Use of Omalizumab for Cold Urticaria Refractory to Therapy

Patricia Choi, M.D. and Nicholas Hartog, M.D.
Spectrum Health/Michigan State University, Allergy and Immunology Department

SPECTRUM HEALTH®

College of Human Medicine
MICHIGAN STATE UNIVERSITY

Background

Cold urticaria is a subtype of physical urticarias. It is a unique subset that can present with life-threatening anaphylaxis with cold exposure. Much like the treatment for other forms of chronic urticaria, antihistamine therapy is the mainstay of pharmacologic therapy for cold urticaria. Second-generation H1 antihistamines are the first line of treatment for cold urticaria; however, some patients may be refractory to maximum antihistamine therapy. Omalizumab is a humanized monoclonal anti-IgE antibody that was approved for treating chronic spontaneous/idiopathic urticaria in 2013. The use of omalizumab continues to expand. We hypothesize that the patients who failed first line therapy for cold urticaria will improve with omalizumab therapy.

Cases

- **Patient 1**. 6 y.o. male who was found to have hives when playing outside during winter and coming out of the swimming pool.
- **Patient 2**. 10 y.o. female who developed anaphylaxis after coming out of the swimming pool and hives with exposure to air conditioning.
- **Patient 3.** 22 y.o. male who had shortness of breath, generalized hives, and syncope after jumping into a lake.
- All patients failed maximum second-generation H1 antihistamine and anti-leukotriene therapy (+/- H2 inhibitor).

Results

- After being started on omalizumab, all three patients have shown decreased frequency of urticarial eruptions, better tolerance to cold exposure, and no episodes of anaphylaxis.
- Patient 1 is able to go outside at recess during winter.
- Patient 2 is able to tolerate air conditioning and no cases of anaphylaxis since initiation of omalizumab therapy.
- Patient 3 specifically showed significant reduction in response to the 5-minute ice cube test, which was limited to erythema after the first does of omalizumab.

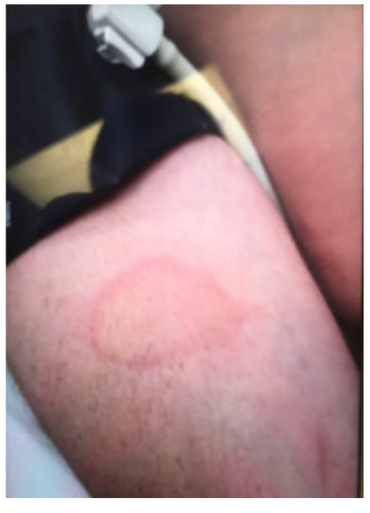
Table1. Summary of the symptoms and treatment course for all three patients

	Patient 1 (6 y.o. M)	Patient 2 (10 y.o. F)	Patient 3 (22 y.o. M)
ICD 10 code for approval	Chronic urticaria. L50.8	Urticaria due to cold. L50.2	Urticaria due to cold. L50.2
Ice cube test	Positive (hives in 7 min)	Positive (hives in 5 min)	Positive (hives in 2 min)
Symptoms			
With air conditioning	None	Hives	Hives
With water exposure	Hives	Anaphylaxis after swimming	Hives after shower/Anaphylaxis after swimming
Cold exposure during winter	Hives	Hives	Anaphylaxis
History of anaphylaxis	None	Yes	Yes
Epinephrine use	No	Yes	Yes
Treatment			
Medications failed	Cetirizine, ranitidine, montelukast	Cetirizine, montelukast	Cetirizine, ranitidine, loratidine, montelukast
Duration of failed therapy	8 months	3 years	No delay
Omablizumab dose	150 mg every 28 days	300 mg every 28 days	300 mg every 14 days*
Ice cube test (post-omalizumab)	negative	not done	improved

*Recently changed from 300 mg every 28 days due to incomplete symptom resolution

5-minute Ice Cube Test

Pre-omalizumab



Post-omalizumab

5-minute Ice cube test on **Patient 3** showed that, compared to pre-omalizumab, post-omalizumab ice cube test after just one dose of omalizumab 300 mg demonstrated improvement with absence of swelling or significant itchiness. There is, however, residual erythema.

Conclusion

- Cold urticaria accounts for one-third of all cases of physical urticarias, and it is considered one of the more dangerous urticarias with potential life-threatening anaphylaxis reaction[1].
- Some cold urticaria patients do not fully respond to first line therapy, second-generation H1-antihistamine.
- When the first line therapy fails, omalizumab should be considered as it can potentially prevent further critical anaphylactic events.
- There are only a few cases on the use of omalizumab as a therapy for cold urticaria[2,3].
- We have not observed any cases of anaphylaxis in our patients since the initiation of omalizumab.

References

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