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Letter to the Editor

Safety of Omalizumab During Pregnancy and Breast-Feeding With Assessment of Placental Transfer: A Case Report

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Asthma exacerbation in pregnant women is associated with obstetrical complications such as fetal growth restriction, preterm delivery and preeclampsia.[1] Omalizumab is a recombinant humanized monoclonal antibody approved for the treatment of severe persistent allergic asthma.[2,3] Data on its safety during pregnancy, based on case series and registries, are limited.[4,5] In this case report, we provide an assessment of omalizumab placental transfer and discussed its safety.

We report here the case of a 34-year-old woman of 51 kg with allergic asthma, bronchiectasis and right pneumonectomy because of recurrent bronchitis. Her treatment included an inhaled corticosteroid (fluticasone), a long-acting beta-2-agonist (salmeterol) and a muscarinic antagonist (tiotropium). Since she had persistent severe asthma with an initial total immunoglobulin E (IgE) level increased to 246 UI/mL, omalizumab (300 mg *i.e.* 6 mg/kg every 4 weeks subcutaneously) along with azithromycin was administered, allowing clinical improvement. Nevertheless, her lung function remained poor with fixed airway obstruction. Percent predicted forced expiratory volume in 1 second (ppFEV1) was 52% and the FEV1:FVC ratio was 65%. She became pregnant while on omalizumab, which was continued because of her respiratory condition. During pregnancy, she further experienced 2 asthma exacerbations requiring oral corticosteroids. Her lung function progressively impaired with a minimum FEV1 of 28%. Obstetrical monitoring and fetal growth were unremarkable. Labor was induced at 37 weeks of gestational age due to a new asthma exacerbation. A healthy girl (Apgar score 10/10/10, weight 2,600 g) was delivered vaginally. Serum samples from mother and cord blood were obtained, the last omalizumab injection being performed 4 weeks earlier. Omalizumab plasma concentration was assayed using a home-made sandwich enzyme-linked immunosorbent assay. Maternal serum level was 29.3 μg/mL, while it was 31.3 μg/mL in the umbilical cord (cord/maternal serum concentration ratio 1:1). There was no complication during the postpartum period. The clinical neonatal examination and platelet count were normal. Breast-feeding was allowed after pharmacologist consulting because the omalizumab antibody-based structure is expected to be destroyed after oral ingestion

Disclosure

There are no financial or other issues that might lead to conflict of interest.

and maintained until 4 months without any adverse event. After 15 months of life, her development was normal.

Omalizumab selectively binds to the Fc portion of circulating IgE leading to decreased circulating free IgE levels. Since omalizumab has an IgG1κ structure (molecular weight 149 kDa), it is expected to be actively transported across the placenta, which is mediated by endocytosis using FcRn receptors on the syncytiotrophoblast.[6] Our report showed that omalizumab crosses the human placenta and is largely transferred to the fetus. Recently, similar findings have been published showing an omalizumab cord/maternal serum concentration ratio of 2.3.[7] Considering its very long elimination half-life of 26 days, omalizumab exposure of the neonate would persist for weeks after birth. In preclinical studies, no maternal toxicity, embryotoxicity or teratogenicity effects were observed, except neonatal thrombocytopenia in primates. Experience in pregnant women is based on case reports and on the the Xolair Pregnancy Registry (EXPECT) study, a registry from the company licencing omalizumab which enrolled 230 pregnancies.[8] There was no apparent increase of major congenital malformations among the women treated with omalizumab.

Finally, the use of omalizumab during pregnancy and breast-feeding appear to be safe, although more data are needed. The risk-benefit ratio for treating pregnant women with omalizumab must be assessed every time, as neonates will be exposed for weeks after birth.

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