

CASE REPORT

Cross-Reactive Carbohydrate Determinants (CCDs) Causing Interference in Allergen-Specific IgE Antibody Analysis

Jian-Qing Zhang¹, Hong-Gang Sun², Hong Chen¹, Li-Fang Wu³

¹ Department of Dermatology, Shaoxing People's Hospital, Shaoxing, Zhejiang Province, China

² Department of Medical Laboratory, Shaoxing People's Hospital, Shaoxing, Zhejiang Province, China

³ Department of Orthopedic (Joint Sports Medicine and Foot and Ankle), Shaoxing People's Hospital, Shaoxing, Zhejiang Province, China

SUMMARY

Background: The use of CCD antibody adsorbents specifically adsorb CCDs, reducing non-specific IgE interference in chemiluminescence assays, thereby making the detection results of true allergen-specific IgE more accurate.

Methods: Chemiluminescence assays were used to quantitatively detect allergens (total IgE and specific IgE) in patient serum, with heterophile antibody removers to exclude the interference of heterophile antibodies, and anti-CCD IgE adsorbents to exclude the interference of CCDs.

Results: The detection results after using allergen heterophile antibody removers showed no difference from the original results, while the specific IgE returned to normal after using CCD-specific IgE adsorbents, with no significant change in total IgE.

Conclusions: When multiple allergen sIgE are positive simultaneously, or when the allergen detection results do not match the patient's clinical symptoms, history of allergen exposure, or skin test results, it is necessary to perform anti-CCD IgE adsorption tests to improve the accuracy of allergen diagnosis.

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Correspondence:

Li-Fang Wu
Department of Orthopedic
(Joint Sports Medicine and Foot and Ankle)
Shaoxing People's Hospital
Shaoxing, Zhejiang Province, 312000
China
Phone: +86 13858440906
Email: wmdxs2009@126.com

KEYWORDS

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INTRODUCTION

Allergy, also known as an allergic reaction, is an abnormal immune response of the body caused by substances that are usually harmless to people [1,2]. Allergies are the immune system's overreaction to certain substances (such as pollen, pet dander, certain foods, etc.). When exposed to these allergens, the immune system releases chemicals including histamine, leading to the occurrence of symptoms. Allergic symptoms may involve multiple systems. Respiratory tract: sneezing, nasal congestion, rhinorrhea, tearing or red eyes. Skin: urticaria, swelling, itching. Digestive system: oral tingling, swelling, diarrhea. Severe reactions: severe allergic reactions may include loss of consciousness, low blood pressure, severe shortness of breath, and other

symptoms, which is an emergency that can be life-threatening. The main pathogenesis of allergic diseases is mainly mediated by IgE antibodies in type I immediate hypersensitivity reactions [1]. Therefore, the *in vitro* detection of allergen sIgE is an important means of diagnosing allergic diseases. By detecting sIgE in patient serum, allergen detection has the advantages of being rapid, accurate, and painless. This method can qualitatively and quantitatively detect allergens (total IgE and specific IgE.) in patient serum or plasma. It can clarify whether the patient has an allergy risk and the types of allergens, which is of great significance for the prevention, diagnosis, and treatment of diseases. In addition, regular detection of total IgE during the course of the disease is also a useful indicator for follow-up changes in the condition. Specific IgE can accurately screen for allergens causing the disease and is the most specific diagnosis of allergic diseases [3]. For example, specific IgE can accurately detect the value of each allergen, such as how high the IgE value is for egg allergy, which is of great significance for clinical treatment. Our hospital uses chemiluminescence allergen detection technology, which has important clinical application value in the diagnosis of allergic diseases due to its high sensitivity and specificity. The application of chemiluminescence immunoassay technology in the detection of dust mite and peanut allergens has demonstrated its effectiveness and accuracy. However, there is a high rate of discrepancy between its detection results and clinical symptoms, causing great confusion in clinical diagnosis.

CASE PRESENTATION

A patient, male, 3 years old, was hospitalized for adenoid hypertrophy and rhinitis. The patient's blood routine test, biochemical test, and preoperative infectious disease test showed no obvious abnormalities, and there were no obvious allergic symptoms. The results of the allergy test are shown in Table 1. The patient's history does not include pet breeding or any related animal contact. This could be important in a medical context to rule out potential sources of allergens, infections, or other health issues related to animal exposure.

DISCUSSION

Common interfering factors in the detection process of allergens include heterophile antibodies and cross-reactive carbohydrate determinants.

Heterophile antibodies may react with animal proteins in the reagent, leading to abnormally high or low detection results, or even false positives or false negatives, making the detection results inconsistent with clinical diagnosis [4]. Heterophile antibodies are a class of immunoglobulins produced by the human body that have sufficient titer and can weakly bind to immunoglobulins of multiple species with multiple specificities. They

mainly interfere with the test by non-specific binding, bridging capture antibodies, labeled antibodies, or labeled antigens [5]. The patient had no history of pet breeding and no history of related animal contact. The ineffectiveness of heterophile antibody removers excludes the interference caused by heterophile antibodies. As shown in Table 2.

After using anti-CCD IgE adsorbents, specific IgE returned to normal, and total IgE showed no significant change (Table 3). The cause of the patient's abnormal results may be cross-reactive carbohydrate determinants. Cross-reactive carbohydrate determinants are an important cause of false positives in serum allergen detection [6]. Studies have found that some allergic patients have sugar molecules with similar structures in their bodies that can produce specific IgE antibodies similar to allergens, showing positive reactions when detecting allergens [7-9]. However, CCDs do not cross-link two corresponding IgE molecules bound to the surface of mast cells like real allergens, so they cannot cause mast cell degranulation and do not produce clinical symptoms.

The production of cross-reactive carbohydrate determinants is related to various factors, mainly including:

1. Molecular structure similarity: Some allergic patients have sugar molecules similar to allergen structures in their bodies, which can produce specific IgE antibodies and may cause positive reactions when detecting allergens [10].
 2. Cross-reactivity in the immune response: In the immune response process, due to the common sugar structures between some allergens and non-allergens, the immune system may not be able to distinguish these structures, thus producing antibodies against these common structures, leading to cross-reactivity.
 3. Genetic and environmental factors: An individual's genetic background and environmental factors may also affect the production of CCDs. Certain genetic traits may make individuals more likely to produce cross-reactive antibodies, and environmental factors such as infections and diet may also affect the immune system's reactivity to sugar structures [11].
 4. Multispecificity of the immune system: Some antibodies in the immune system, especially IgE, may have multispecificity, meaning they can recognize and bind to a variety of different antigens, including non-allergen substances with similar structures.
 5. Contamination during allergen processing and purification: If there is contamination during the processing and purification of allergens, it may introduce non-target components containing CCDs, which may lead to false positive results in allergen detection [9].
- Excluding the interference of cross-reactive carbohydrate determinants (CCDs) in allergen detection can be done using specific methods. Treating samples with anti-CCD antibody adsorbents can significantly reduce false positive results caused by CCD interference without affecting true positive results. This treatment can improve the accuracy of detection results and help clin-

Table 1. Original results of patient allergen test.

TIgE	D1	D2	E1	E5	F10	F13	F14
58.15	1.00	0.61	1.05	0.91	1.15	1.07	1.00
F2	F23	F245	F27	F3	F4	F88	H1
0.65	0.56	0.56	1.3	1.37	1.04	1.29	0.96
I6	M3	M6	T12	W1	W6	F24	
1.02	1.06	0.92	1.02	1.06	0.92	1.02	

D1 - House dust mites, D2 - Dust mites, E1 - Cat epithelium, E5 - Dog epithelium, F10 - Sesame, F13 - Peanuts, F14 - Soybeans, F2 - Milk, F23 - Crab, F24 - Shrimp, F245 - Egg, F27 - Beef, F3 - Cod, F4 - Wheat, F88 - Lamb meat, H1 - House dust, I6 - Cockroach, M3 - Aspergillus fumigatus, M6 - Alternaria alternata, T12 - Willow, W1 - Ordinary ragweed, W6 - Artemisia annua, reference range (0.00 - 0.35 IU/mL). TIgE - Reference range (0.00 - 105.29 IU/mL).

Table 2. Allergen detection results after treatment with heterophilic antibody treating agent.

TIgE	D1	D2	E1	E5	F10	F13	F14
57.16	0.94	0.59	1.09	0.92	1.19	1.10	1.04
F2	F23	F245	F27	F3	F4	F88	H1
0.63	0.59	0.57	1.32	1.39	1.01	1.28	0.97
I6	M3	M6	T12	W1	W6	F24	
1.00	1.04	0.95	1.33	0.75	1.02	1.27	

D1 - House dust mites, D2 - Dust mites, E1 - Cat epithelium, E5 - Dog epithelium, F10 - Sesame, F13 - Peanuts, F14 - Soybeans, F2 - Milk, F23 - Crab, F24 - Shrimp, F245 - Egg, F27 - Beef, F3 - Cod, F4 - Wheat, F88 - Lamb meat, H1 - House dust, I6 - Cockroach, M3 - Aspergillus fumigatus, M6 - Alternaria alternata, T12 - Willow, W1 - Ordinary ragweed, W6 - Artemisia annua, reference range (0.00 - 0.35 IU/mL). TIgE - Reference range (0.00 - 105.29 IU/mL).

Table 3. Allergen detection results after using anti-CCD IgE adsorbents.

TIgE	D1	D2	E1	E5	F10	F13	F14
58.05	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10
F2	F23	F245	F27	F3	F4	F88	H1
< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10
I6	M3	M6	T12	W1	W6	F24	
< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	< 0.10	

D1 - House dust mites, D2 - Dust mites, E1 - Cat epithelium, E5 - Dog epithelium, F10 - Sesame, F13 - Peanuts, F14 - Soybeans, F2 - Milk, F23 - Crab, F24 - Shrimp, F245 -Egg, F27 - Beef, F3 - Cod, F4 - Wheat, F88 - Lamb meat, H1 - House dust, I6 - Cockroach, M3 - Aspergillus fumigatus, M6 - Alternaria alternata, T12 - Willow, W1 - Ordinary ragweed, W6 - Artemisia annua, reference range (0.00 - 0.35 IU/mL). TIgE - Reference range (0.00 - 105.29 IU/mL).

ical doctors determine specific allergens, effectively preventing and controlling allergic diseases. The application value of CCD antibody adsorbents in chemiluminescence detection is mainly reflected in the following aspects:

1. Reduce false positive results: CCD antibody adsorbents can effectively reduce false positive results caused

by CCDs. In chemiluminescence detection, the presence of CCDs may lead to non-specific binding, thus producing false positive signals. Pre-treating samples with CCD antibody adsorbents can significantly reduce this interference and improve the accuracy of detection results [12].

2. Improve detection specificity: CCD antibody adsor-

bents specifically adsorb CCDs, reducing the interference of non-specific IgE, making the detection results of true allergen-specific IgE more accurate. This is particularly important for chemiluminescence immunoassay methods because these methods rely on the specific reaction between antigens and antibodies [13].

3. Clinical application value: In clinical practice, the application of CCD antibody adsorbents helps doctors more accurately determine specific allergens, thus more effectively preventing and controlling the development of allergic diseases. This is of great significance for the clinical application of chemiluminescence detection methods because it improves the reliability and practicality of detection results [14].

4. Technological progress: With the advancement of CCD antibody adsorbent technology, the sensitivity and specificity of chemiluminescence detection methods are expected to be further improved. This will help the wider application of chemiluminescence detection in fields such as environmental monitoring, food safety, and drug analysis. CCDs exist in a variety of plant or animal-derived allergens, and due to the similarity of results, some unique cross-reactions occur [15].

Therefore, when multiple allergens sIgE are simultaneously positive, or when the allergen test results do not match the patient's clinical symptoms, allergen exposure history, skin test results, etc., it is necessary to perform anti CCD IgE adsorption test to improve the accuracy of allergen diagnosis. The application of CCD antibody adsorbent in chemiluminescence detection, especially in allergen specific IgE detection, plays a crucial role in improving the accuracy and reliability of detection. By reducing false positive results caused by CCD, CCD antibody adsorbents can help improve the clinical application value of chemiluminescence detection methods.

CONCLUSION

When multiple allergens sIgE are simultaneously positive, or when the allergen test results do not match the patient's clinical symptoms, allergen exposure history, skin test results, etc., it is necessary to perform anti CCD IgE adsorption test to improve the accuracy of allergen diagnosis.

Source of Support:

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Declaration of Interest:

All authors declare that they have no conflict.

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