

Dupilumab for the treatment of severe atopic dermatitis in a pregnant patient: A case report



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INTRODUCTION

Atopic dermatitis (AD) is an inflammatory skin condition affecting 3% to 10% of adults and 10% to 20% of children globally.¹ Systemic therapies such as cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil have variable levels of efficacy and potential adverse effects.²

Dupilumab is the first biologic treatment approved in the United States for the treatment of moderate-to-severe AD in patients aged 6 years and older. Dupilumab is a human monoclonal antibody of the IgG 4 subclass that inhibits the signaling of interleukin (IL)-4 and IL-13.³ The most common side effect of dupilumab is injection site reaction,¹ and the most specific side effect is conjunctivitis.^{1,2}

AD is the most common gestational dermatosis, accounting for 36% to 49% of all pregnancy dermatoses.⁴ Systemic therapeutic options for AD during pregnancy include oral corticosteroids, azathioprine, cyclosporine, and phototherapy.⁴ However, little is known about the impact of dupilumab in pregnancy. We report a case in which dupilumab was used to treat severe AD in a pregnant patient.

CASE REPORT

A 28-year-old gravida 3, para 2 woman with a lifelong history of AD presented at 20 weeks of pregnancy. Her pregnancy was complicated by hypertension and a small-for-gestational-age fetus; her prior 2 pregnancies were uncomplicated. After no response to topical steroids and phototherapy, she was treated with courses of 40 mg to 60 mg of prednisone. At the time of her visit, she was taking 40 mg of prednisone daily. Her skin examination was

Abbreviations used:

AD: atopic dermatitis
 IL: interleukin
 Th1: T-helper
 TNF: tumor necrosis factor

significant for diffuse AD with an Investigator Global Assessment score of very severe.

Cyclosporine was not indicated given the patient's baseline hypertension and small-for-gestational-age fetus. After thoroughly discussing the risks and benefits of dupilumab with the patient, her obstetrician, and a maternal fetal medicine specialist, the decision was made to start dupilumab. At 24 weeks of pregnancy, the patient received a loading dose of 600 mg followed by 300 mg every other week.

The patient was lost to dermatology follow-up for several months and was managed by her obstetrician. Because of concern of her skin flaring, she remained on 40 mg/d of prednisone for the next 3 months. She tapered off the prednisone 3 weeks before giving birth. Gestational diabetes occurred during her pregnancy.

During the remainder of her pregnancy, the patient tolerated dupilumab well. She noted eye irritation for 1 to 2 days after dupilumab injections but had no other side effects. She had an uncomplicated delivery and delivered a 5-pound, 14-ounce healthy male infant at 37 weeks and 6 days gestational age. Her skin dramatically improved during the course of her pregnancy.

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The patient was seen 1 month after delivery. At this visit, she was experiencing a flare of her AD that began shortly after she gave birth. Her exam was notable for AD with an Investigator Global Assessment score of moderate. She continued to take 300 mg of dupilumab every 2 weeks and remained off oral steroids. The patient was counseled that she could breastfeed while on dupilumab; however, she chose to stop breastfeeding shortly after delivery.

DISCUSSION

Pregnancy is cited as a frequent trigger for AD.⁴ In a normal pregnancy state, the balance between the T-helper (Th)1/Th2 cytokine response is altered; to prevent fetal rejection, the maternal cell-mediated immune function and Th1 response decreases, whereas the Th2 response becomes stronger. This adaptation is thought to increase the severity of AD.⁵

Topical corticosteroids and ultraviolet phototherapy can safely be used during pregnancy for AD. Short courses of oral corticosteroids can be used as second-line treatment.⁴ Cyclosporine is considered a third-line treatment option; however, it may increase the risk of low birth weight in infants.³

Postmarketing data on dupilumab in pregnancy is limited. One recently published case report of a pregnant patient with AD treated with dupilumab in Germany depicted good outcomes for the patient and her baby.⁵ This study referenced data from the European Medicines Agency; however, it is challenging to draw conclusions from the data, as the overall case number is low.

Mouse studies found that IL-13 expression in the eye is responsible for stimulating the proliferation of mucus-secreting goblet cells.⁶ Thus, decreased IL-13 secondary to dupilumab could theoretically cause goblet cell hypoplasia, which may result in decreased mucin production and mucosal epithelial barrier dysfunction.⁷ It is also possible for dupilumab, an antibody of the IgG4 subclass, to cross the placenta, enter the fetus's bloodstream, and possibly affect conjunctival goblet cell production in the fetus. Thus, ocular surface disorders could manifest in the newborn. The theoretical risk of goblet cell hypoplasia would be lower in the third trimester, as the goblet cells have already matured. Our patient's baby did not show signs of ocular dysfunction at delivery or subsequent examinations.

Moreover, conclusive data on the safety of breastfeeding while on dupilumab are lacking. Breastfeeding by mothers treated with tumor necrosis factor (TNF)- α inhibitors is considered safe because of low amounts of the medication in breastmilk and further protein degradation by the

infant's gastric acid.⁸ Although no specific breastfeeding data are available on dupilumab or IL-12/23 IL-17 inhibitors, breastfeeding safety data on TNF- α inhibitors may theoretically be generalized to these newer biologic agents.⁸

It is unknown how dupilumab exposure in pregnancy affects the immune system of the neonate. TNF- α inhibitors are more actively transported from maternal to fetal circulation in the third and second trimesters compared with the first. Thus, it is recommended to hold live vaccines for the first six months of life in children exposed to TNF- α inhibitors in the later trimesters.⁹ However, dupilumab has not been shown to have adverse effects on nonlive immunizations given to adult patients and immune responses against these antigens developed normally.¹⁰ Although there are no data on live vaccinations with dupilumab treatment, the authors predict that it would not cause safety issues for the infant, given that IL-17 and IL-23 blockers have less effect on systemic immunity.¹⁰

This is the first case report, to our knowledge, depicting a pregnant patient with AD treated with dupilumab in the United States. Maternal and fetal outcomes were excellent. Much more research is needed to establish the safety of dupilumab during pregnancy and breastfeeding.

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