Case Report

Successful and safe treatment of severe steroid dependent eosinophilic asthma with mepolizumab in a woman during pregnancy

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ABSTRACT

A 26-year-old female with steroid dependent eosinophilic asthma and nasal polyps who had successfully been treated with mepolizumab for 17 consecutive months with complete steroid withdrawal and symptoms control, stopped biologic treatment due to pregnancy efforts. Mepolizumab discontinuation resulted in frequent exacerbations and daily symptoms despite high dose ICS/LABA and re-initiation of oral steroids. Mepolizumab was initiated again, followed by improvement of asthma control and gradual withdrawal of steroids within 2 months. The patient became pregnant during the fourth month of mepolizumab re-initiation. The patient presented two asthma exacerbations during pregnancy treated with short course (3 days) oral steroids and delivery was uneventful (female, Apgar 9, weight 2750 g, length 59 cm) in week 40 by caesarean section.

1. Background

Asthma is the most common respiratory disorder complicating pregnancy. In the United States, 5%–8% of pregnant women have asthma and worldwide up to 13% of pregnancies may be complicated by asthma [1–3]. Maternal asthma, especially when severe, is associated with an increased risk of adverse perinatal outcomes, therefore changes in the course of the disease are to be expected and can be unpredictable during pregnancy [4,5]. Optimizing asthma management in pregnancy is paramount for protecting the health of both mother and baby.

Studies examining the effect of first-line controller asthma medications have not shown risks induced to the fetus [4]. Whether newer medications for severe asthma, such as biologics, have any effect on the pregnancy and conditions of the fetus is the subject of observational studies. Up to now, omalizumab is the only biologic agent for severe asthma with safety data in pregnancy but it is indicated only in atopic patients with high levels of IgE [6]. Data for newer agents such as mepolizumab are still scarce. Mepolizumab is an IgG1/k class-humanized monoclonal antibody which blocks circulating interleukin-5 (IL-5) which is responsible for the development, maturation, and survival of eosinophils [7]. Several randomized controlled and a few real-life trials have shown the efficacy and safety of mepolizumab in patients with severe eosinophilic asthma [8,9]. Data about the safety of mepolizumab during pregnancy...
and lactation comes from experimental studies on animals; no embryotoxic and teratogenic effect has been found when mepolizumab is administered throughout pregnancy and no adverse effects were observed on fetal or neonatal growth when administered throughout late gestation, delivery and nursing [10].

This study presents a case of a woman who became pregnant and gave birth to a healthy baby while on/during treatment with mepolizumab.

2. Case presentation

The subject was a 26-year-old woman, nonsmoker, with a history of asthma since she was 16 years old. She had undergone polyectomy for nasal polyps at the age of 22 and she had persistent peripheral eosinophilia (600-1500 cells/µL) that was thoroughly investigated for other diseases by a hematologist and rheumatologist. Although she mentions being allergic to NSAIDs, grass and dust, her IgE levels were constantly low (<20IU/ml) while being off oral steroids. Following an upper respiratory infection, her asthma control deteriorated in 2017 and she started treatment with high doses of Beclomethasone/Formoterol, Tiotropium and Montelukast. Due to inadequate control (daily and nocturnal symptoms, limitation in activities, low FEV1 (=56%) and frequent exacerbations, she was started on oral corticosteroid maintenance therapy (OCS), specifically 8mg methylprednisolone. Any effort to reduce OCS treatment resulted in worsening of symptoms (ACT = 16) and exacerbations (4/year). The patient was referred to a tertiary hospital and was investigated for uncontrolled severe asthma (including bronchoscopy). Any other disease was excluded, and she started treatment with mepolizumab 100mg given subcutaneously at monthly intervals.

Two months after initiation of mepolizumab, the patient demonstrated remarkable improvement in asthma control (ACT = 22), pulmonary function (FEV1 = 100%) and complete withdrawal of OCS. During the following 17 months, she was almost asymptomatic while receiving medium dose ICS/LABA. Eosinophils levels remained low (<2%, <100/µL) at several consecutive measurements. She had only two moderate exacerbations treated with short courses (3 days) of oral steroids.

In June 2019 the patient informed her treating physician that she was planning to get pregnant and expressed concerns regarding her treatment with mepolizumab. After being informed, mepolizumab treatment was discontinued and the patient was placed on high dose ICS, LABA and LAMA, as well as montelukast. Within 6 months her asthma control deteriorated, demonstrating daily symptoms, rapid decline in pulmonary function and 3 moderate exacerbations treated with oral steroids. Despite re-initiation of daily oral steroids (Prednisolone 10–15mg) the patient still had poor asthma control with 5 more moderate to severe exacerbations in the following 17 months and daily symptoms, while her efforts to become pregnant were unsuccessful.

In May 2021, upon shared decision with the patient, we reinitiated mepolizumab treatment. Steroids were withdrawn gradually within 3 months, and the patient became pregnant on the fourth month of treatment. During pregnancy, asthma control was generally improved, without any need for OCS, but the patient did not reach the level of control she had prior to mepolizumab discontinuation. In details, she had well controlled asthma (ACT 20–23), mild symptoms but no limitations to daily activities and low peripheral eosinophil levels. However, lung function was only partially improved (FEV1 70–90%) and she presented with 2 exacerbations requiring short term OCS treatment (3 days each time). The patient delivered a healthy girl (Apgar 9, weight 2750 g, length 59) in week 40 by caesarean section. Both the mother and the baby had blood eosinophils <1,5% the day after delivery. The child was breastfed during her first weeks and to this day, she is healthy and shows no symptoms of allergic diseases.

3. Discussion

The use of any drugs during pregnancy causes concern from the mother and often from her doctors [11]. Nonetheless, exacerbations and poor asthma control that may come as a result of treatment withdrawal or poor compliance during pregnancy, are associated with worse outcomes for both the baby (increased perinatal mortality, preterm delivery, low birth weight) and the mother (preeclampsia) [12]. It is therefore vital to achieve good asthma control during pregnancy. Most available asthma medications have a safety profile that has been established by numerous observational studies and the advantages of treating asthma in pregnancy far outweigh any potential risks from treatment [4].

Unlike the widely used inhaled steroids, short/long-acting beta agonists and montelukast, the safety data on biologic therapy for the treatment of severe asthma are scarce [13]. Severe asthma treatment is based on differentiating T2-high from T2-low asthma based on specific clinical features and biomarkers [14]. Severe allergic asthmatic women in pregnancy can be probably treated safely with omalizumab as a registry study found no evidence of increased risk for the fetus [6]. Although asthma phenotypes often overlap there is definitely a group of patients with eosinophilic non-allergic asthma [15]. Pregnant women with eosinophilic non-allergic asthma can only receive oral steroids or anti-eosinophilic treatment, such as mepolizumab.

To our knowledge, there are no published reports concerning mepolizumab usage during pregnancy to date. In one report, two women became pregnant while on treatment with mepolizumab: the first switched mepolizumab to oral steroids on 5th week of gestation and the second terminated the pregnancy because of the unknown possible effects of mepolizumab on the fetus [16]. A registry regarding pregnant women exposed to mepolizumab is being drawn up in the USA with no data published yet [17].

In our case mepolizumab re-initiation resulted in complete OCS withdrawal and fewer asthma exacerbations during pregnancy, but asthma control did not reach the level prior to mepolizumab discontinuation. There is robust data that approximately one-third of asthmatic women are adversely affected by pregnancy, especially females with severe asthma, probably as a result of hormonal changes. Particularly increases in progesterone and cortisol levels may be one of the mechanisms leading to altered control of asthma [18]. Our patient decided to continue mepolizumab during lactation although no information was available on its clinical use during breastfeeding. Because mepolizumab is a large protein molecule with a molecular weight of 149,000 Da, the amount in milk is likely to be very low. It is also likely to be partially destroyed in the infant’s gastrointestinal tract and absorption by the infant is probably
minimal [19]. A task force consisting of respiratory experts from Europe, Australia and New Zealand concluded that mepolizumab is possibly acceptable during breastfeeding [20].

In this report, we present the first case of a young woman with severe eosinophilic non-allergic asthma that had excellent asthma control on mepolizumab, became pregnant, continued treatment during pregnancy and gave birth to a healthy baby without any complications to the mother or the baby. Our case supports evidence that mepolizumab may be safe during pregnancy. More data are needed to support this hypothesis.

3.1. Learning points/take home messages

Management of severe uncontrolled asthma is difficult and challenging, especially when severe asthma is complicated by pregnancy.

Treatment options in severe asthma have been enriched in recent years with the emergence of biologics but unmet needs still exist, especially in pregnant women with eosinophilic non-allergic asthma.

3.2. Patient’s perspective

When my doctor suggested a new therapy, I was full of doubts and concerns, considering I hadn’t yet become a mother. Overcoming the psychologic factors I decided to go for it.

My asthma symptoms were so intense that I have to admit I had lost quality of life.

The first experience with mepolizumab was so exciting, because it was the first time after months that my doctor and I could control my severe asthma.

As time passes by, due to this therapy I have the opportunity to face my life with optimism and to hold in my arms my 90-day year old beautiful daughter, although my asthma still has its ups and downs.

I strongly believe in the scientific innovations that help us as human beings and hope to have helped the next generation.

Declaration of competing interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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