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Self-reported hair loss in patients with chronic spontaneous urticaria treated with omalizumab: an under-reported, transient side effect?

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Key words

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Summary

Omalizumab has been recently approved for treating patients with refractory to H1- antihistamines chronic spontaneous urticaria (CSU). Although hair loss is listed among omalizumab side effects, there are no available data to estimate its frequency. We describe for the first time hair loss as a side effect associated with omalizumab administration in three women, 38, 62 and 70 years old, suffering from refractory to H1-antihistamines CSU. This information was retrieved from their Chronic Urticaria Quality of Life Questionnaires. Despite this side effect, all patients agreed to continue omalizumab regular administration. Hair loss appeared to be transient, lasting up to four months. All cases finally benefited from omalizumab continuation.

Introduction

Omalizumab is a recombinant humanized IgG1 monoclonal antibody that selectively binds to the receptor-binding portion of circulating, free immunoglobulin E (IgE) antibodies, regardless of its specificity. Omalizumab may suppress histamine-induced skin reactions, through the reduction of the number of the high-affinity receptors for the Fc region of IgE (FcεRI) on mast cells and basophils, which seem to downstream relevant cellular activation mechanisms (1).

Omalizumab is currently approved for treating adult and adolescent patients 12 years and older with severe or moderate to severe allergic asthma, in more than 90 countries including the US since 2003, and in the EU countries since 2005. In the EU, it has been additionally approved for the treatment of severe persistent allergic asthma in children 6 years old and above. Recently, in March 2014, the European Commission approved the use of omalizumab as an add-on therapy for the treatment of chronic spontaneous urticaria (CSU) in adult and adolescent (12 years and above) patients with inadequate response to H1-antihistamine treatment (2). The approved dose is 300 mg by subcutaneous injection every four weeks. This dose was concluded after evaluation of the efficacy and safety of omalizumab in three Phase III clinical trials: ASTERIA I (3), ASTERIA II (4), and GLACIAL (5) in nearly 1,000 CSU patients not responding to antihistamines.

In adult patients with allergic asthma, the most common side effects (seen in between 1-10%) associated with omalizumab include headache and injection site reactions (swelling, redness, pruritus and pain). Similarly, in patients with chronic spontaneous urticaria, the most common side effects, additionally to the aforementioned ones, include sinusitis, arthralgia and upper respiratory tract infection (2). In the Summary of Product Characteristics (SmPC) [available online in (2)], there are side

effects without enough available data to estimate their frequency. These include muscle pain, joint swelling and hair loss. We describe three patients with chronic spontaneous urticaria treated with omalizumab, all of which experienced hair loss after the first administration of 300 mg omalizumab.

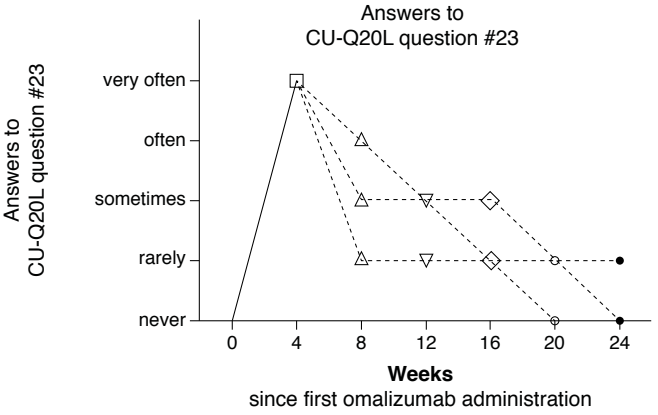
Case Series Presentation

Three women, 38, 62 and 70 years old suffering with chronic spontaneous urticaria (CSU) with angio-edema for 6, 5 and 3 months, respectively, were referred for further evaluation and treatment. All had CSU refractory to treatment with H1-antihistamines, with no other significant illnesses and no surgeries in the past apart from the oldest lady who was on 100 μg levothyroxine sodium daily the last 12 months due to Hashimoto's thyroiditis.

At the initial assessment their urticaria control tests (UCT) were 5, 6 and 6, respectively (6). None of them responded satisfactorily to a four-week course of a fourfold dose of levocetirizine (10 mg bid) (7) in addition to ranitidine 150 mg bid and montelukast 10 mg sid. During these four weeks, all of them required at least one 3-day course of methylprednisolone 8 mg bid due to angio-edema of the lips and/or eyelids and severe pruritus (8). All patients had positive autologous serum skin test (ASST) (9) and were offered the option to be treated with a course of cyclosporine. They all refused due to the described side effects, therefore omalizumab was prescribed. Urticaria activity scores (10) summed over a week (UAS7) at the day of first administration of omalizumab were 25, 27 and 30, respectively. All patients filled out the chronic urticaria quality of life questionnaire (CU-Q2oL) (11). In this questionnaire the last question "Do you suffer side-effects from the medications you take for hives?" was answered with "never" from all patients. Four weeks after the first administration of omalizumab, the UAS7 was slightly improved to 20, 21 and 25 respectively.

Interestingly, all of them changed their report about any side effects in the CU-Q2oL from "never" to "very often". This occurred on early November, mid-December and mid-April, respectively. Only in the oldest patient the reported hair loss was evident by scalp inspection. All patients were informed that hair loss might be a rare side effect of omalizumab and they were all referred for a dermatological examination which in all cases revealed Telogen Effluvium; however, all three agreed to continue omalizumab regular administration. The older lady was referred to her endocrinologist for reevaluation of her thyroiditis, which was found to be under control. Interestingly, this side effect was proven to be transient in all patients, with no need for any special relevant treatment, and to be correlated with urticaria improvement. The improvement course of the hair loss is presented in **Figure 1**. By week 20, all patients had UAS7 < 16 and UCT > 12. All patients are still on omalizumab. One patient still reports mild, but acceptable hair loss that does not seriously affect her quality of life.

Figure 1 *- Scores (0: , 1: , 2: , 3:) from the replies to the question number 23 of the CU-Q2oL questionnaire ("Do you suffer side-effects from the medications you take for hives?") the three patients with hair loss reported since the first administration of omalizumab (week "0").*



We describe for first time, to our knowledge, three cases of mild to moderate hair loss as a side effect associated with omalizumab administration. Since the approval of omalizumab for CSU, 80 patients (46 females) in total have been treated with omalizumab in our center. Although hair loss is listed among the side effects in the SmPC of omalizumab, there are no available data to estimate its frequency. Intriguingly, only the patient with the evident hair loss complained about this side effect, while the other two reported it only when they were in particular asked about their reply to the relevant question of the CU-Q2oL questionnaire. This highlights the importance of the CU-Q2oL questionnaire when assessing urticaria patients, and the fact that hair loss may potentially be underreported when it is not so severe.

All three patients characterized hair loss as a major, distressing side effect, significantly affecting their quality of life, even when there was no evident consequence of it. This side effect could not be attributed to a known trigger from the specialists; however it was still distressing, even as a self-reported side effect.

It is very difficult to pathophysiologically explain why this side effect occurs. It could be speculated that since mast cells appear to have some influence on hair cycle regulation (12), downregulation of mast cell releasability (13) by omalizumab may interfere with this regulation. However, it is interesting that this symptom was transient and it was associated in all cases with significant CSU improvement.

Conclusion

Hair loss, even as a self-reported side effect, might worsen the quality of life in patients with already deteriorated quality of life due to severe CSU. However, this symptom doesn't seem to be a good reason to stop treatment with omalizumab since it appears to be transient, lasting for 3 to 4 months, in patients who seems to finally benefit from continuous regular administration of omalizumab.

Abbreviations

CSU: chronic spontaneous urticaria
SmPC: Summary of Product Characteristics
UCT: urticaria control tests
UAS7: urticaria activity scores summed over a week
CU-Q2oL: chronic urticaria quality of life questionnaire

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