IN-DEPTH REVIEWS

Psoriasis in Pregnancy: A Review

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ABSTRACT

Psoriasis is a complex autoimmune disease, most commonly characterized by silvery scale erythematous plaque. During pregnancy, there is a physiologic change of immunology status, which shifts from an inflammatory state to an anti-inflammatory state, in order to avoid fetal rejection. As a result of this immunomodulatory changes, the majority of pregnant patients experience improvement of their psoriasis. The treatment of psoriasis in pregnancy can be challenging, mainly because there is only a few evidence-based studies. The objective of this paper is to review the relevant data on psoriasis in pregnancy and its treatment.

INTRODUCTION

Psoriasis is chronic inflammatory skin disease that most commonly characterized by silvery scale erythematous plaque.[1,2] It may be associated with other comorbidities such as joint, ocular, and systemic disorders. The treatment of psoriasis is varied depending on the disease severity, comorbidities, and patient preference.[2,3] In the case of pregnancy, treatment of psoriasis can also be challenging. Generally psoriasis improves during pregnancy, however, many pregnant patients still need treatment. Pregnant women must use caution when using any medications, and doctors must decide what treatment options are best for mother and fetus.[4]

REVIEW

Immunopathology of psoriasis

Psoriasis is a complex autoimmune and autoinflammatory disease that is characterized by rapid epidermal growth resulting in a number of clinical manifestations, most commonly sharply demarcated erythematous scaling plaques.[5] The major cells that play a central role in the pathogenesis of psoriasis are keratinocytes, endothelium, dendritic cells, and T cells.[6] Alteration of keratinocyte function, vascular structure, innate and adaptive immune systems contribute to the manifestations of psoriasis.[7] Dendritic cells are a key factor of inflammation in psoriasis, in particular, plasmacytoid dendritic cells producing interferon-alpha (IFN-alpha), which stimulate the activation of myeloid dendritic cells. Myeloid dendritic cells produce interleukin-

12 (IL-12) and IL-23, which promote the development of T-helper 1 (Th1) and Th17 cells.[6,7] Th1 cells produce proinflammatory cytokines, including IFN-gamma, IL-2, and tumor necrosing factor-alpha (TNF-alpha), that have roles in inflammation and psoriasis-like changes in skin. The activation of Th17 cells stimulates the production of IL-17A and IL-22, both of them promoting keratinocyte activation and growth.[7] Recent data suggest Il-17 cytokines as key factors in the development of psoriasis.

Immunological changes during pregnancy

The state of pregnancy has the potential to be severely detrimental to the female immune system being that the father's foreign antigens, which are contained within the fetus, are capable of eliciting a robust immunological response from the mother. It follows, therefore, that during pregnancy, the mother's immune responses must shift from an inflammatory state to an anti-inflammatory state, in order to avoid fetal rejection.[8] Pregnant women experience an overall increase in white blood cells, mainly neutrophils. However, there is a decrease in total T cell numbers and activated T cells [9]

Characteristics of psoriasis in pregnancy

As a result of immunomodulatory changes of pregnancy, the majority of pregnant patients experience improvement of their psoriasis. However, some may also experience worsening of psoriasis, which is still poorly understood.[10] In pregnancy, the maternal immune system is shifting toward Th2 immunity, causing a lower level of Th1 cytokines that are responsible for the inflammatory immune response in psoriasis.[11]

Psoriasis is also correlated with hormonal changes that women undergo during pregnancy, with high level of estrogen and progesterone as the central players for improvement.[12,13] Throughout pregnancy other hormones including human chorionic gonadotropin, glucocorticoid, prolactin, and human placental lactogen, are increased. These hormones are all known to have immunosuppressive effects, which is also a reason for improvement of psoriasis in pregnancy.[10,14]

Psoriasis treatment in pregnancy

There are few evidence-based studies on treating psoriasis in pregnancy. Topical treatments are the most commonly recommended treatment options for pregnant women with psoriasis.[15] Moisturizing agents and emollients such as petroleum jelly and mineral oil have been found to reduce psoriatic plaques. They can help reduce inflammation of the skin, reduce skin cell generation, and clear affected skin plaques.

Topical corticosteroids are first line therapy for psoriasis in pregnant patients.[16] Nonetheless, there is always a risk of systemic absorption which may vary from 0.5 to 7% in intact skin, and may be greater in inflamed or damaged skin.[17] Therefore, it is recommended to use low to moderate potency corticosteroids rather than potent and very potent corticosteroids in pregnant woman with psoriasis.[18]

Other common topical treatments in psoriasis including salicylic acid, coal tar and tazarotene, are not recommended during pregnancy.[16] Calcipotriene is also not recommended in pregnancy (pregnancy category C). However, if there is no other alternative treatment, limited use of topical calcipotriene is still permissible.[19]

Phototherapy with narrowband ultraviolet B (NB-UVB) is the second-line treatment for pregnant women with psoriasis.[20] UVB, which is present in natural sunlight, is an effective treatment for psoriasis as the light can penetrate the layers of the skin and help reduce the growth of affected skin cells. Phototherapy, both narrowband and broadband UVB, is considered safe and effective in pregnancy due to limited penetration to the mother's skin.[21] The data for phototherapy during pregnancy are limited, nevertheless it has not been associated with any increase risk of abnormal delivery or fetal abnormalities.[20] The only consideration of phototherapy in pregnancy is the potential photodegradation of maternal folate, which can cause neural tube defects in the fetus. Therefore, folic acid supplementation is even more highly recommended for these patients.[22]

Nowadays biologic agents are the cornerstones in the treatment of psoriasis. Although this treatment shows promise in treating the disease, the risk of alteration of the immune system is the major concern particularly in pregnant patient.[23] Currently there are four classes of biologic agents that are approved for psoriasis, tumor necrosis factor inhibitors (TNFi), an IL-12/23 inhibitor, IL-17 inhibitors, and Il-23 inhibitors. Fundamentally, these therapies are monoclonal antibodies or fusion proteins which block cytokines or receptors associated with psoriasis, which play roles in the pathogenesis of psoriasis.[23] The potential antibody transfer from mother to fetus is the major concern that limits the use of biologic agents in pregnancy. Monoclonal antibody can actively cross the placenta with the help of neonatal fragment crystallizable (Fc) receptor that are found on trophoblasts, especially during second and third trimesters.[24] This transfer may result in immunosuppression of the newborn, resulting in higher risk for infection. However, pregnant women are usually excluded from clinical trials including study for biologic agents. Therefore, knowledge about safety of these treatments are very limited.[25] Among TNFi, certolizumab pegol is the only biologic agent that has supporting data of safety to be used in both pregnancy and breastfeeding, due to its lack of Fc portion. Without the Fc portion, certolizumab is not actively transported across the placenta.[26] Ustekinumab, an IL-12/23 inhibitor, has very limited data with only few case reports and case series that showed no increased risk of congenital defects or adverse events in pregnant women.[27] Both IL-17 inhibitors (secukinumab, ixekizumab), and IL-23 inhibitors (tildrakizumab, guselkumab, risankizumab) have extremely limited data with no human studies for psoriasis in pregnancy.

CONCLUSION

Psoriasis is a chronic skin condition with a variety of treatments that impacts conception, pregnancy, and postpartum care. While there are some treatments already known to be safer than others, the precise effects of psoriasis on pregnancy are still mostly incomplete due to insufficient available studies. A large scale of systematic review in the treatment of psoriasis in pregnancy is still needed.

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