

# Case Series: Refractory Cases of Hyper-serum IgE Achieve Transformative Decrease by TCM Therapy

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## Case report

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# **Abstract**

## **Background:**

Chronic conditions from IgE-mediated hypersensitivity reactions affect over 150 million Americans, but affordable and effective treatment options remain largely unavailable to the pediatric population.

Traditional Chinese medicine has been shown to reduce IgE levels in refractory cases of hyper-serum IgE and have transformative effects in pediatric patients with chronic allergic inflammation.

## **Presentation:**

Here we present ten patients with chronic atopic conditions and refractory hyper-serum IgE who were treated with TCM therapy. The patients had at least two atopic conditions as well as multiple allergic sensitivities to foods and environmental allergens: all of the patients presented with food allergies (FA) and atopic dermatitis (AD), 60% of patients presented with an environmental allergy (EA), 40% of patients presented with asthma (AS), 10% had celiac disease (Celiac), and 10% had eosinophilic esophagitis (EoE). All of the affected patients had IgE levels greater than 5,000kIU/L (normal =300kIU/L) prior to treatment. None of the patients had an IgE of greater than 5,000kIUL after treatment. We treated 10 children with IgE-mediated hypersensitivity reactions using topical and oral TCM and found an average reduction of 3,723kIU/L IgE per patient ( $p=0.01$ ) or 79%.

## **Conclusion:**

We present a ten-patient case series on the effective lowering of hyper-serum IgE using Traditional Chinese Medicine in otherwise refractory pediatric cases of chronic atopic inflammation. TCM is an affordable and safe alternative for chronic atopic conditions compounded with hyper-serum IgE. Future research via random controlled trials should be used to test the efficacy of TCM.

## **Background:**

In less-developed countries, elevation of serum immunoglobulin E (IgE) is associated with the immune response to parasitic infection, whereas in industrialized countries, IgE elevations are most commonly associated with type one hypersensitivity (anaphylactic) allergic reactions. In these acute IgE-mediated hypersensitivity reactions, a harmless allergen triggers aberrant production of IgE, which induces mast cell and basophil degranulation and causes an immediate inflammatory response such as the bronchospasm seen in anaphylaxis (7). It has been well-documented that IgE antibodies are associated with the acute inflammatory response.

There are also chronic causes of elevated IgE including an autosomal dominant mutation in the STAT3 gene, which causes Job Syndrome. In Job Syndrome, the chronic elevation of serum IgE comes at the expense of other antibodies, and the lack of antibody diversity causes frequent upper-respiratory and skin infections, while the chronically elevated IgE causes chronic inflammatory conditions such as eczema.

However, Job syndrome is exceedingly rare, with only about 250 reported cases since its discovery in 1966.

A far more common cause of chronic IgE elevation is associated with IgE-mediated immunogenic hypersensitivity conditions such as atopic dermatitis, asthma, and food allergy. In chronic IgE mediated hypersensitivity the elevated serum IgE is caused by chronic chemokine and cytokine secretion. Serum levels of IgE in healthy individuals ranges from 50kIU/L to 300kIU/L, while some chronically atopic individuals may have up levels of up to 20,000kIU/L (4). Chronic conditions from IgE-mediated hypersensitivity affect over 150 million Americans.

Despite the prevalence of these conditions, the present management for chronic IgE-mediated hypersensitivity is limited. Food avoidance remains primary treatment for food allergy. Some patients with multiple food and environmental allergies can safely try omalizumab, an anti-IgE monoclonal antibody, but it is restricted to certain age groups and a specific range of serum IgE. Like many biologics, the cost of treatment is a limiting factor in therapeutic modalities. Traditional Chinese medicine (TCM) has a longstanding history as an anti-inflammatory agent and may be a safe and financially viable alternative for patients with chronic IgE-mediated hypersensitivity.

## Presentation:

In this report based on a retrospective analysis, we present a series of 10 patients with IgE levels greater than 5,000kIU/L (normal =300kIU/L) who were administered TCM topical and oral treatments and achieved transformative results. This chart review was conducted according to the IRB approval "Retrospective chart review: practice based traditional Chinese medicine therapy effect on laboratory safety and clinical and immunological outcomes", Protocol #12798. At the time of initial treatment, the median patient age was 7.5 years, and the majority of the study population were Caucasian (70%). This series consists of 4 male and 6 female patients. In this cohort, all patients had at least two atopic conditions as well as multiple allergic sensitivities to foods and environmental allergens: all of the patients presented with food allergies (FA), while 60% of patients presented with an environmental allergy (EA), 40% of patients presented with asthma (AS), 10% had celiac disease (Celiac), and 10% had eosinophilic esophagitis (EoE) (Table 1).

All cases had previously been treated with at least one standard therapy prior to TCM treatment. Complete blood counts with differential, liver function tests, serum blood urea, nitrogen, and creatinine levels were in normal ranges at baseline were obtained. After TCM therapy, patients continued to follow-up with their referring provider, who ordered blood work again at 6 months of treatment.

All patients with a serum IgE greater than 5,000 kIU/L were eligible for TCM therapy, however this cohort had a mean IgE of 18,033kIU/L at baseline. After administration of TCM topical or oral treatments, all ten patients experienced a rapid and significant drop in serum IgE (Figure 1), mean decrease of 3,723kIU/L IgE per patient ( $p=0.01$ ). This corresponds to an average decrease of 79%. Prior to administration of TCM, each patient had a baseline IgE level of greater than 5,000 kIU/L.

## **Discussion And Conclusion:**

Omalizumab is a common pharmaceutical agent used in the treatment of severe IgE hypersensitivity and various allergic conditions (8). It functions as a humanized monoclonal IgE antibody halting the process of the allergic response (8). While omalizumab is effective in minimizing symptoms associated with IgE hypersensitivity, treatment studies have shown negligible reduction of immunoglobulin production in refractory patients (8).

IgE-mediated hypersensitivity has become increasingly prevalent in recent years and continues to be on the rise, however effective and affordable treatment options remain scarce for the pediatric populations. The results of this case series demonstrate that TCM therapy should be investigated as a IgE-lowering agent in atopic children as a possible adjunct to current therapies.

The significant anti-inflammatory effects of TCM therapy experienced by these patients has been well demonstrated. TCM has been shown to inhibit mast cell activation and pro-inflammatory cytokines/signaling pathways (TNF- $\alpha$ , IL-8, NF- $\kappa$ B) by disrupting binding sites on IgE (7). This is a possible mechanism to explain how TCM was able to suppress inflammatory signal pathways and lower IgE in these atopic patients. TCM's utility is likely not just limited to IgE related food allergies (7). With this novel approach to refractory IgE hypersensitivity, further avenues for safe practice of TCM in clinical practice should be pursued.

## **Abbreviations:**

TCM: Traditional Chinese Medicine

FA: food allergies

EA: Environmental allergies

AD: Atopic dermatitis

AS: Asthma

EoE: Eosinophilic esophagitis

TNF- $\alpha$ : Tumor necrosis factor - $\alpha$

IL-8: Interleukin 8

NF- $\kappa$ B: Nuclear factor kappa B

## **Declaration:**

- Ethics approval and consent to participate: All patients provided consent.

- Consent for publication: Written informed consent for publication was obtained from the patients. A copy of the consent form is available for review by the Editor of this journal.
- Availability of data and material: The datasets of this case series are available from the corresponding author on reasonable request.
- Competing interests: The authors do not have any competing interests.
- Funding: There was no funding given for this case series.
- Authors' contributions: J.N had analyzed the data, T.M had interpreted the data, S.U: collected data and drafted the manuscript P.E/D.C/X.L: had reviewed and revised the manuscript

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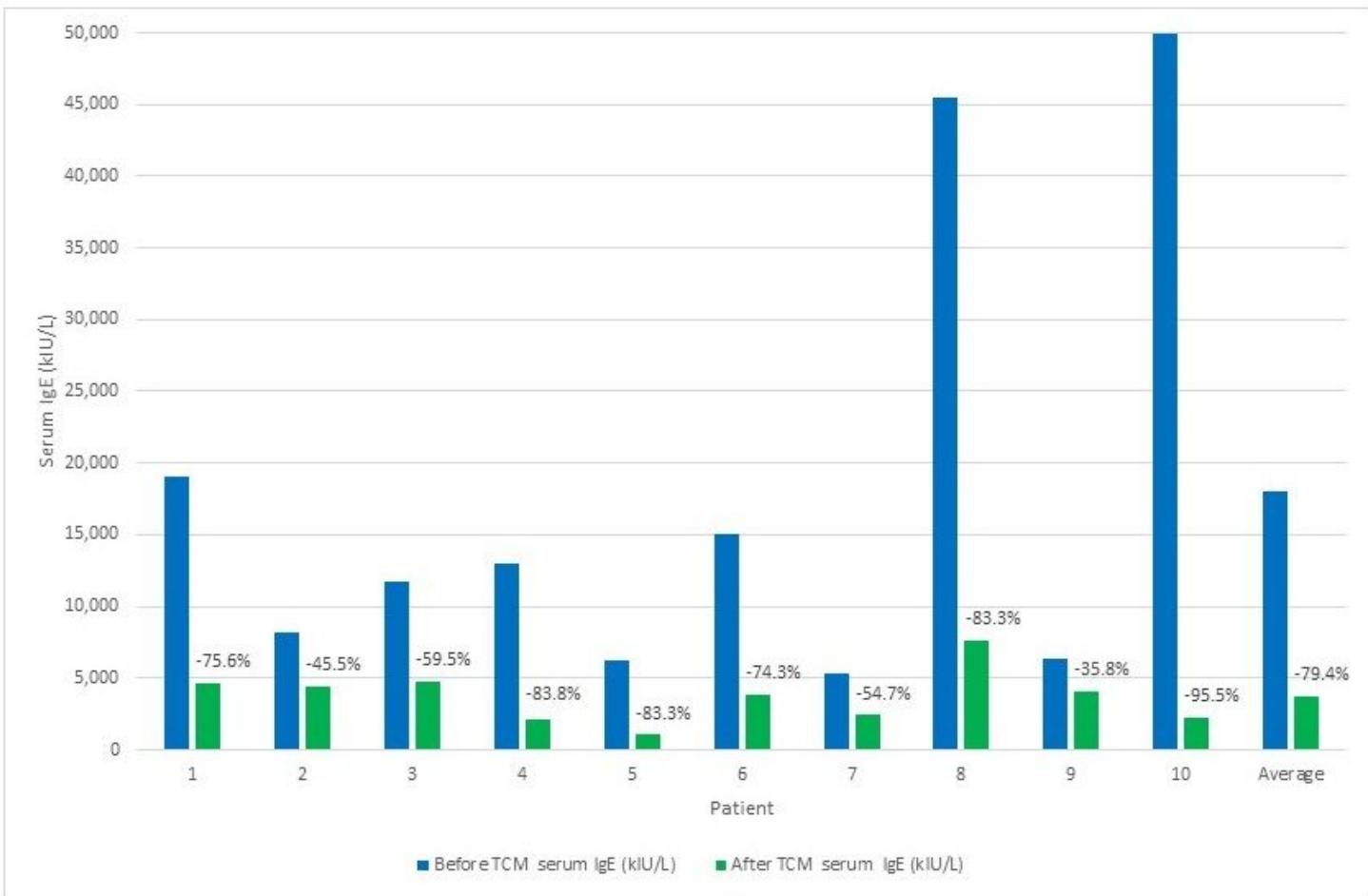
## Table:

Table 1

Patient Characteristics FA, food allergy; EA, environmental allergy; AD, atopic dermatitis; AS, asthma; EoE eosinophilic esophagitis; Celiac, celiac disease

Patient #	ID Number	Age	Sex	Ethnicity	Atopic History
1	WL52087	7	M	White	FA, AD, EA
2	KD234065	10	F	White	FA, AD, AS, EA
3	MR903552	9	M	White	FA, AD, AS, EA, EoE, Celiac
4	ET318691	7	M	Asian	FA, AD, AS
5	JO536367	8	F	White	FA, AD, AS, EA
6	CK17100	3	F	Asian	FA, AD, EA
7	FG921273	1	F	White	FA, AD, AS, EA
8	N/A	3	F	Asian	FA, AD, EA
9	EF761057	13	F	White	FA, AD, AS
10	EW584297	11	M	White	FA, AD, AS

## Figures



**Figure 1**

Percent reduction of serum IgE before and after treatment with TCM ( $P=0.01$ ,  $\sigma$  after TCM = 1771 kIU/L,  $\bar{x}$  after TCM = 3723 kIU/L)