A Case of Pemphigus Vulgaris Improved by Cigarette Smoking

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 27-year-old white man presented to our clinic with a 3-year history of pemphigus vulgaris. The initial treatment for erosions of the buccal mucosa and blisters on his face and body included oral prednisone, intramuscular gold salts, and oral auranofin. After the patient was given a course of aurothioglucose (Solganol) by intramuscular injection, treatment with oral prednisone (100 mg every other day) and oral auranofin (6 mg/d) was initiated, during which all blisters cleared. Eventually, this regimen proved ineffective. In retrospect, the patient recalled that he began to smoke cigarettes because of stress prior to the improvement of his disease. He also reported that he stopped smoking at the time of disease exacerbation. When his disease flared again, he was treated with intramuscular injections of aurothioglucose (75 mg weekly), without improvement.

Examination revealed a 4 × 4-cm erosive plaque with yellow crusting on the patient’s right cheek and a 2 × 2-cm area of erosion on his left cheek (Figure 1, left). A punch biopsy specimen from the lesion on the right cheek demonstrated an epidermis with a split that extended to adnexal structures, as well as mild acute and chronic inflammation in the superficial dermis (Figure 2). Indirect immunofluorescence was positive for epidermal antibodies at a titer of 1:240.

The dosage of prednisone was increased to 80 mg/d, and cyclophosphamide was added to the regimen at a dosage of 25 mg/d. Because of the lack of clinical effect, the dosage of cyclophosphamide was increased to 100 mg/d, and dapsone was added to the regimen at a dosage of 75 mg/d. Despite this aggressive regimen, our patient’s condition failed to improve.

SOLUTION

The patient reported an inverse relationship between smoking and pemphigus flares. He observed a worsening of the pemphigus when he stopped smoking. Nicotine patches were prescribed, but he began smoking cigarettes again instead. On average, he smokes 15 cigarettes per day. One week after he began smoking again, his pemphigus rapidly started to clear. The dosages of prednisone and cyclophosphamide were tapered, and treatment with both drugs was discontinued over a 2-month

Editorial Comment: An inverse relationship between cigarette smoking and the activity of certain diseases, most notably ulcerative colitis, has been recognized. Similarly, nicotine patches have been used in the treatment of pyoderma gangrenosum. Although the exact mechanism of the “beneficial” effect of smoking and/or nicotine on the activity of these diseases has not been definitively elucidated, nicotine has been found to affect the production of certain proinflammatory cytokines.

As physicians, we must not forget the positive association of smoking with lung carcinoma and cardiac and peripheral vascular disease, as well as with impaired wound healing; therefore, improvement in certain inflammatory diseases cannot be used as a rationale for smoking. Rather, as new inverse associations, such as the one reported by Mehta and colleagues, are found, they should foster further investigations toward determining the exact factors involved and the mechanisms responsible for the effect, and ultimately result in more specific clinical interventions.

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period. Dapsone therapy was discontinued immediately. Figure 1, right, shows the patient 5 months after he began smoking again and 3 months after treatment with all medications had been discontinued. He was unable to directly apply the nicotine patch to the lesion because of the proximity of the lesion to his eyes.

COMMENT

To our knowledge, there are no reports in the literature regarding the improvement of pemphigus vulgaris with cigarette smoking. Other diseases, however, have demonstrated this negative association. In a double-blind, placebo-controlled, randomized, multicenter trial, Pullan et al\(^1\) compared the effects of nicotine transdermal patches and placebo on 72 patients with ulcerative colitis. These patients had been receiving routine medicines for ulcerative colitis but had experienced recurrences of their colitis during treatment. The dosage of nicotine was increased in 5-mg increments to a maximum of 15 mg, or 25 mg if a clinical benefit was not observed at 15 mg. Seventeen of the 35 patients in the nicotine group were able to achieve complete remission of their disease, compared with only 9 in the placebo group. Although the mechanism of action of nicotine in this disease is still unknown, it is plausible that this treatment is beneficial for patients who are resistant to conventional therapy.\(^1\)

Recently, a case report described a 35-year-old man with inflammatory bowel disease and pyoderma gangrenosum. While his bowel disease improved during treatment with steroids and immunosuppressive agents, his cutaneous lesions were unaffected. Therapy with a 10-mg nicotine patch directly applied to the ulcer caused dramatic improvement of the cutaneous lesions; interestingly, this patient was also an ex-smoker, as are a significant number of patients with inflammatory bowel disease.\(^2\)

Another condition reported to have a negative association with smoking is aphthous stomatitis. The cause is unclear, but may be the result of increased keratinization of the oral mucosa making the surface more resistant to formation of ulcers. It is possible that the byproducts of combustion act together to increase keratinization of the epithelial surface in the mouth, which, in turn, may prevent antigenic substances from penetrating and activating the immune system to form aphthous ulcers.\(^3\)

Immune effects associated with smoking include reduced immunoglobulins, helper-suppressor T-cell ratio, lymphocyte transformation, and natural killer cytotoxic activity.\(^4\) By stimulating the hypothalamic-pituitary-adrenal axis, nicotine may elevate levels of endogenous glucocorticoids, thus producing an immunocompromised state.\(^5\) Also, benzopyrine, a tobacco-related polycyclic aromatic hydrocarbon, has been noted to suppress B-cell lymphopoeisis\(^6\) and cytotoxicity in lymphokine-activated killer cells.\(^7\) These immune-mediated mechanisms may play some role in the effect of smoking on pemphigus.

We find these results surprising and desire further evaluation of the active therapeutic agent in cigarette smoke that facilitates this immune response.

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REFERENCES


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