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Case Report

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The Lifestyle and the Usefulness of Patch Tests among Elderly Male Patients; Reflections on the Role of T Helper 2 Profile in Allergic Contact Dermatitis

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Abstract

Allergic contact dermatitis (ACD), a T-cell-mediated inflammatory disease, appears in predisposed individuals as a result of exposure to allergens in the environment. This condition is frequently seen as a feminine problem. This investigation presents three examples of male subjects over 60 who recently experienced ACD onset, as determined by the standard series of the European Baseline Series. Our data demonstrate that due to their actual lifestyle and repeated exposures, elderly male patients can develop an ACD to "traditionally female allergens". Patch tests (PT) in older participants indicate equal effectiveness as compared to every adult. However, allergists should consider the additional reading outside the 48 hours following PT application and interpret mild reactions as positive ones. Our data support the idea that when an initial disease history is ineffective, patch testing may help allergists identify the responsible allergen(s) and help patients further prevent exposure to them. In line with literature reports, our findings indicate that the penetration of concentrated allergens into subepithelial tissue, particularly when the epithelial layer is damaged, may result in an allergic reaction and even the development of ACD, which is probably linked to a T helper 2 response (including the synthesis of IgE). Due to the IgE-mediated antitoxic effect, this alternative might assist organisms by allowing exposure to increased allergen levels. However, further research must be done before this thesis can be evaluated.

Keywords: Allergic Contact Dermatitis, Patch Tests, Elderly Patients, Lifestyle, Epithelial Layer, T Helper 2 Response.

1. Introduction

Contact dermatitis from irritant and allergic sources comprises 6% to 10% of all dermatologic visits [1]. Allergists often view allergic contact dermatitis (ACD) as a female issue and agree that allergic symptoms lessen as people age [2-4]. According to recent studies, fresh ACD can occur at any age as a result of exposure to daily cosmetics, new esthetics procedures, and protracted employment [1-5]. A patch test (PT) is used to diagnose ACD and identify the culprit allergens [1–5]. This study presents three examples of male individuals over 60 who recently experienced ACD, as determined by the standard series of European Baseline Series (Chemotechnique Diagnostics). Besides highlighting the significance of specific exposure situations in disease development and diagnosis, this work also sheds light on the conditions that could lead to T helper (Th)2 response, even in ACD.

2. Case reports

1. A 65-year-old subject complained about erythema and itching of upper extremities during the recent month. The objective examination revealed diffuse erythema and confluent edematous infiltrative lesions on dorsal surfaces of forearms, fewer in the lower legs. The patient had also prominent lesions at the perianal/perineal zones like those observed in the upper extremities. Only after the PT application did the patient referred us to the frequent use of moist wipes for hygienic purposes because of the COVID-19 pandemic. PT also confirmed the sensitization to Fragrance Mix I, Euxil K400, and Kathon CG in moist wipes.

2. A 61-year-old subject occupied in building construction during the last years complained about facial, hand, and abdominal ACD symptoms only during the recent 5-6 months. First, topical corticosteroid creams improved allergic symptoms, but yet again, the patient had symptoms worsening. PT resulted positive for Nickel sulfate and Potassium dichromate, which are part of cement.

3. A 66-year-old subject with a recent occurrence of head itching and erythema, who had been suffering from dog-induced allergic conjunctivitis, came to our clinic. The patient mentioned having had a hair transplant only several months before, and then weekly hair coloring. The PT was positive for p-Phenylenediamine, which is present in the hair color.

3. Discussion

The population demography is changing throughout the majority of social strata in every nation. Besides the rising number of senior people worldwide [1, 2], lifestyles are changing, and many aesthetic interventions that were once only made for women are now being made for both men and the elderly. Continuing a job after the age of 60-65 years requires improved personal hygiene, which may result in first exposure to cosmetics and other environmental allergens. Such lifestyle factors may increase allergen exposure and trigger the onset of a clinical reaction.

Fragrances, preservatives, or metals are typical ACD allergens that affect up to 30% of elderly patients (EP), like our case findings [5]. Benzoic acid, methylisothiazolinone, wood tar, nickel sulfate, fragrance mix, diamino diphenylmethane, lanolin alcohols, paraben mix, Euxyl K400, quinoline mix, and balsam of Peru were the most prevalent contact allergens among EPs [1, 2]. As mentioned, female subjects represent the majority, with a rising proportion of males.

Despite the confirmed PTs' usefulness in the elderly (reaching a maximal positivity rate of up to 85%) [4, 5], it is debatable whether the positivity prevalence to at least one allergen in the EP group is lower or equal in comparison to the other adult patients [3, 4]. Positive PT reactions have been less intense in EPs than in younger patients, with a higher percentage of mild (+) positive reactions. Additionally, more commonly than younger patients, EPs displayed a dynamic pattern of rising PT reaction intensity at the second reading after 3 days compared with the first reading after 2 days [3]. The highest reaction intensity to PT allergens is seen between 72 and 96 hours after application in two of the three cases included in this investigation. Some authors agree that even mild or uncertain reactions should be interpreted as true positive PT reactions and that the delayed onset of an allergic response in EPs may need an extra reading after 7 days [3].

The allergist and patient may learn more about the offender and relative exposure variables due to a positive PT test when an initial disease history is inconclusive. One of our patients utilized the wet wipes to refresh the affected forearms, believing them to be a good, hygienic tool, not realizing the severity of the condition. PT revealed a simultaneous allergic sensitivity to Fragrance mix I, Kathon CG, and Euxyl K400. Only when informed about the presence of culprit allergens in moist wipes, the patient reported their extensive use for hygienic or refreshing purposes during the COVID-19 pandemic [6]. In the other case, the positive PT result identified the culprit allergen (p-Phenylenediamine) in the hair color. The patient showed only an undefined pruriginous erythema on the head.

ACD is a T-cell-mediated inflammatory reaction that develops in predisposed individuals because of environmental exposure to allergens [1]. Despite the prevailing view of ACD as a Th1-mediated condition, the in vivo or in vitro reactivity to responsible allergens correlated with a mixed Th1, Th2, Th17, Th22, and T regulatory (Treg) cytokine response [7, 8]. In particular, the intensive reactivity to nickel among ACD subjects correlated more strongly with peripheral blood mononuclear cell production of interleukin (IL)-4 or IL-13 as compared to IL-2, interferon-γ (IFN-γ), or IL-10 [7]. Besides these cytokines, experimental ACD in mice is associated with increased levels of IL-6, IL-17, IL-22, IL-23, and transforming growth factor-β (TGF-β) [8, 9]. These models demonstrated that ACD chronicization induces a striking shift in the cutaneous/plasmatic cytokine milieu to Th2, including an extreme increase of IL-4 and immunoglobulin (Ig) E levels [8, 10]. As mentioned above, such an immune switch occurs under IL-10-related regulatory processes [7, 8, 11, 12].

The association of disease chronicization or intensive skin lesions with a Th2 response (including IgE synthesis) can be explained with the postulates of a) exposure intensification after the damage of barrier integrity [13]; and b) an IgE-related antitoxic effect [14]. The mechanism of BIDEAR (Barrier Integrity Damage-Elicited Allergic Response) considers intensive exposure to the allergen because of previous epithelial damage (independent of immediate or delayed allergy type) as the trigger of the immune deviation and related disease onset [13]. In our case, the damage to epithelial integrity during transplantation may have allowed the allergic response to hair color allergens. This subject had pet-related allergic conjunctivitis, showing a predisposition for IgE response. Recently, we observed similar behavior in several cases: the immediate or delayed allergic pathology (allergic rhinitis, urticaria, anaphylaxis, or ACD) occurred only when allergen exposure happened in epithelia-damaged areas [13]. Further, Th2-mediated allergic reactions to latex have a greater incidence in children with spina bifida. Similar to the situations stated above, repeated surgical procedures, the implantation of latex-containing products, and catheterization might expose compromised epithelial barriers to large latex concentrations [15].

The intensive penetration of allergens into the deep layers of the living epidermis and increasing antigen uptake in concert with the pro-allergic immune response(s) are key factors in eliciting an allergic response in affected subjects [13, 16-18]. The increased allergen concentrations around antigen-presenting cells can induce Th2 polarization because of the modulation of the dendritic cell (DC) function. This is possible because DCs placement at the interface between body surfaces and the environment is ideal for allergen capture and, thereafter, for the induction of tolerance or the initiating and persisting of the immuno-inflammatory response [13, 18-20]. As mentioned above, the Th2 response may have an antitoxic effect on allergen exposure. According to a recent report, the treatment of bee venom (BV) with supernatant collected from IgE-activated human peripheral blood-derived cultured mast cells (MC) decreased the plenty of BV toxins, including the major allergens, demonstrating proteolytic degradation and thus an antitoxic effect [14]. Subcutaneous sublethal injections of venom also induce a Th2 immune response associated with the production of specific IgE-s, which together with IgE-dependent effector cells, can play an important role in acquired immunity against next exposure to potentially lethal BV amounts. These findings confirm that venom-specific IgE can efficiently increase the magnitude of the BV-induced MC response as a protective measure against the venom proteins [14]. In agreement with this effect, a successful pregnancy also requires a Th2-biased profile to keep internal states steady and balanced (even against toxins), independent of underlying inflammatory conditions [21, 22]. Another example

of the Th2 response that happens after exposure to large allergen concentrations is the development of sensitization in animal models of allergic disorders as a result of repeated parenteral administration of ovalbumin, as well as intensive latex exposure in children with spina bifida due to diverse chirurgical procedures [8, 12, 15, 23, 24].

In summary, these findings show that the antibody-mediated enzymatic activity by Th2 effector cells and the consecutive antitoxic effect could be expressed both in immediate and delayed allergic reactions [14, 25]. This may be much more distinct when the effector cells placed on conjunctive tissue are exposed to increased allergen concentrations because of the precedent trauma (or subcutaneous inoculation), or disease-associated epithelial damage [7-9, 13, 15]. Like IgE-mediated pathologies, the Th2 response during exacerbating or chronicization of ACD can play an essential role, while the respective mediators can be reliable markers and probable beneficial effectors [7]. Immune cells placed in the conjunctive layer cannot notice what happens with the adjacent epithelia in such cases, but the extensive allergen exposure can be perceived as a more toxic (gradient-wise) concentration outside the body [Figure 1]. Thus, the organism may consider a Th2-mediated antitoxic response as a more appropriate immune model for the situation.

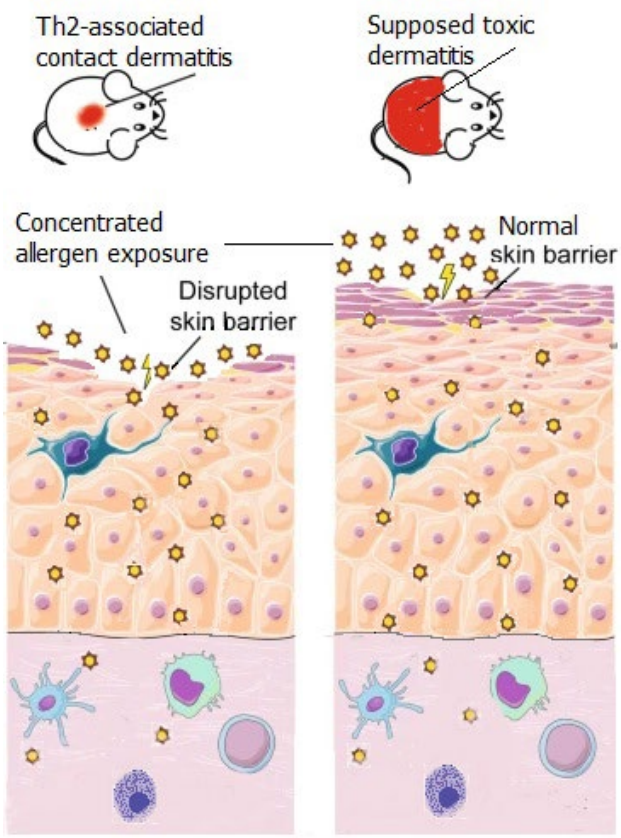

Figure 1

Figure legend: Although Th1-mediated disease is the prevalent theory, ACD also exhibits a mixed Th1, Th2, Th17, Th22, and Treg cytokine response. The condition in the Th2-related ACD is depicted in the model on the left, along with epithelium destruction and connective tissue cells being exposed to higher allergen concentrations. The right-hand model depicts the organism-related assumed situation, which interprets the elevated allergen concentration around connective tissue cells as a case of exposure to toxic allergen levels outside the adjacent intact epithelial layers, and the Th2 and IgE response as a more appropriate instrument to address the situation. Being unable to observe what is happening to the surrounding epithelium, in these situations immune cells located in the conjunctive layer can activate the MCs, inducing the IgE-related catalytic activity and the degrading effect of granular enzymes. The profile of immune response (not depicted in the figure) and allergen concentration in the connective tissue are identical in both models. In contrast, the model to the right has a substantially larger allergen concentration on the epithelial surface: penetrating through an intact epithelium, the allergens reach the same concentration in the connective tissue as on the left.

4. Conclusion

ACD can occur first in the elderly, and male subjects can experience an ACD even with "traditionally female allergens" due to their actual lifestyle and frequent exposures. PTs in older subjects are also effective and recommended for every adult. Guidance from patch testing greatly assists allergists identify the responsible allergen(s) and help patients further prevent exposure to them. Allergists should consider the additional reading outside the 48 hours after applying PT and even interpret mild reactions as valid positive ones. The intensive allergen penetration into the subepithelial tissue may cause an allergic response and develop ACD, likely associated with a Th2 profile (including a surprising IgE synthesis). This scenario may help organisms allow exposure to toxic allergen levels. Still, further studies are necessary to test our suppositions.

Author contribution: AB collected the case reports and helped with helpful discussions; EÇM ideated and drafted the manuscript.

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