

The Use of Dupilumab in Severe Atopic Dermatitis During Pregnancy: A Case Report

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Abstract

Atopic dermatitis accounts for most cases of gestational dermatoses. The rising prevalence of atopic dermatitis poses a significant health and economic burden. Current treatments include topical and systemic glucocorticoids and cyclosporine. Presently, the only biologic approved for atopic dermatitis is dupilumab with limited data available regarding its safety profile in pregnancy. We report a case of severe atopic dermatitis treated safely with dupilumab with no adverse maternal or fetal outcomes and resolution of atopic dermatitis postpartum in the absence of maintenance dupilumab therapy. Further research is needed to elucidate the role of dupilumab in the management of atopic dermatitis during pregnancy.

Introduction

Atopic dermatitis (AD), a chronic inflammatory skin disorder that manifests with severe pruritis in the setting of eczematous lesions, is one of the most common skin disorders in adults and children. Globally, the prevalence of AD continues to increase with up to 20% of children and 3% of adults affected¹. In pregnancy, AD is the most common skin disease accounting for 36–59% of all dermatoses^{2,3}. The rising prevalence of AD poses a significant economic burden with an estimated annual cost in Canada of \$1.4 billion dollars⁴. Additionally, AD results in significant morbidity and adversely affects quality of life^{5–7}. Current treatment options for moderate to severe AD in pregnancy include oral corticosteroids, azathioprine, cyclosporine and phototherapy^{3,8}. Presently, the only biologic approved for moderate to severe AD is dupilumab. Dupilumab is a fully monoclonal antibody of the immunoglobulin G(IgG)4 subclass that exerts its effect through the disruption of interleukin(IL)-4 and IL-13 signaling pathways, key modulators in the pathogenesis of AD⁹. Although a growing body of evidence supports the use of biologic agents in pregnancy for dermatological conditions, there remains a sparsity of data evaluating the impact of dupilumab in the pregnant population and the subsequent effects on fetal outcomes¹⁰. We describe a case of severe AD treated safely with dupilumab during pregnancy with subsequent resolution of symptoms in the post-partum period.

Case Report

A 33-year-old gravida 1 para 1 with a past medical history of seasonal rhinitis and severe AD dating back to early childhood, presented in the setting of worsening AD refractory to high potency topical corticosteroids, systemic corticosteroids, antibiotics for staphylococcal superinfection, methotrexate, cyclosporine as well as ultraviolet phototherapy. She was subsequently started on hydroxyzine, clarithromycin and triamcinolone cream which resulted in mild improvement, but on discontinuation her AD flared. Her Investigator Global Assessment for Atopic Dermatitis score of 4 was indicative of severe disease. She was subsequently initiated on dupilumab 300mg every 2 weeks with significant improvement in her condition and quality of life and no longer required antihistamine therapy. She became pregnant 12 months later and remained on dupilumab 300mg every 2 weeks until 27 weeks

gestation at which point dupilumab was stopped. Unfortunately, she experienced a severe flare of AD only 2 weeks after discontinuation that was refractory to topical treatments and she was, therefore, restarted on dupilumab at 29 weeks gestation. This was continued until 36 weeks of gestation. At 38 weeks gestational age an ultrasound was concerning for intrauterine growth restriction as well as breech position and the patient underwent urgent Cesarean section with delivery of a healthy female infant (Weight 2480g). Surgical pathology revealed normal umbilical cord vasculature, normal villous maturation compatible with a third trimester placenta with no evidence of villitis or infarct, and no chorioamnionitis. There were no issues postpartum. The patient was reassessed 6 weeks postpartum and had opted to breastfeed. Her AD remained well controlled without recommencement of her dupilumab therapy.

Discussion And Conclusion

Immunity in pregnancy is characterized by a shift from cell-mediated immunity (Th1) to humoral immunity (Th2) and is associated with a reduction in fetal demise/abortion. The upregulation of the Th2 response is similarly seen in atopic diseases which are associated with reduced fertility. It is, therefore, not surprising that pregnancy worsens AD severity. For this reason, adequate control of AD in pregnancy is warranted and may reduce the risk of severe complications such as eczema herpeticum, bacterial infections, and improve quality of life with reduced psychosocial comorbidities¹¹⁻¹³.

The current cornerstones of AD treatment in pregnancy include topical corticosteroids, topical calcineurin inhibitors, and narrowband ultraviolet B (UVB). In the setting of refractory disease, systemic cyclosporine or glucocorticoids can be used as alternative therapies for long term disease control, although the risk of low birth weight in neonates with maternal cyclosporine or long term steroid used must be considered^{3,9}.

Biologic therapies in pregnancy continues to gain traction especially in the management of inflammatory bowel disease, and rheumatoid arthritis where the use of tumor necrosis factor (TNF α) inhibitors is generally considered safe in the first 2 trimesters due to the negligible transfer of maternal antibodies during this period¹⁰. With regards to AD, there remains a paucity of data with only 2 case reports reporting the use of dupilumab in pregnancy. Both case reports demonstrated favorable maternal and fetal outcomes.^{11,14} The effects of dupilumab on breastfeeding infants is unclear and, therefore, is not currently recommended in lactating women⁸. Similarly, the effects of dupilumab on the neonatal immune system are uncertain and the potential for altered newborn immunity exists¹⁰. For this reason, the administration of live vaccines should be delayed for at least 6 months post delivery¹⁰. In this case, the patient demonstrated well controlled AD despite not being on dupilumab maintenance therapy.

This case report adds to current literature regarding the use dupilumab in pregnancy. To our knowledge, this is the first case report of a pregnant patient with AD treated with dupilumab in Canada. Our case is the first to demonstrate symptom resolution without re-initiation of dupilumab in the postpartum setting with excellent maternal and fetal outcomes.

Abbreviations

AD (Atopic Dermatitis)

IGg (Immunoglobulin)

IL (Interleukin)

Th1 (Cell mediated immunity)

Th2 (Humoral immunity)

UVB (narrowband ultraviolet B)

Declarations

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Literature search and drafting of the manuscript (NA, DA, TK), critical revision of manuscript for important intellectual content (AK, DA), senior authorship guidance and supervision (AK)

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