

Pigmented Facial Contact Dermatitis to Benzyl Salicylate: A Comparative Histopathological and Immunohistochemical Study of the Involved Skin and the Positive Patch Test Site

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Abstract: Pigmented contact dermatitis (PCD) is a noneczematous variant of allergic contact dermatitis, and benzyl salicylate is one of its causes. This type of PCD shows nonlichenoid interface dermatitis with pigment incontinence. We aimed to characterize the earliest histopathological changes of this reaction. A 51-year-old man presented with persistent facial eruption composed of hyperpigmented and hypopigmented macules due to exposure to benzyl salicylate present in his aftershave. The biopsies obtained from hyperpigmented and hypopigmented macules, and from the positive patch test site to benzyl salicylate, showed a nonlichenoid focal vacuolar interface dermatitis with mononuclear cells in the papillary dermis and around the pilosebaceous units, along with melanophages. A MART-1 immunostain showed intact melanocytes in all 3 biopsies. A Fontana–Masson stain demonstrated intact melanin in the basal cell layer of a facial hyperpigmented macule and the patch test site, but melanin was reduced in the biopsy taken from a hypopigmented facial macule. There were more epidermal and dermal CD1a+ Langerhans cells in the patch test biopsy than in the other 2 biopsies. Most of the mononuclear cells were CD3+. The CD4+ to CD8+ ratio was approximately 1:1 in the facial macules; yet, CD4+ cells outnumbered CD8+ cells in the patch test biopsy. There were a few TIA-1+ cells in all 3 biopsies. In conclusion, the earliest histopathological and immunophenotypical events in PCD due to benzyl salicylate are similar to those of longer-standing lesions, i.e., a nonlichenoid focal interface dermatitis involving the epidermis and pilosebaceous unit, along with dermal melanophages.

Key Words: pigmented contact dermatitis, benzyl salicylate, interface dermatitis, patch test

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INTRODUCTION

Most cases of allergic contact dermatitis (ACD) are characterized histopathologically by spongiosis.^{1,2} Biopsies of experimentally induced ACD demonstrate spongiosis, which peaks 24–48 hours after application.³ Follicular spongiosis also characterizes early ACD and to be absent in early irritant contact dermatitis (CD).⁴ A less common histopathological

finding in ACD is a lichenoid tissue reaction and pigment incontinence.⁵

Pigmented CD (PCD) is a noneczematous variant of ACD. Benzyl salicylate was one of the common causes of PCD in Japan during 1960–1970. In the late 1970s, major cosmetic companies reduced its usage in their products, and the incidence decreased remarkably.^{6,7} The histopathology of PCD consists of basal cell liquefaction accompanied by the formation of melanophages in the papillary dermis.

A 51-year-old male patient developed facial PCD most likely due to benzyl salicylate present in his aftershave. The histopathology and immunohistopathology of the hyperpigmented and hypopigmented facial macules and of the positive patch test site to benzyl salicylate were studied and characterized, with the aim of delineating the initial histopathological events in this form of PCD.

Case Report

A 51-year-old man presented to our clinic with an 8-month history of worsening nonpruritic hyperpigmented and hypopigmented macules on his face. He reported constant usage of perfume and aftershave. He had no personal or family history of atopy. There were hyperpigmented and hypopigmented macules and patches in a reticular formation on his cheeks, ears, forehead, and neck (Fig. 1). The clinical differential diagnosis included PCD, postinflammatory hyperpigmentation, discoid lupus erythematosus, lichen planus pigmentosus,



FIGURE 1. Hyperpigmented and hypopigmented macules on the left cheek, ear, and temple.

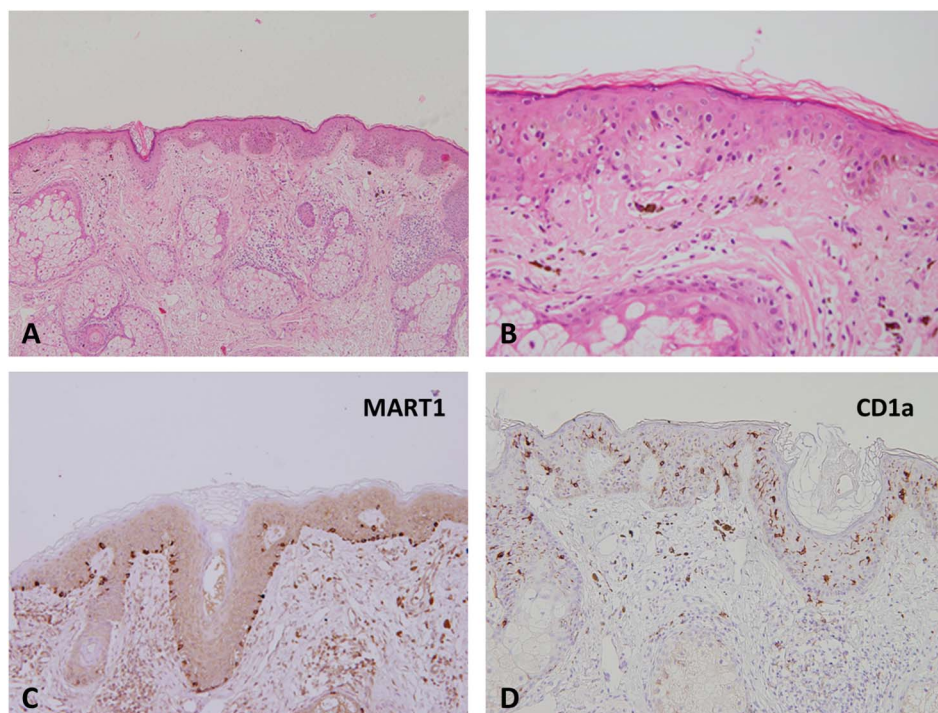
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FIGURE 2. A skin biopsy from hyperpigmented macule on the face. (A) Superficial perivascular and interstitial mononuclear cells infiltrates in the upper dermis with scattered melanophages. (B) Higher magnification, showing lymphocytes, melanophages, and focal vacuolar changes in the basal cell layer of the epidermis. (C) Immunostaining demonstrates numerous MART-1 + melanocytes in the basal layer of the epidermis and infundibula, and (D) numerous CD1a + Langerhans cells in the epidermis and fewer in the dermis.



and lichen actinicus. The patient denied a previous rash before the patches appeared, making postinflammatory changes less likely.

Punch biopsies (2.5 mm) obtained from hyperpigmented and hypopigmented macules on the cheek demonstrated superficial perivascular mononuclear cells in the papillary dermis, scattered melanophages, and focal vacuolar

changes in the basal cell layer of the epidermis. Additional infiltrates of mononuclear cells are seen around pilosebaceous units (Figs. 2A, B). Immunostaining of both biopsies demonstrated numerous MART-1+ melanocytes along the basal cell layer of the epidermis and infundibula, and scattered CD1a Langerhans cells in the epidermis, papillary dermis, and infundibula (Figs. 2C, D). Most of the mononuclear cells

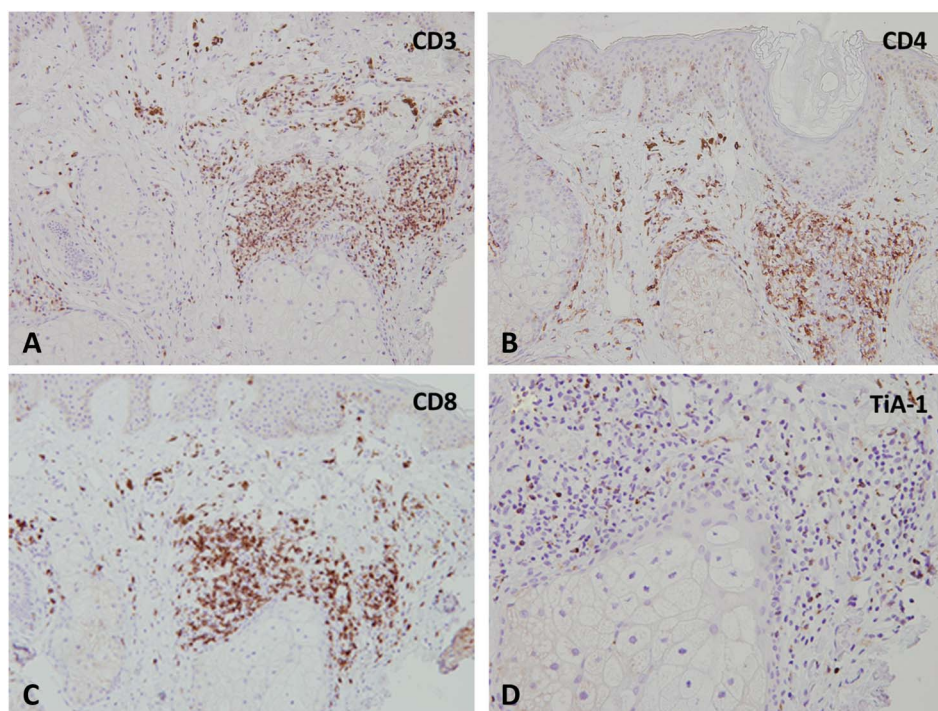


FIGURE 3. (A) Immunostaining demonstrates that most of the mononuclear cells in the upper dermis and the dense infiltrate around a pilosebaceous unit stain for CD3. (B and C) There are equal numbers of CD4+ and CD8+ cells in the infiltrate, and (D) a few TiA-1+ cells.

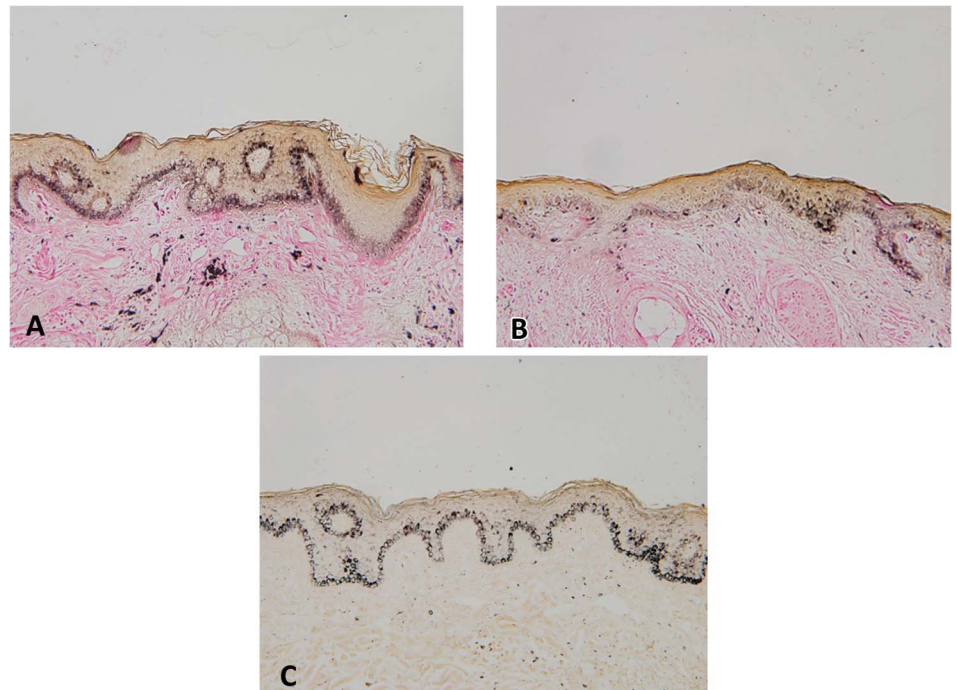


FIGURE 4. Fontana–Masson stain of the (A) hyperpigmented macule, (B) hypopigmented macule, and (C) patch test site showing decreased melanin in the hypopigmented skin as compared to the hyperpigmented skin and the patch test site.

stained for CD3, with equal numbers of CD4⁺ and CD8⁺ cells, and a few TiA-1⁺ cells (Fig. 3).

A Fontana–Masson stain demonstrated intact melanin in the basal cell layer of the facial hyperpigmented patch and the patch test site, but melanin was reduced in the biopsy taken from the hypopigmented facial patch (Fig. 4).

Patch test was performed with the following series: European Baseline Series, Cosmetic Series, Fragrance Series, and Plant Series (Chemotechnique Diagnostics AB, Vellinge, Sweden). The patch test showed a positive reaction (+) to benzyl salicylate (Fig. 5). Benzyl salicylate was found in the patient's aftershave.

A skin biopsy obtained from the positive patch test site, 96 hours after the application of benzyl salicylate, showed perivascular and interstitial mononuclear-cell infiltrates in the

papillary dermis and around a pilosebaceous unit. The mononuclear-cell infiltrate abutted focally the epidermis and a pilosebaceous unit, and were accompanied by mild focal vacuolar changes in the basal cell layer. There were also several melanophages in the papillary dermis (Figs. 6A, B). A Fontana–Masson stain demonstrated intact melanin in the basal cell layer (Fig. 4). Immunostaining showed numerous MART-1⁺ melanocytes in the basal cell layer of the epidermis and infundibula, and numerous CD1a⁺ Langerhans cells in the epidermis and dermis (Figs. 6C, D). Most of the mononuclear cells stained for CD3⁺, and there were more CD4⁺ than CD8⁺ cells. A few TiA-1⁺ cells were also present (Fig. 7).

Compared with the facial biopsies, the patch test site biopsy showed more epidermal and dermal CD1a⁺ Langerhans cells and a dominance of CD4⁺ over CD8⁺ cells by a ratio of 3 to 1 (Figs. 2, 3, 6, 7).

DISCUSSION

PCD is a noneczematous variant of ACD first described by Osmundsen in 1970. He described a group of textile industry workers who developed hyperpigmentation due to exposure to a new textile whitener.⁸ Pigmented cosmetic dermatitis is a variant of PCD first described in Japan during 1960–1970 by Nakayama.^{6,9} The common allergens implicated in PCD include aniline dyes, bactericides, fragrances, and fragrance fixatives, such as benzyl salicylate in cosmetics.^{6,7} Benzyl salicylate is a solvent present in cosmetics and fragrances, used as odorant, fixative, and UV absorber. The incidence of PCD decreased remarkably in Japan after major cosmetics have reduced the usage of benzyl salicylate.⁷ However, it is still being used in some fragranced cosmetic products. There needs to be awareness of the potential risk of PCD,

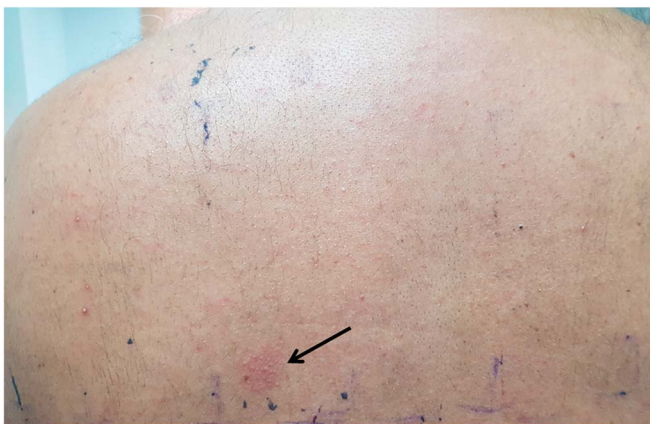
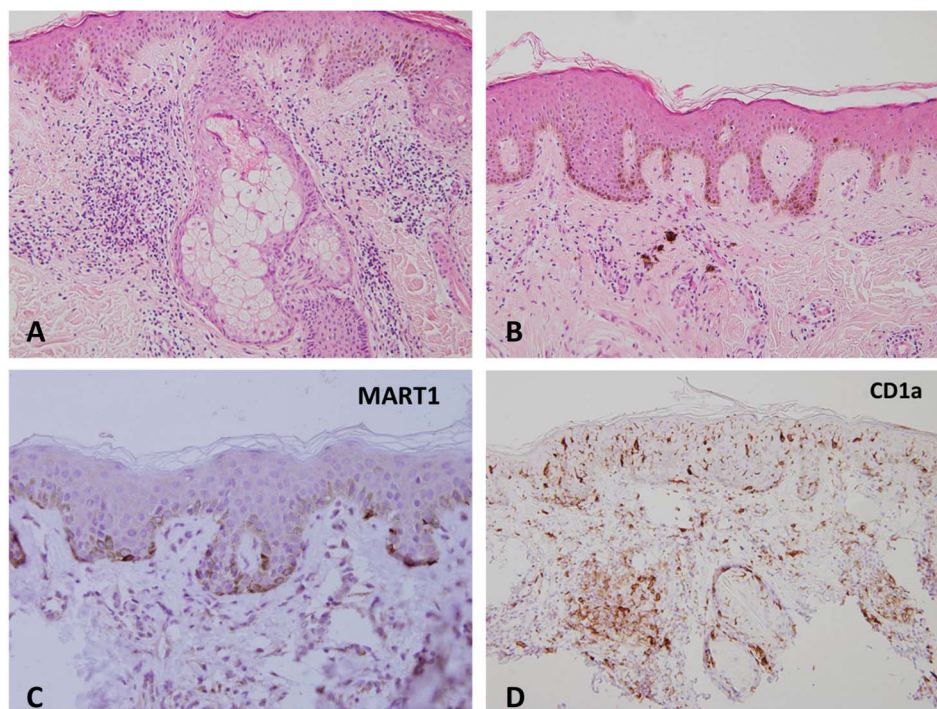


FIGURE 5. Positive reaction to benzyl salicylate (arrow) 96 hours after application.

FIGURE 6. A skin biopsy obtained from the site of the positive patch tests to benzyl salicylate, 96 hours after application. (A) There are perivascular and interstitial mononuclear-cell infiltrates in the papillary dermis. A dense mononuclear-cell infiltrate also surrounds a pilosebaceous unit. (B) The interstitial infiltrate abuts the epidermal basal cell layer with mild vacuolar changes, and melanophages are present in the papillary dermis. (C) Immunostaining demonstrates numerous MART-1+ melanocytes in the basal layer of the epidermis and infundibula, and (D) numerous CD1a + Langerhans cells in the epidermis and fewer in the dermis.



mainly in darker skin types in which the pigmentation can be very marked, as in our case. The pigmentation usually takes a long time to resolve, in some case reports more than a year, and occasionally it may persist despite allergen avoidance.⁵⁻⁷

The pigmentation in pigmented cosmetic dermatitis has been described as diffuse, patchy, reticulate, or occasionally follicular, with predilection for the face and

forehead. The main histology is basal cell liquefaction accompanied by the formation of melanophages in the papillary dermis. Nakayama et al⁶ suggested that the liquefaction may be provoked by accumulation of low concentrations of fragrances producing type 4 allergic cytolytic reaction in the epidermal basal layer. The melanin from destroyed cells is sprayed into papillary dermis and ingested

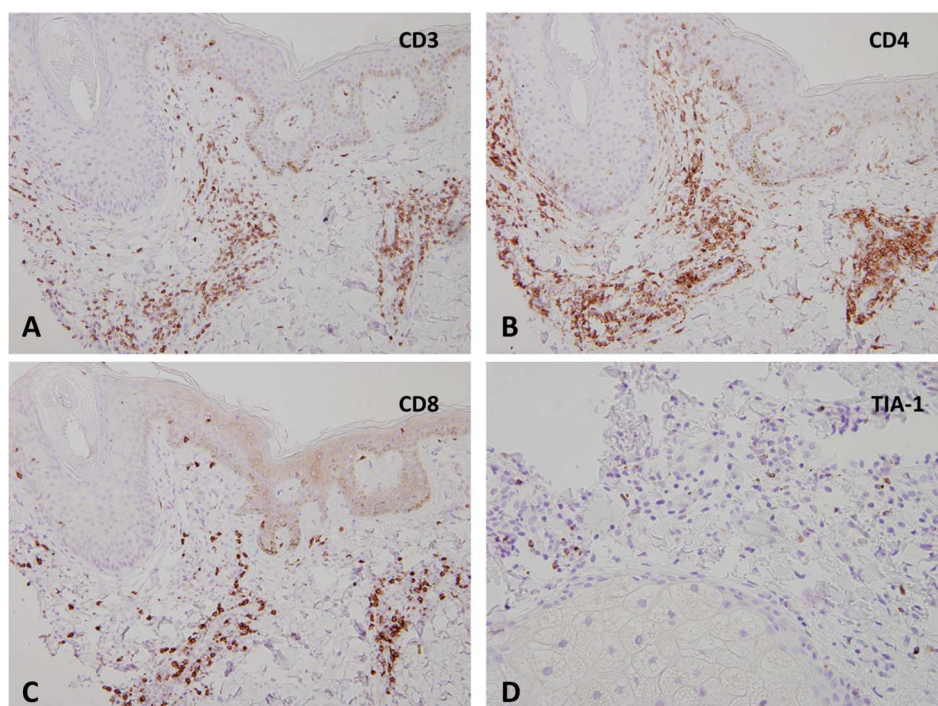


FIGURE 7. (A–C) Immunostaining shows that most of the mononuclear-cell stain for CD3 and there are approximately 3 times more CD4+ than CD8+ cells. (D) There are a few scattered TIA-1+ cells.

by macrophages. This is suggestive of a lichenoid allergic reaction rather than a toxic reaction.⁶

Biopsies from positive allergic patch tests skin sites are often characterized by follicular spongiosis.⁴ In our case, the biopsies of the affected skin and the patch test site showed similar findings, which included mild focal vacuolar interface dermatitis involving the epidermis and pilosebaceous units including mononuclear cells and dermal melanophages. In all 3 biopsies, the inflammatory process involved the upper pilosebaceous unit, which may indicate that the allergen also penetrates the hair follicles.

All cases described of pigmented cosmetic dermatitis due to benzyl salicylate manifest clinically as hyperpigmentation. Our case demonstrated both hyperpigmented and hypopigmented macules, which were similar histopathologically, including preservation of basal cell layer melanocytes. However, the melanin was reduced in the biopsy taken from a hypopigmented macule compared with the hyperpigmented one. These pigmentary changes may, therefore, be attributed to the presence of melanophages and disturbed melanin production.

Although all 3 biopsies in our case showed basically similar histopathological findings, there were some immunohistochemical differences: CD4⁺ cells dominated over CD8⁺ cells in the patch test site, whereas in the longstanding hyperpigmented and hypopigmented lesions, they were roughly equal with a mild tendency toward CD8⁺ cells. TiA1+ cytotoxic T cells were present in small numbers in the dermal infiltrates of all 3 biopsies, most likely involved in the vacuolar interface dermatitis. CD1a + Langerhans cells were much more abundant in the epidermis and dermis of the positive patch test site reflecting, perhaps, a higher concentration of the antigen in the patch test site than in the 2 long-standing lesions.

Dhingra et al¹⁰ studied the molecular profile of contact dermatitis induced by different allergens. The conclusion was that individual allergens can induce distinct immune responses; therefore, ACD does not represent a single immune event. Our case showed lichenoid tissue reaction with some involvement of cytotoxic T cells.

In conclusion, the earliest histopathological and immune phenotypical events in PCD due to benzyl salicylate are similar to those of longer-standing lesions, that is, nonlichenoid focal interface dermatitis, involving the epidermis and pilosebaceous units along dermal melanophages.

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