

Atopic Dermatitis is a Multi-Organ Disorder Disease Involving not only the Skin but also the Intestinal Tract and Cervical Spine

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ABSTRACT

Atopic dermatitis (AD) has traditionally been regarded as a skin disorder; however, accumulating clinical evidence suggests that it may represent a multi-organ disease involving the intestinal tract and cervical spine. This article reviews the authors' long-term clinical experience and observations regarding the systemic involvement of AD, particularly in relation to *Staphylococcus aureus* colonization and superantigen-mediated inflammation. Previous studies have demonstrated a high prevalence of *S. aureus* on the skin of AD patients, elevated serum IgE levels, and positivity for antibodies against staphylococcal enterotoxins. The authors further investigated gastrointestinal and cervical spine abnormalities in AD patients through duodenal biopsy and cervical MRI examinations. Among 32 examined patients, 65.6% showed both duodenal and cervical spine abnormalities, suggesting significant extra-cutaneous involvement. In addition, the article presents a representative case of severe AD treated with standard therapy combined with topical povidone-iodine disinfection therapy. Marked clinical improvement was accompanied by substantial reductions in serum TARC, IgE, and anti-SEA antibody levels over time. These findings support the hypothesis that superantigens produced by *S. aureus* contribute not only to skin inflammation but also to systemic organ involvement in AD. The authors conclude that atopic dermatitis should be considered a multisystem disorder requiring comprehensive evaluation and management beyond the skin alone.

Keywords

Staphylococcus aureus, Superantigens, Povidone-iodine, Atopic dermatitis.

Introduction

Based on test data, we have experienced cases in which atopic dermatitis patients have a high multi-antigen positive rate, which is not seen in patients with allergic diseases such as bronchial asthma and allergic rhinitis. In addition, we often encounter patients with atopic dermatitis who have exorbitant IgE levels. In addition, it is widely recognized that *Staphylococcus aureus*

is detected at a high rate from the skin of patients with atopic dermatitis. *Staphylococcus aureus* produces many toxins, which are named superantigens [1,2]. Dr. Yamada [3] of Kinki University has already reported that many patients with atopic dermatitis have colitis when examining the large intestine of atopic dermatitis. Professor Kira [4] of Kyushu University has already reported that many patients with atopic dermatitis have myelitis. Therefore, we also examined the duodenum and cervical spine of many patients with atopic dermatitis, and experienced many disorders of the intestinal tract and cervical spine in addition to the skin in patients with atopic dermatitis. In addition, we have experienced many

cases in which these two organs were damaged in the same case of atopic dermatitis.

Our experience to date leading to the argument that atopic dermatitis is not only a skin disease but also a multisystem disease.

We thought that sterilization of *Staphylococcus aureus* detected on the skin of patients with atopic dermatitis with disinfectants would increase the therapeutic effect. Therefore, in June 1993, as the first case, in addition to general treatment, we applied a diluted antiseptic povidone-iodine solution to the eruption against *Staphylococcus aureus* detected on the skin. As a result, we experienced improvement in the patient's skin eruptions and symptoms in a short period of time. Therefore, when we tried a combination of disinfection with povidone-iodine solution in combination with general treatment for atopic dermatitis patients in many cases, we obtained many effects. In 1993, we made a presentation at the Japanese Society of Allergology in Kumamoto. This announcement became widely known, and in September of the following year, NHK's TV program: Today's Health was broadcast as My Announcement: Disinfection Therapy for Atopic Dermatitis. After the broadcast, many patients with atopic dermatitis visited our Chiba City Hospital from all over Japan, and we gained a lot of clinical experience. At the Third Asian Pacific Congress on Antisepsis, Sydney, January 1997, our presentation entitled New successful treatment with disinfectant for atopic dermatitis was published in Dermatology 1997; 195(suppl 2) [5]. From these reports [6], Isodine therapy became widely known in Japan.

Also, the November 1998 TBS TV show: Friday TV Stars, Big Hit! titled these are the famous Japanese doctors2, who gave me the opportunity to introduce them to the Isodine therapy. Taking this opportunity, we were able to see many patients with atopic dermatitis and accumulate a lot of clinical experience. And our presentation titled Significance of *Staphylococcus aureus* toxin (superantigen) in atopic dermatitis in 2004 was published in Science of Skin [7] in 2004. In 2003, the previous year, Dr. Ito et al. [8] wrote a paper titled "Is atopic dermatitis a risk factor for intervertebral disc degeneration? " in Journal of the Neurological Sciences. Dr Kino et al. [9], had reported that there is a lesion in the colon of infants of atopic dermatitis with a food allergy. Among them, they have reported to the Pediatric Radiology that it has also improved inflammation of the colon along with the improvement of the rash of patients in 2002.

In 2015, Dr. Kobayashi [10] of Keio University published a paper reporting that *Staphylococcus aureus* is involved in the onset and exacerbation of atopic dermatitis. However, in 2016, we thought that the symptoms of atopic dermatitis may be caused not only by damage to the skin but also by other organs. We wrote a paper on the importance of disinfection as a general treatment against *Staphylococcus aureus* [11-13]. Inspired by Dr. Kobayashi's paper, we wrote a paper in the same year that atopic dermatitis might be a superantigen disease. This article was highly evaluated, and I was able to make a presentation titled "Atopic dermatitis

is one of superantigens diseases" in the lifelong learning course of the online bulletin of Chiba University School of Medicine. After that, our article [14], including the fact that the frequency of community-acquired infections of MRSA [15] increased, was published in the course that was renewed (<https://inohana.jp/hq/?p=4517>). Based on the data we have reviewed so far, both duodenal injury and cervical spine injury were observed in 21 of 32 (65.6%) patients with atopic dermatitis (Table1).

Table 1: Duodenal biopsy and Cervical MRI findings.

Case No	Age	Histological diagnosis	MRI diagnosis	Clinical diagnosis
1	43	Chronic Duodenitis	CS,OYL	CM
2	32	Chronic Duodenitis	CS	CM
3	31	Chronic Duodenitis	CS	CM
4	26	Chronic Duodenitis	WNR	CM
5	21	Chronic Duodenitis	WNR	CM
6	23	Chronic Duodenitis		WNR
7	25	Chronic Duodenitis	CS	CM
8	28	Mild Duodenitis	CS	CM
9	28	Chronic Duodenitis	WNR	CM
10	36	Chronic Duodenitis	CS	CM
11	33	Duodenitis	WNR	CM
12	24	Mild Duodenitis	CS	CM
13	29	Chronic Duodenitis	CS	CM
14	28	Duodenitis	CS	CM
15	26	Duodenitis	WNR	WNR
16	24	Mild Duodenitis	CS	CM
17	28	Mild Duodenitis	CS	CM
18	20	Chronic Duodenitis		WNR
19	26	Chronic Duodenitis	CS	CM
20	21	Chronic Duodenitis	CS	CM
21	32	WNR	CS	CM
22	28	WNR	CS	CM
23	24	Chronic Duodenitis	CS	CM
24	26	Chronic duodenitis	CS	CM
25	28	WNR	CS	CM
26	30	Chronic duodenitis	CS	CM
27	34	WNR	CS	CM
28	21	Chronic duodenitis	CS	CM
29	38	WNR	CS	CM
30	30	Chronic duodenitis		WNR
31	34	Slight du0denitis		WNR
32	22	Mild Duodenitis		WNR

A Case of Recently Experienced Atopic Dermatitis

For patients with atopic dermatitis, we used povidone-iodine as an antiseptic to disinfect the skin, in addition to general treatments such as steroid ointment and moisturizing agents. We present a recent case of treatment that showed dramatic improvement in laboratory data. We will present a case of atopic dermatitis at the age of 47 at the first visit. The serum TARC value at the first visit was very high at 59270 PG/mL and at the treatment day 7 it was halved to 38057 PG/mL. The serum IgE value increased slightly from 62000 IU/mL to 71000 IU/mL in 7 days, and the serum anti-SEA IgE antibody titer (Table 2) increased only slightly at 4.87 IU/mL and 6.13 IU/mL. The serum TARC was 7760 PG/mL, the

serum IgE value was 60000 IU/mL and the serum anti-SEA IgE antibody titer was 4.36 IU/mL in the third examination at the one month of treatment. About 7 months after starting treatment, the serum IgE improved significantly to 22000 IU/mL, the serum TARC to 1314 PG/mL, and SEA to 2.31 IU/mL. About a year after the treatment, the patient happily told me that his life had changed with the improvement of his rash.

Table 2: Changes in allergic tests from the start of disinfection therapy.

	2021.10.26	2021.11.2	2021.12.1	2022.6.2
IgE (IU/mL)	62000	71000	60000	22000
TARC (PG/mL)	59270	38057	7760	1314
SEA (IU/mL)	4.87	6.13	4.36	2.31

TARC: Thymus and Activation-Regulated Chemokine

SEA: Staphylococcal Enterotoxin A

Thus, the serum TARC values and the serum IgE values were dramatically improved over time from the start of treatment. In the second and, the serum IgE value and the serum anti-SEA IgE antibody titer were somewhat higher than the first. It is very interesting that the inspection values will improve so much in a short period of time. We speculate that *S. aureus* was stimulated with a disinfectant and, as a result, produced toxins in large quantities. We had reported that the serum IgE value and the serum anti-SEA IgE antibody titer would change in many cases concurrently with the improvement of the skin lesions from 2 months after the treatment. (Table 2. Changes in allergic tests from the start of disinfection therapy).

Conclusion

Atopic dermatitis is not only a disease of the skin, but *Staphylococcus aureus*, which is highly detected from the skin, is greatly involved in its pathology. *Staphylococcus aureus* produces many toxins. We have experienced that many *Staphylococcus aureus* bacteria are detected in the skin of atopic dermatitis patients who are 0 years old after the onset. In addition, we have experienced many cases in which IgE antibodies against *Staphylococcus aureus* toxins (SEA or SEB) were already positive in blood samples taken from the patient before the age of one year. The toxin acts as a superantigen and causes damage to many organs. *Staphylococcus aureus* is often detected in the skin of children with atopic dermatitis, and antibodies against toxins in the blood are measured early. Therefore, in patients with atopic dermatitis, it is necessary to pay attention to medical care that considers not only the skin but also diseases of the intestinal tract and cervical spine, as we have reported many times.

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