

Chemokine Responses in Palladium-Induced Lichenoid Eruption: Similarities to and Differences From Lichen Planus

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PRECIS

This report on the chemokine profile of a lichenoid eruption secondary to use of palladium offers new insights for the pathogenesis of this entity.

DISCUSSION

A 43-year-old former metal foundry worker presented with a 6-month-long generalized lichenoid cutaneous eruption and oral erosive lichen planus proximal to silver-colored dental amalgams (Fig. 1A). Both areas of involvement occurred about the same time after placement of the patient's dental amalgams. Violaceous ulcers on the plantar aspect of the man's feet were consistent with plantar erosive lichen planus.

Histopathologic findings were compatible with lichen planus; direct immunofluorescence was nondiagnostic. Patch testing revealed positive reactions to palladium (3+), gold thiosulfate (2+), and potassium dicyanoaurate (2+). Histopathologic analysis of the palladium reaction showed interface vacuolar dermatitis with superficial dermal inflammation (Fig. 1B). The material safety data sheet for the patient's dental work confirmed the presence of 3% palladium in the amalgam. The resulting diagnosis was lichenoid eruption secondary to palladium exposure. Although the cause cannot be determined definitively, we hypothesize that palladium present in the

dental amalgams may have leached into the oral mucosa, causing subsequent systemic absorption that resulted in a lichenoid eruption distant to the site of exposure. The patient declined removal of his amalgams and was treated with topical 0.1% tacrolimus that resulted in 50% to 60% improvement after 6 weeks.

Chemokine immunohistochemistry studies (TARC [thymus- and activation-regulated chemokine]/CCL17 and its receptor CCR4; Mig/CXCL9 and its receptor CXCR3; RANTES [regulated upon activation, normal T cells expressed and secreted]/CCL5 and its receptor CCR3) were performed on biopsy specimens from the skin lichenoid eruption, the palladium patch reaction, and 5 control specimens from subjects with lichen planus, using methodology previously described.¹ Two assessors (A.d.S. and D.A.W.) reviewed the slides and categorized results as negative when less than 10% of inflammatory cells were stained.

TARC/CCL17 and CCR4 were positive in all cases. Mig (CXCL9) was positive in the skin lichenoid eruption (Fig. 1C) and in the lichen planus controls but negative in the patch-test reaction; the Mig receptor CXCR3 was negative in the skin lichenoid eruption and the patch-test reaction but positive in 60% of lichen planus controls. All tissues were negative for RANTES/CCL5 and its receptor CCR3, except for a positive CCR3 reaction in the dermis of the lichen planus controls.

Lichenoid reactions are characterized by autoreactive cytotoxic CD8⁺ T cells that presumably recognize autologous keratinocyte antigens, leading to the attack and destruction of basal layer keratinocytes mediated by T helper 1-type cytokines.² Activated plasmacytoid dendritic cells produce interferon γ , inducing expression of chemokines such as Mig, CXCL10, and CXCL11, crucial for T-cell activation and homing to skin.² CXCR3 and Mig are the main chemokines in lichenoid reactions.²⁻⁴

CXCR3 and Mig are upregulated in chemical-induced allergic skin responses but not in irritant contact dermatitis.⁵ CXCR3⁺ cutaneous lymphocyte-associated antigen-expressing CD4⁺ mem-

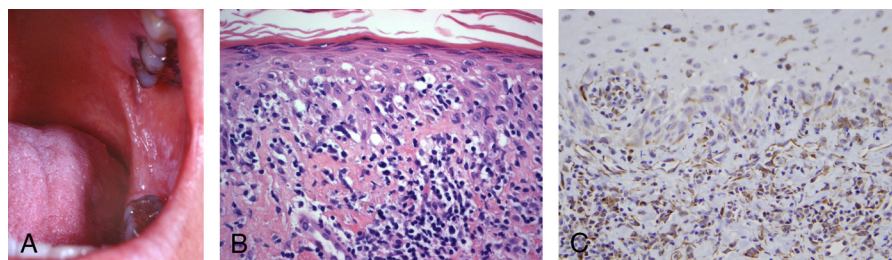


Figure 1. Most relevant clinical and histopathologic findings. A, Buccal mucosa lichenoid eruption adjacent to silver-colored dental amalgams. B, Histopathology showing lichenoid nature of the patch test site (hematoxylin-eosin, original magnification $\times 40$). C, Histopathology showing TARC-positive in the skin lichenoid eruption (immunohistochemistry for TARC, original magnification $\times 40$).

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ory T cells are essential for nickel-specific T-cell proliferation and production of cytokines in vitro.⁵ In vivo studies have shown that stimulation of keratinocytes and dermal endothelial cells with interferon γ produces Mig and CXCR3, amplifying inflammatory responses.⁵

Our results suggest that the chemokine profile of lichenoid contact dermatitis differs from that of lichen planus or allergic

spongiotic dermatitis. However, these conclusions are based on a single case report, so further studies are warranted.

PEARL

This case provides new insights on the pathogenesis of contact lichenoid eruptions.

REFERENCES

1. de Souza A, Gibson LE, Wada DA, et al. Resolution of CD8⁺ lymphomatoid papulosis after surgical excision of the type AB-thymoma. *Am J Dermatopathol* 2009;31(5):475–479.
2. Meller S, Gilliet M, Homey B. Chemokines in the pathogenesis of lichenoid tissue reactions. *J Invest Dermatol* 2009;129(2):315–319.
3. Sells RE, Hwang ST. Paradoxical increase in skin inflammation in the absence of CCR4. *J Invest Dermatol* 2010;130(12):2697–2699.
4. Wang X, Fujita M, Prado R, et al. Visualizing CD4 T-cell migration into inflamed skin and its inhibition by CCR4/CCR10 blockades using in vivo imaging model. *Br J Dermatol* 2010;162(3):487–496.
5. Meller S, Lauerma AI, Kopp FM, et al. Chemokine responses distinguish chemical-induced allergic from irritant skin inflammation: memory T cells make the difference. *J Allergy Clin Immunol* 2007;119(6):1470–1480.

Chemical Leukoderma Occurring After Use of Hair Dye Containing *para*-Phenylenediamine

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PRECÍS

Chemical leukoderma may occur with exposure to *para*-phenylenediamine-containing products. Whereas vitiligo mimics chemical leukoderma, the latter carries a better prognosis, and future occurrences are avoidable.

DISCUSSION

A 50-year-old woman developed an asymptomatic, depigmented area on her scalp with increased number of gray hair roots 2 days

after application of hair dye containing *para*-phenylenediamine (PPD). She had been using the same hair dye for several years. She denied history of preceding trauma or erythema of the region. Medical history and family history were noncontributory for vitiligo, atopic dermatitis, or autoimmune disease. Clinical examination revealed a sharply marginated depigmented patch of the scalp following the hair margin (Figs. 1A, B). Wood lamp examination accentuated the depigmented area as well as one 3-mm depigmented macule along her left eyebrow and two 2-mm depigmented macules on the bilateral antecubital fossae. Liver and thyroid function tests were unremarkable. Allergy patch test was negative for PPD. At her follow-up visit 1 week later, daily application of clobetasol propionate foam 0.05% to her scalp had resulted in increased follicular and generalized repigmentation.

Chemical leukoderma is an acquired depigmentation dermatosis induced by repeated exposure to specific chemical compounds such as topical derivatives of phenols and catechols, PPD, tretinoin, and systemic medications including chloroquine.¹ Depigmentation can occur secondarily to a preceding allergic contact dermatitis or via direct toxic effects. *para*-Phenylenediamine is added to hair dyes to decrease application time and intensify color. Its chemical structure is similar to tyrosine, which may be converted by tyrosine-related protein 1 into compounds toxic to the melanocyte. This leads to loss of melanocytes within the skin and hair follicle, resulting in skin depigmentation and graying of the hair.^{1–3}

In a study of 864 cases of chemical leukoderma, 27.4% of patients experienced depigmentation at the site of hair dye application. Areas of involvement were limited to the contact area in 73.7% but had spread to remote areas in 26.3% cases.¹ This may be due to (i) sensitization or (ii) autotransfer or heterotransfer of the chemical.

The differential diagnosis of depigmented lesions also includes postinflammatory depigmentation, vitiligo, and koebnerized vitiligo. To differentiate between these disorders, one must obtain a thorough history, including previous exposures and antecedent skin reactions at the involved site. Negative allergy patch testing without history of preceding erythema or irritation in the involved area helps rule out postinflammatory depigmentation following an allergic contact dermatitis.¹ Histopathologically, both chemical leukoderma and vitiligo reveal a complete absence of melanocytes. Vitiligo commonly presents as a bilateral, symmetric depigmentation of the face and body, favoring the extensor surfaces and bony prominences.⁴ In contrast, chemical leukoderma occurs at the exposed site, with an ability to develop numerous small depigmented macules at remote sites.¹

In our patient, history of repeated exposure to PPD-containing hair dye resulted in a sharply demarcated depigmented patch at the site of chemical exposure, which is consistent with chemical leukoderma. Repigmentation after discontinuing use of PPD further supports our diagnosis. Interestingly, depigmentation of the

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