk of affecting the fetus. In mild cases with limited skin lesions, treatment with topical medications may suffice, while phototherapy or systemic therapy is reserved for extensive skin lesions and severe cases. For pregnant women, topical treatment and phototherapy are prioritized to ensure maximum safety for both mother and fetus. In cases of good improvement during pregnancy, discontinuing any treatment may be a reasonable strategy.

First-Line treatment

For pregnant women with psoriasis and limited lesions (< 5 - 10% body surface area), treatment can be managed with topical therapy.

Moisturizers/emollients: This is the simplest treatment, well-tolerated and without significant side effects.

Topical corticosteroids: Most topical corticosteroids are FDA-approved for use in

pregnant women. However, it is important to note that corticosteroids may exacerbate stretch marks during pregnancy, and strong topical corticosteroids can lead to low birth weight in newborns.

Second-Line treatment

When topical treatments with moisturizers and corticosteroids are ineffective or when skin lesions are extensive, phototherapy is preferred as an alternative. Narrowband ultraviolet B (NB-UVB) phototherapy at a wavelength of 311 nm is a safe and effective method for pregnant women. However, the major drawback of this method is the need to visit a treatment facility three times a week. If narrowband UVB is not available, broad-spectrum UVB (290 - 320 nm) can be used as a substitute, although it is less effective. For localized skin lesions, laser devices emitting UVB, such as the excimer laser (308 nm), can be employed.

Common side effects of UVB phototherapy include erythema, dry skin, and itching; therefore, using it in conjunction with moisturizers and topical corticosteroids helps enhance treatment efficacy and reduce side effects. Additionally, there are concerns regarding decreased serum folate levels with UV exposure. This deficiency increases the risk of fetal neural tube defects when combined with hyperthermia, so it is important to avoid hot baths, especially during the first 28 days of pregnancy, while monitoring folic acid levels throughout treatment along with adequate vitamin supplementation.

Third-Line treatment

Biologics and cyclosporine may be effective for patients who have failed topical and light therapies. However, data on safety in pregnant women remain limited and careful consideration of benefits versus risks is essential.

TNF-α Inhibitors: Increasing evidence suggests that TNF inhibitors can be used safely during pregnancy. However, risks of preterm birth, low birth weight, and potential infection have also been reported. Among TNF inhibitors, certolizumab is considered the safest due to minimal placental transfer and relatively low risk of immunosuppression in newborns and teratogenic effects.

Adalimumab, etanercept, and infliximab are classified as Category B by the FDA regarding pregnancy. However, because adalimumab, etanercept, and infliximab can cross the placenta and may be detectable in newborns for several months or longer after birth, there are significant concerns about potential postnatal effects on infants. For infliximab, it is recommended to discontinue the drug by 30 weeks of gestation as it can cross the placenta in the third trimester, and to delay live vaccine administration for infants until they are 7 months old.

Ustekinumab, a monoclonal antibody targeting interleukin (IL) 12 and IL-23, is also classified as Category B by the FDA. Safety data on ustekinumab during pregnancy are primarily limited to animal studies, but cases of healthy, uncomplicated births and spontaneous abortions have been reported in patients treated with ustekinumab during pregnancy.

Cyclosporine: A calcineurin inhibitor, cyclosporine is classified as Category C by the FDA during pregnancy. The risk of teratogenicity in women treated with cyclosporine appears to be very low, although cases of preterm birth and low birth weight have been reported. Previously, cyclosporine was indicated for severe or refractory pustular psoriasis. In 2012, the medical

board of the National Psoriasis Foundation recommended cyclosporine as an appropriate first-line therapy for pustular psoriasis. The safe dosage of cyclosporine is 2 - 3 mg/kg/day. Due to side effects like hypertension and kidney dysfunction, patients need regular blood pressure monitoring and kidney function assessments. Cyclosporine can be used alone or in combination with corticosteroids. Due to limited research data on cyclosporine use in pregnant women with psoriasis, its use is usually reserved for severe, refractory cases, requiring careful consideration of benefits and risks

Contraindicated therapies

Methotrexate should not be used to treat psoriasis in pregnant or breastfeeding women due to its potential to cause teratogenic effects and interfere with cellular metabolism in breastfeeding infants. Pregnancy should be avoided for three months following the last methotrexate dose, as the drug can persist in the liver for several months.

Acitretin significantly increases the risk of congenital abnormalities in both humans and animal studies. Additionally, acitretin can be metabolized to etretinate, which remains in body fat for up to 52 months after discontinuation of treatment. Therefore, pregnancy should be avoided for three years after the last acitretin dose.

Tazarotene: The FDA classifies tazarotene as Category X for pregnant women.

Other therapies

Topical Calcineurin Inhibitors (e.g., tacrolimus, pimecrolimus): Based on animal studies and case reports, these medications do not increase the risk of congenital abnormalities. However, oral tacrolimus may increase the risk of low birth weight and preterm birth.

Calcipotriol, calcitriol, and vitamin D derivatives: Animal studies in mice and rabbits show an increased risk of congenital abnormalities. Hypercalcemia from excessive topical use and excessive vitamin D supplementation can lead to skeletal abnormalities in offspring.

Fumaric acid esters are used to treat psoriasis in Europe. While animal studies do not indicate any teratogenic potential, there is very limited data in humans. Thus, the use of fumaric acid esters is not recommended in pregnant women.

Coal tar: Classified as category C by the FDA, topical forms may be considered for use in the second and third trimesters of pregnancy.

Systemic glucocorticoids are not recommended for treating psoriasis due to the risk of severe disease flare-ups upon discontinuation. An exception is for pustular psoriasis during pregnancy, where systemic glucocorticoids are the primary treatment.

Other biologics such as ixekizumab, secukinumab, brodalumab, guselkumab, and secukinumab currently lack sufficient safety and efficacy data for treating psoriasis in pregnant women.

4. CONCLUSIONS

The relationship between psoriasis and pregnancy remains unclear; most studies suggest that pregnancy positively impacts psoriasis, with symptoms generally tending to improve, though they can easily flare in the postpartum period if not well-managed. This presents a challenge due to the increased risk of disease impact and treatment effects on fetal health during this sensitive period. In treating psoriasis during pregnancy, topical therapies should be prioritized over systemic therapies. Mild to moderate topical

corticosteroids are the first-line treatment. Additionally, emollients/moisturizers should be used regularly. For patients with moderate to severe disease, narrowband UVB phototherapy is the best treatment option for pregnant women. However, patients who cannot be managed with topical therapies and light treatment may require systemic therapy for control. TNF-α inhibitors are the best choice, with increasing evidence showing no teratogenic effects or toxicity. In contrast, tazarotene, methotrexate, and acitretin are contraindicated during pregnancy.

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