

# Chronic Acquired Dyskeratotic Papulosis of the Face

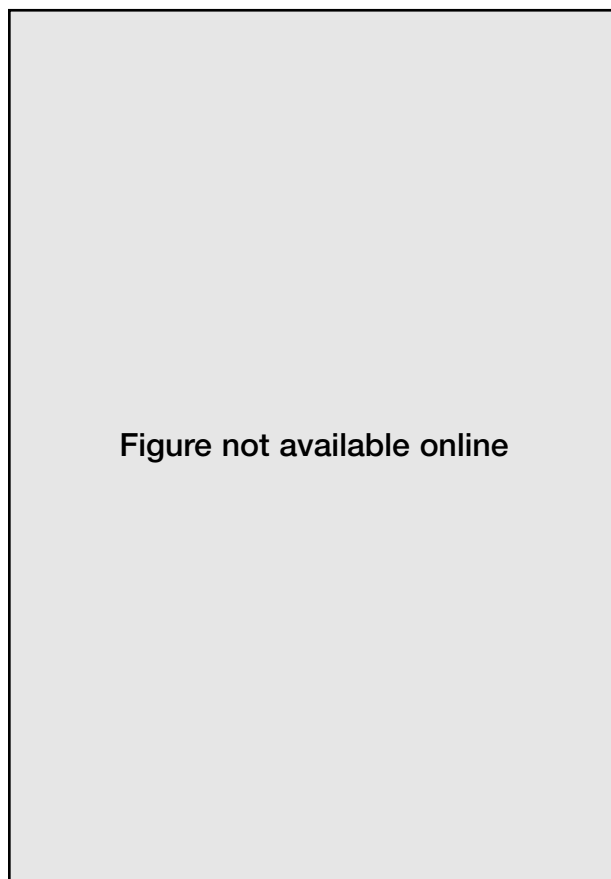
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*A Vietnam veteran who had been exposed to Agent Orange presented with a 28-year history of a papulonodular disease mainly affecting the face. Over those years, pin-sized papules had developed into dark nodules. Multiple biopsies of both fresh and mature papulonodules had been performed for routine histopathology and electron microscopy. Results had been positive for spongiosis with exocytosis, acanthosis, dyskeratotic keratinocytes, and marked incontinence of pigment, which together are suggestive of a previously unreported clinical entity that we term chronic acquired dyskeratotic papulosis.*

## Case Report

A 51-year-old black man presented with a papulonodular disease that had begun as mildly pruritic pin-sized papules 28 years earlier (during his tour of duty in Vietnam) and that had progressed to persistent dark nodules 0.5 to 1.5 cm in diameter. Over the years, new lesions also had developed. The majority of lesions involved the face (Figure 1), but several affected a shoulder and the upper back. The rest of the patient's physical examination was unremarkable.

Since the patient's initial eruption, various therapeutic modalities had been tried, but none had had any effect on the size or color of the lesions or on the development of new eruptions. Treatments had included various topical steroid preparations (1% hydrocortisone cream, 0.1% triamcinolone acetonide ointment, 0.1% mometasone furoate cream), intralesional triamcinolone acetonide (20 mg/mL), and nonsteroidal preparations (0.05% tretinoin cream with sunscreen, metronidazole



**Figure 1.** Multiple discrete pigmented papulonodules, some present for more than 25 years, are photodistributed.

gel, 0.005% calcipotriene cream). Interestingly, the healed skin over several biopsy sites was cosmetically improved, with reversion to almost normal pigmentation. Cryotherapy had not been cosmetically beneficial.

The patient's medical history was significant for exposure to Agent Orange (an herbicide used as a defoliant) and for a case of jaundice during the late 1960s. There was no family history of skin diseases, and neither the patient's siblings nor his child had had skin lesions similar to his. Current medications included sertraline, clonazepam, lisinopril, and

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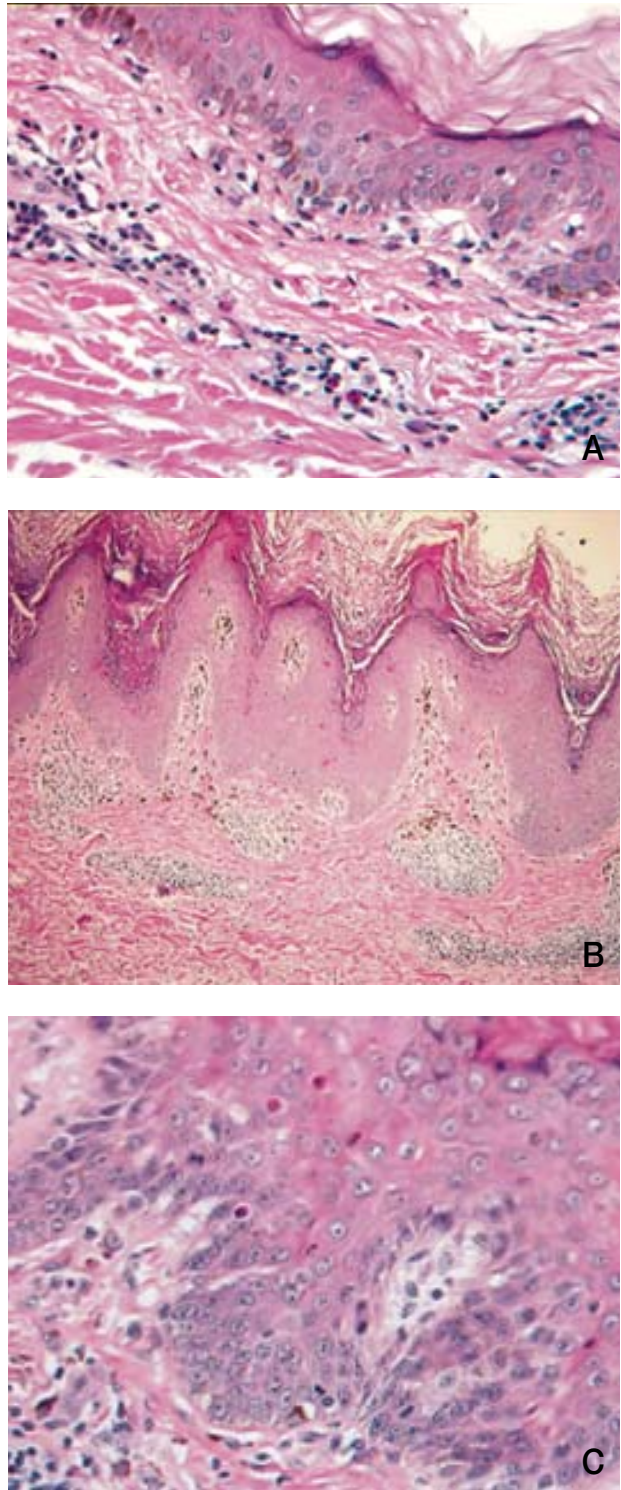
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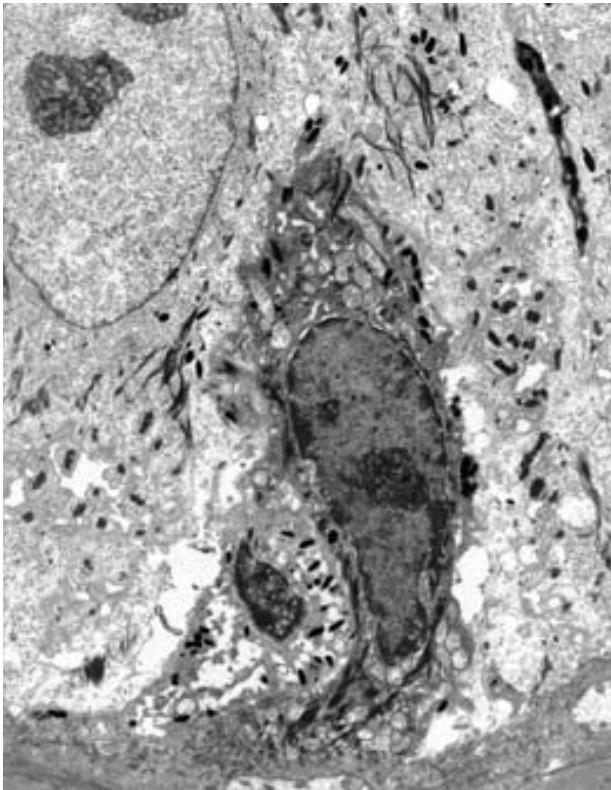
triprolidine for hypertension and posttraumatic stress disorder; the patient denied any medication or drug use around the time of the initial eruption.

Standard laboratory tests were performed: urinalysis; complete blood cell count; renal function studies; VDRL (Venereal Disease Research Laboratory) test; enzyme-linked immunosorbent assay (for human immunodeficiency virus); and tests of serum electrolytes, prothrombin time, partial thromboplastin time, erythrocyte sedimentation rate, rheumatoid factor, and antinuclear antibodies. Results of serum protein electrophoresis showed a minimal increase in the gamma fraction. Results of liver function tests showed occasional elevations of alanine aminotransferase but were otherwise unremarkable. Results of hepatitis screening were positive for antibodies to hepatitis B core antigens but negative for hepatitis B surface antigen—consistent with a case of hepatitis B in the past. Antibodies to hepatitis C were detected by immunoblotting; results of serum polymerase chain reaction (PCR) testing, however, were negative for hepatitis C viral RNA (Clinical Resource Center, Minneapolis VA Medical Center, Minnesota).

We reviewed results of biopsies that had been performed on new pin-sized eruptions and on established pigmented papulonodular lesions over the previous 6 years. Early lesions had been characterized by a dense, perivascular, lymphohistiocytic, and eosinophilic infiltrate around superficial and deep dermal vessels; this infiltrate had been associated with a mildly spongiotic epidermis occasionally containing eosinophils (Figure 2A). Later lesions had been marked by irregular acanthosis, hyperkeratosis, parakeratosis, and the distinctive presence of dyskeratotic cells (Figure 2, B and C). These cells had been found in all layers of the malpighian stratum and often clustered beneath the stratum corneum epidermidis. Incontinence of pigment with numerous melanophages had been prominent in the superficial dermis in late lesions. Given the papular nature of these eruptions and the reversion to normal pigmentation at some healed biopsy sites, we searched for similar histologic abnormalities in hair follicles; in some follicles, we traced dyskeratotic cells and eosinophils to the middermis. On frozen sections, results of immunofluorescent stains had been negative for immunoglobulin G (IgG), IgM, IgA, C3, and  $\kappa$  and  $\lambda$  light chains (BioGenex, San Ramon, California), as had been results of immunoperoxidase stains for hepatitis C (BioGenex). Results of in situ hybridization had been negative for human papillomavirus (Dako, Carpinteria, California). Results of immunoperoxidase staining with CD68,



**Figure 2.** In an early lesion, mildly spongiotic dermatitis with perivascular and intraepidermal eosinophils (A). In a later lesion, verrucous hyperplasia with hyperkeratosis and parakeratosis associated with dyskeratotic cells throughout the epidermis and clustered beneath the stratum corneum epidermidis (B). In another late lesion, incontinence of pigment with dyskeratotic cells and intraepidermal eosinophils (C)(H&E, original magnifications  $\times 400$ ,  $\times 100$ , and  $\times 200$ ).



**Figure 3.** Two basal keratinocytes with pyknotic nuclei and condensed cytoplasm in a late lesion viewed with an electron microscope. Keratin bundles and desmosomes are preserved in some dyskeratotic keratinocytes (osmium tetroxide, original magnification  $\times 2000$ ).

a macrophage marker (Dako), had been positive for intraepidermal and dermal macrophages in some instances.

Results of electron microscopic examination of these biopsies confirmed the presence of dyskeratotic cells throughout the epidermis, including the basal layer (Figure 3); these results are similar to those reported with incontinentia pigmenti (IP).<sup>1</sup> These cells have pyknotic nuclei and condensed cytoplasm with cytoplasmic organelles in various stages of disintegration. Both keratin filament bundles and desmosomes seemed intact. No viral particles were detected.

### Comment

The evolution of our patient's disease rules out the usual differential diagnosis for an acute eosinophilic spongiosis (eg, contact dermatitis, phototoxic dermatitis, drug-caused eruption, dermatophytosis). However, the combination of histologic features (eosinophilic exocytosis, dyskeratotic epidermal cells, prominent incontinence of pigment) in our patient's case is not unique. There are striking clinicopathologic similarities between the evolution of our patient's disease and the evolution from the

vesicular to the verrucose and then to the pigmented stage of IP—pruritic vesicles and pigmented nodules associated with histologic findings of epidermal spongiosis, eosinophilic exocytosis, dyskeratotic keratinocytes, acanthosis, hyperkeratosis, and incontinence of pigment. However, our patient was an adult when these lesions first developed, whereas IP manifest itself in newborns. Further, the IP rash forms a whorl, whereas our patient's eruption has been papular and has occurred mainly over sun-exposed areas of the body. Unlike IP, which is self-limiting, our patient's disease has lasted more than 28 years. Detection of microscopic changes in hair follicles to the middermis was interesting and may explain the chronicity of the disease.

Our patient's experience with Agent Orange may be significant, as his eruption had developed only on body areas that had been exposed to the herbicide. In our search of the literature, however, we did not find any reports of organochlorine-induced dyskeratosis of the skin. The serum protein electrophoresis finding of a slight elevation in the gamma fraction, associated with a waxing-and-waning elevation in alanine aminotransferase, was suggestive of a chronic disease. Although our patient's immunoblotting results were positive for hepatitis C, results of serum PCR testing and of immunoperoxidase staining of skin were negative for this disease. As PCR testing is much more sensitive than immunoblotting, the immunoblotting results were probably false-positive. Nevertheless, our patient's occasional elevation in liver enzymes in the presence of his current hepatitis B profile suggests that liver biopsies may be needed to clarify the issue of chronic active hepatitis B.

Although we have not been able to pinpoint the etiology of the disease affecting the exposed surfaces of our patient's skin, we propose the term *chronic acquired dyskeratotic papulosis* as a description of this previously unreported entity. *Dyskeratosis* is used here to denote squamous epithelial cells with homogeneous eosinophilic cytoplasm and pyknotic nuclei. Other acquired forms of dyskeratosis include isolated dyskeratotic acanthoma (a solitary lesion)<sup>2</sup> and acquired dyskeratotic leukoplakia of the vagina,<sup>3</sup> both of which were recalcitrant to treatment, as was the case with our patient.

### REFERENCES

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