Chronic Nodular Prurigo Associated with Nummular Eczema: Possible Involvement of Odontogenic Infection

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Accepted April 5, 2003.

Sir,
Prurigos are diseases characterized by intensely pruritic papules and nodules caused by a variety of pathomechanisms. Primary lesions are papules, with or without vesicles, or urticular lesions. Unlike eczematous reactions, the lesions of prurigo rarely become confluent or form lichenified plaque. Prurigo lesions do not show pustule formation or desquamation. However, prurigos can co-exist with several eczematous skin diseases, including, in particular, atopic dermatitis (1). The following is a report on cases of nodular prurigo that initially presented as nummular-like eczematous skin lesions. This type of prurigo seems distinct from classic chronic nodular prurigo Hyde, suggesting the existence of a previously undescribed subtype of nodular prurigo occurring in association with focal infection.

CASE REPORT
A 66-year-old male presented with a 16-year history of rashes appearing on his trunk and extremities. Physical examination revealed small serous papules of 2 – 5 mm diameter scattered on his back and lower extremities. The papules tended to aggregate to form round erythematous plaques 3 – 5 cm in diameter with some exudates. The lesions were severely pruritic. Histologically, the epidermis showed mild, irregular acanthosis with minimal intercellular edema. A cellular infiltrate, largely consisting of lymphocytes and a few eosinophils, was observed around the capillaries of the papillary and upper reticular dermis. Lymphocyte invasion of the epidermis was detected in some areas. Laboratory findings, including blood count, liver and renal function tests, and urinalysis were within normal limits, with the exception of increased levels of blood eosinophils 1892/ mm³, lactate dehydrogenase 757 U/l (269 – 467 U/l) and total serum IgE 3700 (<250 IU/ml). Initially, the patient was diagnosed as having nummular eczema. Over time, however, some of the plaques became elevated and formed erosive dark-red nodules. The patient was treated with topical corticosteroids. While small papules showed slight improvement, the nodules became hyperkeratotic and transformed into dome-shaped brown nodules mimicking prurigo nodularis (Fig. 1a, b, c). These nodules were surrounded by ill-defined urticarial erythema. Histological examination of nodules revealed a marked irregular acanthosis with parakeratotic hyperkeratosis. The inflammatory infiltrate was composed of a number of lymphocytes and eosinophils with an increased quantity of collagen fibres in the upper dermis (Fig. 1d).

The chest roentgenogram, computed tomographic scan revealed no abnormal findings. The patient, however, was also suffering from gum bleeding in the left lower 5th tooth. A roentgenogram revealed remarkable bone loss around the tooth, indicating severe periodontitis. Tooth extraction resulted in a transient flare-up phenomenon characterized by intense erythema around nodules, accompanied by severe pruritus. Within a few weeks, dramatic improvement of skin lesions was noted.

To observe immunological changes associated with skin lesions, intracytoplasmic cytokines of peripheral blood lymphocytes were assessed by flow cytometry. Peripheral blood mononuclear cells from the patient were isolated by Ficoll-Paque (Amersham Pharmacia Biotech, Uppsala, Sweden) density gradient centrifugation. Cells were stained with FITC-conjugated anti-human CD4 or CD8 mAb. After fixation with 4% paraformaldehyde, these cells were permeabilized with 0.1% saponin and stained with phycoerythrin-conjugated anti-human IL-2, IL-4, IL-5, or IFN-γ mAb (Pharmingen, San Diego, CA, USA). Flow cytometric analysis was performed on the Cyto ACE-150 (JASCO Corp., Tokyo, Japan). There was a weak increase in the proportion of...
IL-4+/CD4+ lymphocytes (5.7%) when compared with that of a healthy donor (<1%). Two days after tooth extraction, the percentage of IL-4+/CD4+ lymphocytes was significantly increased (18.9%). There was no significant change in the intracytoplasmic levels of IL-2, IFN-γ and IL-5. Two weeks after tooth extraction, the increased level of IL-4+/CD4+ lymphocytes returned to normal, accompanied by gradual improvement of skin lesions.

DISCUSSION

Prurigo is a commonly used diagnostic term that lacks a precise definition. Prurigos can be categorized into three forms: acute, subacute and chronic. Our patient's skin lesions shared clinical and morphological features with chronic prurigo, in particular prurigo nodularis. It should be noted that these prurigo nodules initially exhibited characteristics of nummular eczema, including the appearance of circular or oval eczematous plaques with grouped serous papules. Prurigo and nummular eczema are clinically distinct diseases. However, Rowland Payne et al. (2) classified nodular prurigo into two groups: nodular prurigo Hyde was described as an eruption composed almost exclusively of prurigo nodules, while nodular prurigo eczema was described as an eczematous eruption with prurigo nodules. Furthermore, Rowland Payne et al. also reported a patient with prurigo eczema exhibiting prurigo nodules arising from nummular eczema (2). It therefore appears likely that there is a transitional form of disease that lies on the continuum between prurigo and nummular eczema. This supposition is further supported by another three similar cases which we have experienced to date (Table I).

The precise aetiology of the prurigos is still unknown. A variety of diseases, such as gluten enteropathy, chronic renal failure, obstructive biliary disease, malignant lymphoma, leukaeemia, polycythaemia, malignant solid tumours, and parasitic infections, have been implicated as causative factors in chronic prurigo. It should be noted that these prurigo nodules initially exhibited characteristics of nummular eczema, including the appearance of circular or oval eczematous plaques with grouped serous papules. Prurigo and nummular eczema are clinically distinct diseases. However, Rowland Payne et al. (2) classified nodular prurigo into two groups: nodular prurigo Hyde was described as an eruption composed almost exclusively of prurigo nodules, while nodular prurigo eczema was described as an eczematous eruption with prurigo nodules. Furthermore, Rowland Payne et al. also reported a patient with prurigo eczema exhibiting prurigo nodules arising from nummular eczema (2). It therefore appears likely that there is a transitional form of disease that lies on the continuum between prurigo and nummular eczema. This supposition is further supported by another three similar cases which we have experienced to date (Table I).

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The cause of nummular eczema is also unknown. The role of regional bacterial infection is still controversial. In some cases, particularly in the elderly, xerotic skin seems to contribute to the pathogenesis of nummular eczema.

It should be noted that our patient's tooth extraction induced a transient flare-up phenomenon characterized by intense erythema around the nodules followed by remarkable improvement of skin lesions. Flow cytometric analysis revealed that transient induction of IL-4+/CD4+ T cells was stimulated by the tooth extraction, suggesting that Th2 cells, but not Th1 cells, were involved in this immunological skin reaction associated with periodontitis. The other three cases also suffered from moderate to severe periodontitis. Treatment of periodontitis by tooth extraction improved their skin lesions. Thus, we conclude that this peculiar type of skin reaction is most likely associated with bacterial focal infections, such as odontogenic infection.

Focal infections, including acute or chronic tonsillitis and odontogenic infections, have been implicated as factors precipitating palmoplantar pustulosis, psoriasis and chronic urticaria (7–10). Either bacterial immune complexes, superantigens or toll-like receptor mediated immune reactions may be involved in the induction of these diseases. Anaphylactoid purpura and certain cases of chronic pigmented purpura also occur in association with focal bacterial infections (11). Further study is needed to elucidate the mechanisms responsible for the differing clinical and histological responses to bacterial antigen stimulation.

REFERENCES


Table I. Characteristics of patients with chronic nodular prurigo, nummular eczema and periodontitis

<table>
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<th>Age/sex</th>
<th>Duration (years)</th>
<th>Distribution</th>
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*Presented case