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Case Report

Efficacy and safety of omalizumab in the treatment of chronic urticaria: A case series

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Abstract Chronic idiopathic urticaria (CIU) is a disease with significant impact on the quality of life owing to its morbidity and relative high prevalence. Omalizumab is a recombinant monoclonal antibody against IgE that inhibits binding of IgE to FcεRI on the cell surface of mast cells. Its role has been thoroughly studied in asthma. We present a case series focusing on the role of subcutaneous omalizumab in the treatment of CIU along with its safety profile in terms of immediate and late side effects.

Key words
Omalizumab, chronic idiopathic urticaria, IgE.

Introduction

Urticaria is a condition characterized by localized or widespread pruritic wheals that typically exist for no more than 24 hours, having no apparent external triggers.[1] By definition, acute urticaria lasts no longer than six weeks, whereas chronic urticaria lasts longer than six weeks, often several years. Chronic urticaria that has no detectable cause is termed as chronic idiopathic urticarial (CIU). It is characterized by blanchable, raised, palpable wheals, which can be linear, annular, or arcuate. They can occur on any skin area; are usually transient and migratory; and may coalesce rapidly to form large areas of erythematous, raised lesions that blanch with pressure. Pathogenesis of urticaria involves the release of histamine from cutaneous mast cells, basophils. IgE also plays an important role in chronic idiopathic urticarial.[2]

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Omalizumab is a recombinant monoclonal antibody against IgE that inhibits binding of IgE to FcεRI on the cell surface of mast cells.[3] Its role has been thoroughly studied in asthma.[4,5] We present a case series focusing on the role of subcutaneous omalizumab in the treatment of CIU along with its safety profile in terms of immediate and late side effects.

Case Reports

All cases reported here, had presented in Department of Dermatology, Islamabad Medical Complex Hospital, NESCOM as chronic idiopathic urticaria. These patients were offered treatment with omalizumab, as 3-month trial of conventional therapy with antihistamine was less effective, and they were having daily relapses of urticarial rash. Patients with history of systemic disease, previous biologic treatment, drug allergies and anaphylaxis, abnormal baseline investigation like liver function tests, urea, creatinine, electrolytes, antinuclear factor and full blood count. The severity of urticaria was graded as itch severity score[6] (ISS) taken at baseline, 24 hours and 1 week after omalizumab

injection (**Table 1**). All patients were followed up for side effects, immediate within 24 hours and late after 1 week of injection.

Table 1 Itch severity score [6].

No.	*Pruritus feature*	*Categories*	*Scoring*	*Maximal scoring*
1.	Distribution	Pruritus at a single location	1	3
		Pruritus at multiple locations	2	
		Generalized pruritus	3	
2.	Severity	Pruritus without the need to scratch	1	5
		Pruritus with the need to scratch but without excoriation	2	
		Pruritus unrelieved by scratching but without excoriation	3	
		Pruritus accompanied by excoriation	4	
		Totally restless	5	
3.	Frequency	Four short episodes (<10 min)	1	3
		One long episode (>10 min)	2	
		Continuous pruritus	3	
4.	Sleep disturbances	Each episode of awakening due to pruritus		

Case 1

A 40-year-old male presented with history of pruritus and rash for the past 4 months. He was evaluated and diagnosed as chronic urticaria. There was no specific trigger and he developed severe itching followed by urticarial patches on the skin all over the body. Previously he had been taking antihistamines with no significant relief. Treatment with omalizumab was commenced with dosage of 300mg subcutaneously. ISS noted on baseline was 15, it reduced to 3 after 24 hours and 1 week. He did not report any immediate or late side effects from the treatment.

Case 2

A 35-year-old female presented with history of generalized itching over arms, legs and back, followed by erythematous patches for the past 8 months. It was spontaneous in onset, causing significant disturbance in her daily activities. She had been taking antihistamine, maximum doses with only temporary relief and gradual worsening in frequency of symptoms. She was injected omalizumab 300mg subcutaneously and followed for changes in ISS from baseline. She reported significant improvement with ISS of 14 pre-treatment reducing to 4 after 24 hours to 3 after a week. No immediate or late side effects were reported.

Case 3

A male, 29-year-old came in OPD with 12-month history of generalized body itching, occurring two to three times a day, followed by hives over skin. He also complained of swelling of lips and around eyes. Previously he had been taking antihistamine, standard doses with no improvement in his symptoms for the past 6 months. After omalizumab 300mg subcutaneously he reported improvement in symptoms. ISS recorded at baseline 9, after 24 hours 6 and 3 after 1 week. Patient reported no side effects after 24 hours and 1 week of injection.

Case 4

A 42-year-old male, presented with recurrent episodes of pruritus all over the body for the past 10 months. It was followed by generalized urticarial patches and wheals. He had disturbance in sleep because of increasing

frequency of symptoms almost every night, with no relief in symptoms with conventional therapy. After discussing the treatment option, he was given 300mg omalizumab subcutaneously. He reported remarkable improvement in itch severity score over from baseline of 13 followed by 5 after 24 hours and 2 after one week postinjection interval. There were no side effects reported.

Case 5

A 27-year-old female presented to us with history of urticarial rash occurring over arms and legs, intermittent, 3-4 times a week associated with severe itching for the past 9 months. She had been taking antihistamine to which she showed no improvement in symptoms. Omalizumab 300mg was injected subcutaneously. ISS at baseline was 13, improved to 5 after 24 hours and 3 after 1 week. There were no side effects reported.

Discussion

Our case series included 5 patients who presented with CIU, resistant to conventional therapy. All the patients showed remarkable improvement in symptoms after 300mg omalizumab subcutaneously assessed as per ISS 24 hours and 1 week later. This is consistent with clinical trials that showed improvement in symptoms after initial dose of 300mg omalizumab7-10.[7-10] The improvement in symptoms after omalizumab shows that chronic urticaria is IgE-mediated; other mechanisms include decrease in release of inflammatory mediators from basophils and mast cells.[11]

Omalizumab led to decrease in ISS from a mean of 12.8 to a mean of 4.6 after 24 hours and 2.8 after 1 week, previous clinical trials show decrease in ISS from baseline to mean change -9.8±6 in patients receiving 300 mg omalizumab.[12] In another trial a decrease in ISS was reported by 9.4 points from baseline at 12 weeks after receiving 300mg Omalizumab versus placebo group.[13]

Omalizumab has shown promising results in controlling CIU by various mechanisms. Firstly, it inhibits the binding of IgE to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils.[3,4] Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of allergic response mediators, as degranulation of mast cells and basophils would not be possible.[13] Secondly, it binds to circulating IgE, irrespective of allergen specificity. This results in biologically and functionally inert IgE-anti-IgE complexes that have specifically been shown not to activate the complement system.[5]

Thirdly, it downregulates FcεRI on basophils,[13] mast cells,[14] and dendritic cells.[15] This process leads to reduced expression of FcεRI on these cells resulting in decreased binding of circulating IgE, hence, preventing the release of inflammatory mediators. Although majority CIU patients do not have single identifiable triggers, and not necessarily have high IgE levels, therefore, multiple stimuli can lead to chronic urticaria. Omalizumab has also been shown to reduce the expression of FcεRI on dendritic cells; and attenuates the degree of allergen presentation and processing.[15]

As previous clinical trials reported, patients show no serious side effects, neither early nor late.

References

1. Greaves MW. Chronic urticaria. *N Engl J Med.* 1995;**332**:1767-72. [Erratum, *N Engl J Med.* 1995;**333**:1091.]

2. Vonakis BM, Saini SS. New concepts in chronic urticaria. *Curr Opin Immunol*. 2008;**20**:709-16.
3. Presta LG, Lahr SJ, Shields RL, Porter JP, Gorman CM, Fendly BM *et al*. Humanization of an antibody directed against IgE. *J Immunol*. 1993;**151**:2623-32.
4. Schulman ES. Development of a monoclonal anti-immunoglobulin E antibody (omalizumab) for the treatment of allergic respiratory disorders. *Am J Respir Crit Care Med*. 2001;**164**:S6-11.
5. Owen CE. Anti-immunoglobulin E therapy for asthma. *Pulm Pharmacol Ther*. 2002;**15**:417-24.
6. Reich A, Medrek K, Szepietowski JC. Four-item itch questionnaire – validation of questionnaire. *Przegl Dermatol*. 2012;**99**: 600-4.
7. Naaman S, Sussman G. Chronic idiopathic urticaria: treatment with omalizumab. *Skin Therapy Lett*. 2014**;**19**(6):1-4.**
8. Saini S, Rosen KE, Hsieh HJ, Wong DA, Conner E, Kaplan A, Spector S, Maurer M: A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J Allergy Clin Immunol*. 2011;**128**:567-73.e1.
9. Maurer M, Rosén K, Hsieh H-J, Saini S, Grattan C, Gimenéz-Arnau A *et al*. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;**368**:924-35.
10. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenéz-Arnau A *et al.* Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med*. 2013;**368**:924-35.
11. Chang TW. The pharmacological basis of anti-IgE therapy. *Nat Biotechnol.* 2000;**18**:157-62.
12. Saini SS, Bindslev-Jensen C, Maurer M, Grob JJ, Bülbül Baskan E, Bradley MS *et al*. Efficacy and safety of omalizumab in patients with chronic idiopathic/spontaneous urticaria who remain symptomatic on H_1 antihistamines: A randomized, placebo-controlled study. *J Invest Dermatol*. 2015;**135**:67-75.
13. MacGlashan DW Jr, Bochner BS, Adelman DC, Jardieu PM, Togias A, McKenzie-White J *et al*. Down-regulation of Fc(epsilon)RI expression on human basophils during in vivo treatment of atopic patients with anti-IgE antibody. *J Immunol*. 1997;**158**:1438-45.
14. Beck LA, Marcotte GV, MacGlashan D, Togias A, Saini S. Omalizumab-induced reductions in mast cell Fc epsilon RI expression and function. *J Allergy Clin Immunol*. 2004;**114**:527-30.
15. Prussin C, Griffith DT, Boesel KM, Lin H, Foster B, Casale TB. Omalizumab treatment downregulates dendritic cell FcepsilonRI expression. *J Allergy Clin Immunol.* 2003;**112**:1147-54.