

Title:

Omalizumab use during pregnancy for chronic spontaneous urticaria (CSU): report of two cases

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Editor

Chronic Spontaneous Urticaria (CSU) is a disease characterized by the development of wheals and/or angioedema that associates pruritus lasting six weeks or more. Omalizumab (as add-on therapy) has been approved since 2014 for CSU patients refractory to H1-antihistamines.¹⁻⁶ We describe two women with clearly pregnancy exacerbated CSU where Omalizumab has been a safe and successful therapeutic alternative. The first patient is a 37-year-old woman with CSU since 2006. During severe exacerbations she received treatment with short courses of oral corticosteroids (prednisone 15mg/day) added to H1-antihistamines (higher doses x4). In March 2013 she became pregnant and immediately during the first weeks of pregnancy developed an important exacerbation of their symptoms. A month later she suffered a spontaneous abortion and CSU symptoms improved gradually with Cyclosporine-A (CyA) (300mg/day; 3mg/kg), added to H1-antihistamines. In January 2014 she became pregnant again, and like the previous pregnancy she developed a severe flare of urticaria (*Urticaria Activity Score* of the previous 7 days (UAS7:42; 0-42). Blood tests including infectious serology and the autologous serum skin test (ASST) resulted negative. At this point, after careful consideration of an alternative therapy, it was decided to obtain authorization to start treatment with Omalizumab as off-label use. The patient accepted to be treated after being informed of the unknown safety profile of Omalizumab during pregnancy at that time. Treatment was initiated (300mg/4weeks). Two weeks after the first administration of Omalizumab the patient was completely asymptomatic (UAS7:0) and concomitant medication for CSU (including CyA and corticosteroids) was removed. Our patient gave birth to a healthy girl with no developmental abnormalities. The child was delivered by acute

Caesarean section due to slow progression of labor. We agree with the patient not to breastfeed the baby.

The second patient is a 37-year-old woman with at least one previous episode of CSU long-lasting 7 years (1991-1997) referred in the 2003 to our specialized Urticaria Unit because of a recurrence. An extended diagnostic programme including blood count, infectious serologies, autoimmunity and ASST were performed resulting all normal. The disease was controlled up dosing H1-antihistamine and with sporadic use of corticosteroids. In 2009 the patient showed a worsening of the CSU-symptoms (UAS7:26). At that time, ASST turned positive and CyA (300mg/day; 5mg/Kg) was added to H1-antihistamines with a complete resolution of symptoms (UAS7:0). In October 2011 she presented a sudden and unexplained worsening despite the treatment (UAS7:42) and Omalizumab (300mg/4weeks) was added with immediate complete response. Two years later she became pregnant. Omalizumab was stopped and loratadine introduced. During the following two weeks she presented a severe exacerbation of CSU (UAS7:42). After being thoroughly informed about the potential risks and unknown safety of Omalizumab during pregnancy we decided, together with the patient, to reintroduce Omalizumab (300mg/4weeks). The delivery was by Caesarean section. She gave birth to a healthy boy with no congenital abnormalities. The baby was breastfed and no side effects were reported. On posterior carefully pediatrician review, physical and mental development was also normal until now (24-month-old baby 1 and.....14-month-old baby 2)

The two cases were reported to the official pharmacosurveillance system. Omalizumab is still not approved for use during pregnancy but, it has been recently assigned to pregnancy category B by the FDA⁷ based mainly on the Xolair® Pregnancy Registry (EXPECT), a postmarketing prospective, observational study of

191 asthmatic pregnant women exposed to one or more doses of Omalizumab within 8 weeks prior to conception or at any time during pregnancy without side effects.⁸ In a review of the literature we found only two papers of women with CSU treated with Omalizumab during pregnancy without apparent toxicity for the offspring and achieving disease control during pregnancy.^{9,10} Omalizumab can be considered as a safe and successful therapeutic alternative, after careful consideration of risk–benefit profile in pregnant women with not controlled CSU.

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