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New risks from ancient food dyes: cochineal red allergy

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KEY WORDS

Carmine red; Cochineal red; anaphylaxis; food additives; dyes

Summary

This study reports an unusual case of IgE-mediated hypersensitivity to Cochineal red or Carmine red, a coloring agent of natural origin. Although the risk of anaphylactic reactions is well known, since the nineties the use of this additive seems to be nowadays on the rise. The problem of labeling of additives used in handmade food products is highlighted.

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Introduction

Among food and drug additives, Carmine or Cochineal Red is one of the best known as a cause of allergic reactions (1).

This natural red dye derives from the bodies of female *Dactylopius coccus*, insects that grow on cochineal cacti widespread in Central and Southern America, Southern Europe, and India. This dye has been widely used since sixteenth century as a coloring agent in processed food and drinks, cosmetics and textiles. Nowadays, it is found in hamburgers, sausages, alcoholic and non-alcoholic drinks, sweets and fruit yoghurts. However, its identification in such a various range of products is difficult, particularly in fresh processed food such as those handmade by butchers.

During the past 20 years, several Authors reported about severe allergic reactions following the ingestion of carmine in foods and drinks (2,3). Moreover, allergic rhinitis and asthma in sub-

jects exposed to powdered carmine dye in occupational settings is well known (4,5). IgE-mediated food and respiratory hypersensitivity has been shown (6), and cheilitis following contact with lipsticks colored with carmine has been reported as well (7). Some Authors hypothesize that the presence of the dye in cosmetics could be the reason for the female prevalence of this sort of allergy.

The first identification of allergens of cochineal red was reported by Quirce et al. in 1994 (4). More recently, Japanese researchers characterized and cloned a 38 kDa phospholipase or related enzyme, homologous to other similar proteins in insects, as the major allergen (8).

Case report

A 32 years old woman with no prior history of allergies was referred in 2011 to our clinic for an episode of generalized ur-

ticaria, associated with eyelid oedema and rhinitis occurring immediately after the intake of a protein-vitamin supplement (Car-go; Recordati, Italy). During the previous 5 years she experienced some other similar but less severe episodes after eating sausages or spicy meat (kebab). The label on the vitamin supplement reported Carmine (in addition to amino acids, vitamins of group B, C and E), which led us to suspect a reaction to the dye. Notably, carmine red has been recently removed from the drug. A SPT with the integrator, performed diluting the powder content of one capsule (0.1 mg/ml NaCl) was performed and scored positive, eliciting erythema and a pruritic 5 mm wheal. The same SPT scored negative in five control subjects. Skin tests with inhalant and food allergens, including various kinds of meat and spices, were negative. Specific IgE to red cochineal (ImmunoCAP F340) was 0.19 KU/l. ImmunoCAP for the common foods scored negative. The basophil activation test (Flow CAST from Bühlmann Laboratories, Schönenbuch, Switzerland) to Mix dyes 1 and 2 (including E120 and E124) and with the protein-vitamin supplement "Car-go" was negative. Some months after this episode, the patient experienced a new, more severe, reaction with angioedema of lips and face and slight laryngeal involvement, some hours after ingestion of a handmade turkey hamburger. The butcher confirmed the use of some carmine-colored sausages for the preparation of the hamburger.

Discussion

This case confirms the actual risk of allergic reactions induced by Carmine red present not only in food, but also in dietary supplements and OTC drugs. Its increased use may expose the population to a relevant risk of IgE sensitization. The possible occurrence of symptoms some hours after the ingestion of the dye is reported in the literature, and may result in undiagnosed cases labelled as "idiopathic anaphylaxis".

The natural Cochineal red, classified in Europe as E120, must be distinguished from the synthetic form, the Cochineal Red A also named Ponceau 4R (E124), belonging to the azo-dyes. It is known as histamine-liberator, but not as IgE sensitizing agent. We believe that accurate, more specific and strict regulation on labelling (both at an international and national level) is crucial in safeguarding health.

Only recently the FDA ruled that food, drugs and cosmetic products containing coloured additives like cochineal extracts and carminic acid must be clearly labelled. In Europe, the regulation on food labelling includes additives and dyes: red dyes are listed from E120 to E129 (table 1). The system appears to be efficient at level of industrial products, while handmade foods are more at risk of undeclared manipulation. Further, the existence of two similar Cochineal Red dyes, E120 and E124, may represent a risk of mistake in most of European countries. Notably, the synthetic, non-allergenic one (E124) is not allowed

in Norway and Finland, and also in USA because of a supposed carcinogenic risk.

The potential risk of allergic reactions due to natural cochineal red would deserve greater attention among specialists. The demonstration of the mechanism needs more sensitive diagnostic methods. Although very low, the IgE specific level (0,19 KU/l) obtained in the study can be considered positive, because in the last years the use of the whole quantitative scale of antibodies presence is preferred, rather than the cut-off value of 0,35 KU/l in the CAP-system. A diagnostic extract for skin test is not available.

The identification of the major allergen and the use of recombinant and molecular diagnosis could be of great importance to ameliorate the diagnosis in a next future.

Table 1- Red colouring additives (EU nomenclature).

E 120	Cochineal, Carminic acid, Carmines
E 122	Azorubine, Carmoisine
E 123	Amaranth
E 124	Ponceau 4 R, Cochineal Red A
E 127	Erythrosine
E 129	Allura Red AC

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