Journal of Cosmetics, Dermatological Sciences and Applications, 2023, 13, 33-37
https://www.scirp.org/journal/jcdsa
ISSN Online: 2161-4512
ISSN Print: 2161-4105

Chronic Spontaneous Urticaria on Omalizumab Therapy and Latent Tuberculosis Infection: A New Case Report

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How to cite this paper: Abdulwahhab, W.S. and Al Qaydi, F.M. (2023) Chronic Spontaneous Urticaria on Omalizumab Therapy and Latent Tuberculosis Infection: A New Case Report. *Journal of Cosmetics, Dermatological Sciences and Applications*, **13**, 33-37.
https://doi.org/10.4236/jcdsa.2023.131003

Received: December 31, 2022
Accepted: March 12, 2023
Published: March 15, 2023

Abstract

Background: Chronic Spontaneous urticarial (CSU) is a common dermatological problem characterized by recurrent pruritic or burning wheals last less than 24 hours and treated by many modalities of therapy including systemic antihistamines and in refractory cases with Omalizumab anti-IgE antibody biological injection. Latent tuberculosis infection (LTBI) is diagnosed based on a positive tuberculin skin test or QuantiFERON-TB test without evidence of active tuberculosis. **Aim:** To document a new case report of a patient with a history of CSU and latent tuberculosis on Omalizumab therapy during Isoniazid (INH) prophylaxis. **Case Report:** A-53-year-old woman with a history of CSU and newly identified LTBI who have been treated with INH monotherapy before starting Omalizumab injection followed up over 24 weeks course of therapy for any sign of tuberculosis reinfection. **Conclusion:** Omalizumab injection was used effectively for the treatment of CSU in a patient with latent tuberculosis infection with minimal risk of tuberculosis reactivation.

Keywords

Chronic Spontaneous Urticaria, Latent Tuberculosis, Omalizumab, QuantiFERON-TB Test

1. Introduction

CSU is a heterogeneous disorder with recurrent pruritic wheals and angioedema or both that markedly affects patients' quality of life [1] [2]. At any given time, CSU is believed to affect 0.5% - 1% of the global population [3]. EAACI/GA (2)

LEN/EDF/WAO guidelines recommend approved doses of second-generation H1 antihistamines as first-line treatment for CSU, and up to four times the approved dose as the second-line treatment. However, a significant proportion of patients continue to experience symptoms. Third-line treatment includes add-on therapy with omalizumab [2].

The anti-IgE antibody omalizumab is used in CSU patients resistant to antihistamine treatment [4] and it is currently the only drug approved for use. International and national guidelines recommend its use after the failure of antihistamines at standard and increased doses.

The incidence of tuberculosis varies worldwide, of those infected with *Mycobacterium tuberculosis*, only about 5% - 10% develop active tuberculosis during their lifetime [5] [6]. Most other patients carry latent tuberculosis infection remaining asymptomatic and noninfectious while their host immune response contains the infection. The immune system may then eradicate the LTBI, or the infection may remain and become activated at a later point in time, sometimes several years later [7]. However, patients with LTBI and an impaired immune system, such as those co-infected with the human immunodeficiency virus or those receiving immunosuppressive treatment, have a much higher likelihood of developing active tuberculosis [8] [9].

Biologic therapies, in particular TNF-α inhibitors, pose a risk for opportunistic infections and for reactivating LTBI [10]. Recent guidelines recommend screening for LTBI before initiation of anti-TNF-α biologic therapy. However, non-TNF-α inhibitor biologics do not seem to be associated with the same risk of TB reactivation as TNF-α inhibitors, caution is warranted until longer-term data are available. Until then, it is appropriate to apply the same screening strategies as for traditional TNF-α inhibitors [11].

In the present case report, we are describing an A-53-year-old woman who has a history of severe CSU for 12 weeks duration, refractory to H1-antihistamine therapy, diagnosed accidentally as LTBI and treated with Omalizumab for the 24 weeks duration without any sign for re-activation of tuberculosis infection. The consent form was taken from the patient about the publication of her condition.

2. Case Report

A 53-year-old woman presented to the clinic with a 12 weeks history of daily recurrent intermittent flares of severely pruritic urticaria. The patient's condition is sometimes associated with oedematous swelling of both eyelids and lips with difficulty in breathing. Her symptoms were not triggered by a physical stimulus like scratching the skin, exercise, stress, cold, heat, sunlight, or contact with water or chemicals. She was not on any regular medications and did not have any recent infections or psychological stress. She also denies having a family history of urticaria. Her condition was associated with a severely impaired quality of life. On physical examination, generalized erythematous wheals are seen with a negative skin provocation test. Angioedema involves both upper eye-

lids. According to the patient, the rash would disappear spontaneously within 24 hours and reappear again throughout the body. Urticaria activity score (UAS7) was calculated at the initial presentation which revealed severe urticaria with a score of 40. Laboratory tests showed high total IgE levels > 3000 IU/ml, Normal eosinophils and basophils, and a negative result on the antinuclear antibodies (ANA) test. Thyroid antibodies were also negative. The diagnosis of severe chronic spontaneous urticaria was confirmed. She underwent treatment with second-generation H1 antihistamines in up to four-fold of the dosing but remained symptomatic. Omalizumab, 300 mg subcutaneously every 4 weeks was initiated as an add-on treatment. At the time of the diagnosis, incidentally, during routine blood tests, LTBI was diagnosed (positive Quantiferon test (QuantiFERON-TB test (Cellestis, Carnegie, Vic., Australia), positive TST, and a negative chest x-ray, consistent with LTBI). The patient was referred to the pulmonology clinic where she was started on INH prophylaxis therapy and simultaneously we started with Omalizumab 300 mg subcutaneous injection administered every 4 weeks. After treatment with 3 doses of Omalizumab injections administered in 12 weeks duration, the patient was free of symptoms (no new wheals or angioedema) and UAS7 improved significantly (0). Omalizumab was discontinued after the administration of 6 doses in 24 weeks where the patient achieved complete urticarial clearance. The patient did not experience any adverse effects during the treatment. A 12-week follow-up was planned for re-evaluation of the patient and therapy without any signs of relapse. Regarding LTBI, the patient did not experience any signs of TB re-activation throughout her treatment course.

3. Discussion

The recent clinical guideline for tuberculosis screening regarding Omalizumab therapy for CSU recommended no TB screening required [12] [13]. While treatment with other biologics for example in psoriasis the National Psoriasis Foundation recommends that patients with psoriasis who are candidates for biologic treatment should be screened for LTBI and, where appropriate, receive anti-tuberculosis prophylaxis before initiating biologic therapy [8]. Waqas *et al.* recently demonstrated a low risk of TB reactivation in 3 case reports of psoriasis diagnosed with LTBI treated with Ustekinumab biology during INH prophylaxis [14]. The risk of TB re-activation in cases of LTBI during therapy with Omalizumab studies is unclear and not discussed in detail. However, this is the first case report documenting a case of CSU and LTBI treated with Omalizumab injection without signs of TB reactivation during the course therapy. The safety profile of omalizumab is favorable [15]. But appropriate caution must be taken with all biologics regardless of their safety.

Screening for LTBI and prophylactic therapy if there is evidence of infection is currently the standard for all patients who are candidates for biological therapy. Recommendations for the management of LTBI in patients treated with biologics are mostly concerned with TNF inhibitors while the risk of TB in those using

non-anti-TNF targeted biologics is negligible or absent. As a consequence, it is expensive to perform the TST and IGRAs in patients undergoing treatment with biologics characterized by a mechanism of action not interfering with TNF-α [16]. In addition, data from clinical trials indicate the absence of TB risk in patients treated with omalizumab, hence suggesting that LTBI detection tests may be unnecessary. We suggest taking into consideration environmental and host-related risks for tuberculosis in patients with CSU requiring biological therapy. The literature confirmed a low or absent risk for non-anti-TNF targeted biologics [17].

4. Conclusion

Omalizumab injection can be used effectively for the treatment of CSU associated with LTBI with minimal risk of tuberculosis reactivation. However, because there are no clear guidelines or recommendations regarding prophylaxis for LTBI in patients treated with omalizumab, and due to the limited number of clinical trials and absence of available data, it is difficult to know the certain risk of LTBI reactivation treated with omalizumab. This case report is not enough to draw any definitive safety conclusions. Conduction of more studies with larger sample sizes is recommended to demonstrate the safety of Omalizumab biology in cases of CSU diagnosed with LTBI and to assess the risk of TB reactivation and to obtain more information on the long-term safety and therefore allow definitive conclusions about TB risk associated with Omalizumab.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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