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Carmine red (E-120)-induced occupational respiratory allergy in a screen-printing worker: A case report

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Abstract. *Carmine red (E-120)-induced occupational respiratory allergy in a screen-printing worker: A case report.* Here we present a case report of a patient suffering from occupational rhinoconjunctivitis and asthma due to IgE-mediated carmine red allergy. This is the first description of carmine red allergy in a screen-printing worker in which the diagnosis was documented by quantification of specific IgE antibodies, by skin tests, by a flow-assisted basophil activation test, and by a carmine red challenge test.

Introduction

Carmine (E-120, colour index no. 75470) is a natural red pigment extracted from dried female *Dactylopius coccus var. Costa* or *Coccus cacti* (cochineal) arthropods. Carmine is widely used to colour foods, beverages, cosmetics, and drugs, and it is also used as a histological dye. There have been reports of occupational respiratory disease, including rhinoconjunctivitis, asthma, and extrinsic allergic alveolitis in employees at factories that manufacture natural dyes,[1,2] at spice blenders,[3] and in butcher shops.[4,5] However, there have been no cases reported among screen-printing workers. Screen printing, also known as serigraphy, is a technique in which an image is created on paper, on a textile, or on another type of object by pressing ink through a screen that has some areas blocked so that it is much like a stencil. Reports that carmine can be a food allergen remain anecdotal.[6-8] However, cases of carmine-induced food allergy may increase as natural dyes become even more widely used.

Case report

A 48-year-old woman was referred to our department because of increasing occupational rhinoconjunctivitis and asthma. A detailed medical history, quantification of specific IgE antibodies, and skin tests for aeroallergens excluded traditional inhalant allergies. However, inquiries about her occupational history revealed that she had been working for years as a screen printer and that the respiratory symptoms were probably related to her exposure to carmine red and/or cyan blue powder. None of her co-workers reported similar symptoms.

Quantification of carmine-specific IgE showed levels of 0.92 kUA/L (*f340*, ImmunoCAP, ThermoFisher Phadia, Uppsala, Sweden). In this test, a value ≥ 0.35 kUA/L is considered positive. Skin prick tests with carmine red resulted in a wheal and flare reaction of 5/9 mm, whereas a skin test with cyan blue was negative (< 3/3 mm). Both dyes were provided by the patient and dissolved in saline buffer. Skin prick tests with the two dyes in 2 healthy control individuals were negative. Flow cytometric analysis (FACSCanto II, BD, Immunocytometry Systems, San Jose, CA, USA) of activated peripheral blood basophils was performed using Alexa Fluor 448-coupled anti-IgE (Sigma-Aldrich, Chemic GmBH, Steinheim, Germany) to identify the cells and phycoerythrin-conjugated anti-CD63 (Pharmingen, BD Biosciences, Erembodegem, Belgium) to assess their activation status. The test included a negative control (stimulation buffer without any allergen), a positive control (anti-IgE), carmine red, and cyan blue. To exclude nonspecific basophil activation, the test was also performed using blood from two healthy control individuals who had negative skin prick tests for the dye. Upon challenge with the carmine red, 19% and 28% of the patient's basophils were positive for CD63 after stimulation with 1 and 10 μg/mL carmine, respectively. In contrast, carmine failed to induce expression of CD63 by basophils from the two control subjects under these stimulation conditions. The basophil activation

test for cyan blue was negative in the patient. Specific challenge tests with carmine red that were performed 2 weeks after the last exposure to the powder were positive, resulting in nasal obstruction and a 20% decrease in FEV1. Rhinomanometry was not performed; however, nasal symptoms that included sneezing, a runny nose, and obstruction occurred when the patient came in contact with carmine red. Pulmonary peak flow measurements revealed a personal best value of 400 L/min that dropped to 290 L/min (-27.5%) during exposure to carmine red at the printing office (when the patient was in the vicinity of the printing machine). Due to progressively worsening symptoms, the woman quit her job. The allergic reaction was reported to the Fund for Occupational Diseases.

Discussion

Allergic rhinitis occurs after allergen exposure due to IgE-mediated inflammation of the membranes lining the nose. This inflammation results in nasal symptoms that can include sneezing, nasal obstruction, and mucous discharge.[9] In Belgium, the most prevalent causes of allergic rhinitis are house dust mites and grass pollen.[10,11] Occupational rhinitis (OR) is defined as the episodic work-related occurrence of sneezing, nasal congestion, rhinorrea, and itching. It often coexists with occupational conjunctivitis and/or asthma. OR is categorized as allergic OR or as non-allergic OR. Allergic OR can be IgE-mediated and is induced by either high-molecular weight (HMW) agents or low-molecular weight (LMW) agents. Allergic OR can also be non-IgE-mediated and induced by LMW agents that act like haptens. Currently, the allergic mechanism underlying non-IgE-mediated OR is not fully understood. However, non-allergic OR is mediated by non-immunologic mechanisms and is likely to be caused by irritants (e.g. tobacco smoke or pollution), annoying smells (e.g. perfumes and cleaning agents), and corrosive agents (e.g. ammonia and chloride bleach).[12] The exact prevalence of OR in workers exposed to occupational allergens and chemical agents is not known,[12-14] but Table 1 shows the estimated prevalence of some important causes of OR. The risk factors associated with the development of OR are exposure level, length of exposure, atopy, and smoking.[12] Occupational rhinoconjunctivitis and asthma constitute important medical health issues that are associated with significant morbidity, work absences, and negative effects on the quality of life of affected patients. Timely and correct diagnosis and therapeutic management are thus extremely important.

The diagnostic approach to OR starts with taking a detailed and comprehensive medical and occupational history.[12-14] A visit to the workplace can help identify the exact cause(s) of OR, as patients may be unaware of some of the many substances they are exposed to. Data sheets that list all of the substances to which workers may be exposed must be available at the workplace.[13] In the case of an IgE-mediated allergic OR skin prick test, quantification of serum-specific IgE (sIgE) and basophil activation tests (BATs) should be performed.[12-14] Direct nasal challenges, either at the workplace or in the office or laboratory, can be added to the diagnostic workup, especially when skin tests and sIgE assays yield equivocal or negative results. The responses can be quantified by either symptom scoring or by objective methods such as rhinomanometry, acoustic rhinometry, and peak nasal inspiratory flow.[12,13] Removing the patient from situations in which exposure to the allergen is likely can be an important step in preventing progression to occupational asthma.[13,14]

Here we report a case of a patient suffering from OR and asthma after exposure to carmine red and cyan blue powder, two dyes used for screen printing in the patient's workplace. Carmine is a natural red colorant obtained from aqueous extracts of cochineal. It is used widely in the food, dyeing, cosmetic, and pharmaceutical industries. IgE-mediated carmine red reactions can include the following symptoms as the result of inhalation or ingestion: rhinitis, conjunctivitis, asthma, extrinsic allergic alveolitis, urticaria, angioedema, and anaphylaxis. Carmine red allergy has been reported in professionals that work as employees at a factory makes natural dyes, in butchers, in workers that help produce coloured cosmetics, and in spice blenders. However, to the best of our knowledge, this is the first case of an IgE-mediated carmine allergy in a screen-printing worker. At present, the allergenic components responsible for carmine allergy remain largely unknown.

Diagnosis of IgE-mediated carmine red allergy, as in our patient, includes history taking that shows symptoms such as nasal congestion, rhinorrhea, sneezing, nasal and eye itching, coughing, and shortness of breath that are exacerbated by occupa-

Table 1
Aetiological agents and prevalence of occupational rhinitis (adapted from Moscato *et al*.[12])

Occupation	Agent	Prevalence (%)
High molecular weight agents		
Laboratory workers	Laboratory animals (e.g. rats, mice, rabbits, guinea pigs, hamsters)	6-33
Hospital workers	Latex	2-20
Pharmaceutical and detergent industry workers	Biological enzymes	3-87
Bakers	Flour, α-amylase, grain mites	18-29
Fishery workers	Fish and seafood protein	5-24
Workers who come into contact with plants (e.g. tobacco leaves, cayenne pepper, tea, coffee, cocoa, dried foods, saffron)	Other plant allergens	5-36
Low molecular weight agents		
Painters	Diisocyanates	36-42
Chemical workers	Anhydrides	10-48
Joinery workers	Wood dust	10-36
Jewelry workers	Platinum	43
Medics, paramedics, pharmacists	Drugs (e.g. psyllium, spiramycin)	9-41
Hairdressers, shoe manufacturing workers, reactive dye production workers	Chemicals	3-30

tional exposure to carmine. Such symptoms may resolve during weekends or vacations. Confirmatory testing involves quantification of sIgE antibodies, skin tests, BATs, and challenge tests. In BATs, basophils are stimulated with allergen extracts and in vitro basophil activation is quantified by flow cytometry. The principles and clinical application of BATs are summarized elsewhere.[15] A review of BAT indicates that this technique is useful for diagnosing IgE-mediated allergies for which no serological tests are available or when the serological tests yield equivocal results.

An important step in managing occupational allergic rhinoconjunctivits and/or asthma is to reduce or completely eliminate further exposure to the offending agent(s). In symptomatic treatment, nasal steroids are considered first-line therapy for cases of persistent allergic rhinitis. Additional antihistamines may be given as needed.

Conclusion

Here we describe the first reported case of occupational rhinoconjunctivitis and asthma due to carmine red allergy in a screen-printing worker. The clinical suspicion of allergy was confirmed by sIgE, skin prick test, BAT, and by a carmine red challenge test.

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