



# Omalizumab Treatment in Chronic Spontaneous Urticaria During Pregnancy: Report of A Case and Review of the Literature

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## ABSTRACT

Omalizumab is a safe and effective treatment option for chronic spontaneous urticaria (CSU). Although cohort studies in patients with asthma show no increased risk of congenital abnormalities, very little data exist in the literature regarding the use of omalizumab for CSU during pregnancy. Herein, the safe and successful use of omalizumab up dosing in a pregnant woman with CSU along with a review of the published literature is presented.

**Keywords:** Chronic spontaneous urticaria, omalizumab, pregnancy, up dosing

## INTRODUCTION

Omalizumab, a monoclonal antibody directed against IgE, is recommended as a third line treatment option in CSU. Its effectiveness and safety have been repeatedly demonstrated in clinical trials and subsequent real-life data (1,2). Despite being classified as a category B medication, omalizumab is not approved for use during pregnancy. The literature data on the use of omalizumab in pregnant women with CSU are sparse. Herein, we report the successful and safe use of omalizumab up dosing in a pregnant woman with CSU for the first time to our knowledge.

## CASE REPORT

In October 2018, a 36-year-old female presented to our clinic with a 10-month-history of CSU. She was previously treated with second generation antihistamines (desloratadine, bilastine and ebastine) at standard or higher doses up to 4-fold of standard doses and systemic corticosteroids which provided no benefit. She was otherwise healthy and had no associated chronic inducible urticaria or atopy. Laboratory tests including

complete blood count, C-reactive protein and erythrocyte sedimentation rate were within normal range. Although she claimed to have residual ecchymosis following the resolution of wheals, the diagnosis of urticarial vasculitis was excluded through histopathological examination of a skin biopsy.

Omalizumab treatment was commenced with a dose of 300 mg every 4 weeks as an add-on therapy to ebastine 40 mg/day. Following seven months of treatment, the symptoms were only partially controlled and thus omalizumab was up dosed to 600 mg every 4 weeks. Omalizumab up dosing led to rapid control of the symptoms within a few weeks. Omalizumab (600 mg/4 weeks) was continued for a further six months with good control of the disease (i.e. UCT  $\geq$  12). However, omalizumab was discontinued shortly after the sixth dose because the patient found out she was 6 weeks pregnant at the end of October 2019 (the last dose of omalizumab had been administered at the third week of September 2019, making embryonic exposure to omalizumab probable). Treatment with loratadine (10-20 mg/day) during the first trimester provided no significant improvement. Considering the severity of the symptoms,

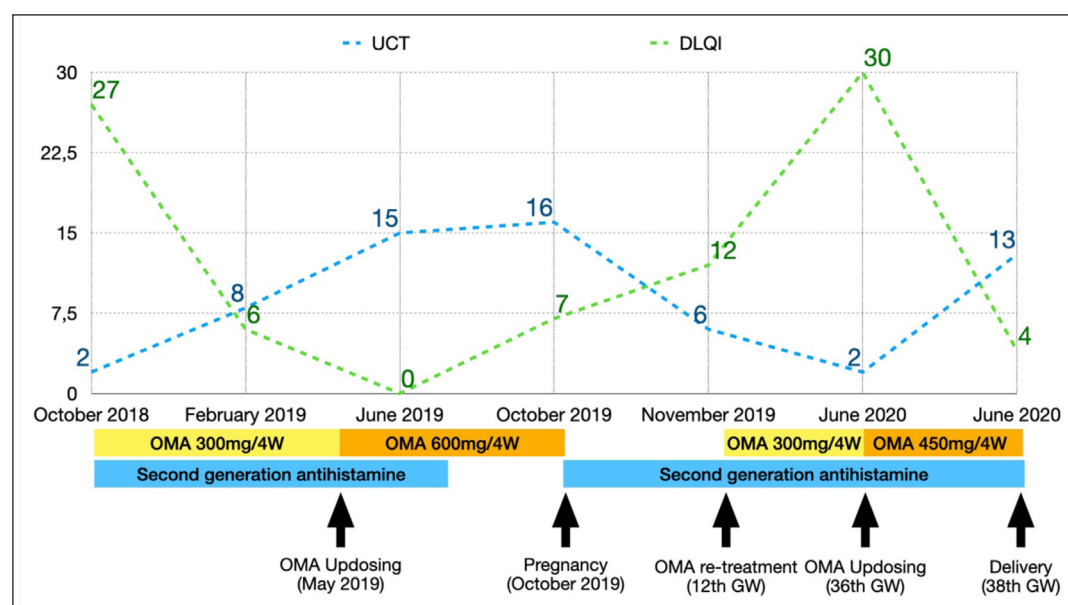
re-treatment with omalizumab (300 mg/4 weeks) was planned following a personalized benefit-risk assessment and informed consent at the 12<sup>th</sup> week of pregnancy around the end of December 2019. Since only a partial response could be obtained with five doses of omalizumab at 300 mg, updosing to 450 mg instead of 600 mg owing to pregnancy and safety considerations was decided at the 36<sup>th</sup> gestational week. Since the recommended and approved dose for omalizumab is 300 mg every 4 weeks in our country, an approval from the Ministry of Health for the off-label use of omalizumab at higher doses was obtained by referring to the existing literature data. The symptoms were almost fully controlled just before the delivery. Two weeks after the last dose of omalizumab, the patient gave birth to a healthy girl with no congenital abnormalities by cesarean section at the 38<sup>th</sup> gestational week. The changes in the urticaria control test (UCT) and dermatology life quality index (DLQI) throughout the treatment period are summarized in Figure 1.

## DISCUSSION

CSU is characterized with the presence of wheals and/or angioedema for >6 weeks (3). Owing to its chronic, relapsing and remitting course along with the occasionally disabling symptoms, CSU has a substantial negative impact on the various aspects of the patients' quality of life including physical and emotional well-being, daily social

activities and sleep (4). Persistence or exacerbation of CSU might occur during pregnancy and this combination might be even more exhausting for the patient. The exacerbation of CSU during pregnancy has been reported in 43.3% of the patients in a recent study (5). The current international guidelines for the management of CSU recommend a stepwise treatment algorithm consisting of non-sedating 2<sup>nd</sup> generation antihistamines at standard or higher doses, omalizumab and cyclosporine (3). Although the avoidance of all systemic treatments during pregnancy, particularly in the first trimester, is a prudent approach, the use of the same algorithm following a patient-based benefit-risk assessment is recommended (3). Considering the high rates of refractoriness to antihistamines in patients with CSU (6), treatment with omalizumab might be required in pregnant women with CSU as well.

The safe use of omalizumab during pregnancy in asthma has been demonstrated in large studies (5,7). A recent study of 250 patients with asthma and exposure to omalizumab [Observational Study of the Use and Safety of Omalizumab during Pregnancy (EXPECT) cohort] and a disease-matched comparison group without omalizumab exposure showed no increased risk of major congenital abnormalities (7). However, the data on the use of omalizumab during pregnancy in patients with CSU are very limited. A review of the literature revealed five reports comprising 10 patients in whom CSU was treated



**Figure 1.** The treatment course of the patient and the changes in patient-reported outcome measures during the treatment. *DLQI*: Dermatology Life Quality Index, *GW*: Gestational week, *OMA*: Omalizumab, *UCT*: Urticaria control test, *W*: Week)

**Table I: Characteristics of the patients reported in the literature who received omalizumab for CSU during pregnancy.**

Reference	Number of Patients	Dose	Time of exposure	Treatment Outcome	Pregnancy Outcome	Breastfeeding
Vieria dos Santos et al. 2014 (8)	1	150 mg monthly and 150 mg every 15 days	Starting from the 4th month of pregnancy	Complete response	No complications or congenital anomalies	Yes
Ghazanfar M. and Thomsen S. 2015 (9)	1 (two consecutive pregnancies)	150 mg every 2 weeks and 300 mg every 4 weeks	During pregnancies	Complete response	No complications or congenital anomalies	No
Cuervo-Pardo L et al. 2016 (10)	4	300 mg every 4 weeks	During pregnancies	Complete response	No complications or congenital anomalies	Not reported
Gonzales-Medina M et al. 2017 (11)	2	300 mg every 4 weeks	During pregnancies	Complete response	No complications or congenital anomalies	No/Yes
Ensina L et al. 2017 (12)	2	150 mg and 300 mg every 4 weeks	During pregnancies	Complete response	No complications or congenital anomalies	Yes/Yes
Present report	1	600 mg, 300 mg and 450 mg every 4 weeks	During the first month and restarting from the 4th month of pregnancy	Well-controlled disease	No complications or congenital anomalies	Yes

successfully with omalizumab during pregnancy without any maternal or fetal complications (Table I). All patients showed complete response to treatment with omalizumab (150 mg–300 mg/2- 4 weeks), unlike our patient in whom updosing to 450 mg was needed for the adequate control of the symptoms (8-12). Although almost 30% of the patients in the EXPECT cohort received omalizumab at doses higher than 300 mg every 4 weeks (7), this is the first report, to our knowledge, demonstrating the safety and effectiveness of omalizumab updosing in CSU during pregnancy. Despite the short duration of omalizumab updosing in our patient during pregnancy, updosing of omalizumab might be considered before commencing immunosuppressive treatments in pregnant patients with CSU unresponsive to omalizumab at standard doses as the literature data show the effectiveness of omalizumab updosing in CSU (13). Only four of the previous babies were breastfed and no complications were reported on long-term follow-up (6–14 months) (11,12). Likewise, our patient is also breastfeeding her baby without any short-term (1 month) complication.

In conclusion, the present report and review of the literature along with the data from asthma studies indicate the safety of omalizumab during pregnancy, although

larger cohort studies are warranted in patients with CSU. Despite the successful use of omalizumab at higher than 300 mg in our case for a relatively short period, more data are needed to recommend the routine use of updosing in pregnant patients.

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