Systemic contact dermatitis due to compositae.

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Abstract

A 62-year-old-woman presented with dermatitis of the face, eyelids, and neck. Patch testing results after 96 hours revealed positive reactions to benzoyl peroxide, 2-n-octyl-4-isothiazolin-3-one, compositae mix II, and propylene glycol. Upon further evaluation of her history, it was found she had regular ingestion of sunflower butter, dandelion teas, artichokes, and Echinacea tablets. After complete clearance of the substances, her dermatitis cleared. Re-exposure to these edibles led to recurrence.

Keywords: Systemic contact dermatitis, Patch testing, Delayed-type hypersensitivity, Compositae.

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Introduction

Contact dermatitis (CD) is a hypersensitivity reaction where cutaneous exposure to a compound elicits dermatitis. Systemic contact dermatitis (SCD) requires previous sensitization to an allergenic compound, wherein subsequent re-exposure results in a delayed elicitation phase. SCD causes a variety of clinical presentations, often involving recalcitrant, widespread, or recurring dermatitis [1]. SCD has been reported with a variety of allergens including nickel, balsam of Peru, and propylene glycol [1]. However, there have been few reports of SCD to compositae/sesquiterpene lactone mix allergens, particularly chamomile teas [2-4].

Case Report

A 62-year-old Caucasian woman was presented with worsening dermatitis of the face, eyelids, and neck. Previous treatments of prednisone and aclometasone resulted in temporary and fleeting improvement of her condition and the patient was subsequently referred for patch testing (Figure 1).

She was patch tested to 110-allergen series with standard readings at 48 and 96 hours. At 48 hours, positive reactions were seen to the following: benzoyl peroxide 2+, 2-n-octyl-4-isothiazolin-3-one, and dithiomorpholine ± macular erythema. At 96 hours, positive reactions were seen to the following: benzoyl peroxide 2+; 2-n-octyl-4-isothiazolin-3-one, compositae Mix II, and propylene glycol 1+. Allergens considered relevant were the 2-n-octyl-4-isothiazolin-3-one, compositae mix and propylene glycol.

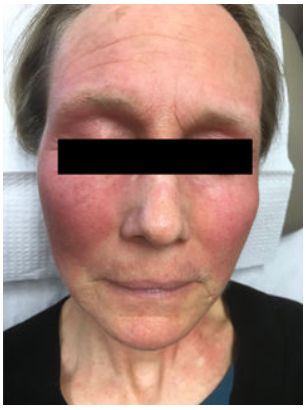

Figure 1: Systemic contact dermatitis.

After thorough topical avoidance of her allergens for six weeks, she had some improvement; however she still required systemic steroids for two episodes of recurrent flares unexplained by topical exposures. The patient denied occupational exposure to her allergens, a history of a leg ulcer, or previous usage of acne medications. Upon further questioning and discussion of systemic exposures to her allergens, she described regular ingestion of compositae-related foods and supplements which were associated with her facial, eyelid, and neck dermatitis flares. The most provocative agents were sunflower butter, dandelion teas, artichokes, and Echinacea tablets. The latter was being taken with regularity when the reaction first occurred. After avoidance of the eliciting compounds, the patient's dermatitis cleared significantly. Upon re-challenge with sunflower butter she noted a recurrent eruption 2-3 hours later.

However, she returned to clinic weeks later with recurrent dermatitis despite avoidance of compositae products. Per the patient, she had recently been exposed to a plethora of surgical scrubs and disinfectants after caring for an ill relative-product that likely contain known allergens such as isothiazolinone, chlorhexidine, and masking fragrances. Isothiazolinone, in

particular, matches her patch testing profile and this substance is in a large variety of substances [5]. Methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI) are well known allergens and are recognized to be strong sensitizers. Notably, there is significant cross-reactivity between the two and solitary reactions to one of the two occur in only a minority of cases [6]. Thus, MI and MCI allergies should be appropriately addressed considering their prevalence in consumer items. This patient's clinical presentation highlights the complexity of ACD and the necessity of patch testing with subsequent allergen awareness and avoidance strategies.

Discussion

The pathogenesis of SCD is not fully explicated, but is thought to involve a type IV hypersensitivity reaction that consists of a sensitization and elicitation phase. The sensitization phase occurs when allergenic compounds come into contact with the epidermal layer. Allergens bind with proteinaceous compounds to form haptens and are recognized by dermal dendritic cells (DCs) and Langerhans cells (LCs). These cells act as antigen presenting cells and recognize the hapten complexes. These cells then migrate to lymph nodes where they activate naïve T lymphocytes to become allergen-specific. Following clonal expansion of the allergen-specific T cells, migratory markers lead the T cells to peripheral tissues such as the skin, gut, and lung. Upon re-exposure (in this case, oral consumption of compositae-related foods), a T cell-mediated inflammatory reaction results in dermatitis [1].

Current literature establishes that $CD8^+$ T cells are the primary effector cells of allergic contact dermatitis (ACD). However, the immunology behind hypersensitivity reactions is much more complex. Depending on the cytokine environment, $CD4^+$ cells have the capability of differentiated into Th1 or Th2 cells, but their role is not entirely understood. Some studies have shown that $CD4^+$ Th1 cells propagate the $CD8^+$ effector response *via* the production of IFN-gamma and TNF-alpha. However, $CD4^+$ cells are also noted to have a regulatory function in minimizing the effector cell response. It is well documented that IFN-gamma (the result of LC and Th1 activation) is necessary for the development of CD and IFN-gamma, in conjunction with IL-5, appear to contribute to the development of systemic allergy [7]. Macrophage migration inhibitory factor is increased in ACD, when compared to healthy subjects, and is produced by both Th1 and Th2 cells. The role of Th2 cells is not as clear, as it appears the Th2 response is only elicited in exceptional circumstances [8].

B cells play an integral role the activation of $CD4^+$ cells. One study demonstrated that the absence of B cells inhibited $CD4^+$ activation and subsequent production of proinflammatory cells [9,10]. Conversely, B cell activation by helper T cells is necessary in the augmentation of T-cell dependent antibody response, an occurrence known as 'linked recognition [11]. Reports have also indicated a role for Th17 cells in the development of contact hypersensitivity (CHS). One study showed that IL-17 deficient mice had reduced CHS. However, restoration of Th17 cells, thus IL-17 showed a restored CHS [12].

Mast cells comprise an additional component of the innate immune system. Their involvement in allergy and type I hypersensitivity is well documented. However, their role in CHS appears to be more controversial. Recent studies have demonstrated hapten-specific IgM and complement (C5a) are capable of activating mast cells, as well as C5a being an essential element in the T cell contact effector response, both of which contribute to the elicitation phase of contact sensitivity [13]. Mast cell activation has been shown to perpetuate DC migration and activation, further highlighting the synergistic roles between the innate and adaptive immune systems [14]. Of note, IgE bearing LCs promote expansion of Th2 memory T cells and increase production of IL-3, IL-4, IL-5, and IL-13 leading to increased levels of IgE, mast cells, and eosinophilia [15].

The most common groups of substances that cause SCD are metals, drugs, and plant products [1]. However, there is a multitude of compounds with varying allergenic potentials capable of causing SCD [16]. In this case, a thorough history and associated positive patch test elucidates compositae as the likely cause of this patient's dermatitis. Compositae, also known as Asteraceae, is made up of more than 22,750 species and is considered the second largest flowering plant family. Species noted to cause CD include chamomile, dandelion, chrysanthemum, artichoke, daisy, and many more (Table 1).

Table 1: Compositae (Asteraceae) species with known sensitization potential

Asian pennywort	Dandelion	Orange
Bergamot	Eastern poison oak	Peruvian lily
Bitterweed	Elecampane	Poison Ivy
Black mustard	Endivie	Poison sumac
Cabbage	Feverfew	Primula
Caper bush	Fleabane	Radish
Capweed	Garlic	Ragweeds
Carrot	Ginkgo tree	Silk oak
Carrot weed	Globe artichoke	Sneezeweed
Cashew nut tree	Horseweed	Sticky elecampane
Cauliflower	Japanese lacquer tree	Stinkwort
Chamomile	Lemon	Sweet chamomile
Chicoriy, Escarole	Lettuce	Tulip
Chrysanthemums	Mango	Western poison oak
Common ivy	Marguerites	Wormwood
Congress grass	Montain tobacco	Yarrow
Dahlia	Mugwort	

Given the wide diversity of this family, there are a multitude of compounds responsible for causing CD. While sesquiterpene

lactones are primarily responsible for eliciting SCD, epoxythymol-diesters and polyacetylenes are also recognized sensitizers. Contact with such compounds is necessary to develop SCD; however, the exact route of sensitization is unclear. Proposals include airborne particles such as pollen/debris, direct contact with the plant, or inhalation/ingestion. In this particular patient, there is a clear temporal relationship with the ingestion of compositae-containing foods/supplements with flares of her dermatitis.

The gold standard for diagnosis of SCD is patch testing and both the American and European baseline series include sesquiterpene lactone mix 0.1 pet [16]. Upon recognition of a compositae allergy by patch testing, avoidance strategies of the eliciting compound are necessary to prevent recurrence of the dermatitis.

Conflict of Interest

Author 1 [Dr. Chandler W. Rundle] declares that he has no conflict of interest. Author 2 [Dr. Brian C. Machler] declares that he has no conflict of interest.

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