A Possible Role of Interleukin-8 in the Induction of Psoriasis-like Lesions in Torre-Muir Syndrome

Sir,

Torre-Muir syndrome is an autosomal dominantly transmitted genodermatosis associated with visceral malignancies, including colonic adenocarcinomas and their in situ precursors (1). The cutaneous neoplasms associated with this syndrome are sebaceous adenoma, sebaceous epithelioma, or keratoacanthoma in the majority of cases. We describe a case of Torre-Muir syndrome with a family history of malignancies, presenting psoriasis-like erythematous plaques which disappeared or were exacerbated in parallel with the recurrence of his colon cancer.

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CASE REPORT

A 65-year-old male with colon sigmoideum cancer with liver metastasis was referred to our outpatient clinic. His father had died of bladder cancer, and his older brother also had colon cancer. On physical examination, he presented with seborrheic dermatitis-like lesions on his scalp and face. Several yellowish-white, slightly umbilicated papules were scattered on his cheeks. A keratotic nodule was under the right eyelid. A slightly elevated, scaly erythematous lesion, 2 cm in diameter, was seen on the upper back. Similar lesions were noted on his chin and dorsum of the right hand. A histologic feature of the papules on the cheeks was an enlarged sebaceous gland with numerous branching

lobules, compatible with sebaceous hyperplasia. The keratotic nodule showed irregular epidermal proliferation, with downward invagination, compatible with keratoacanthoma. The psoriasis-like lesions also showed hyperkeratosis with parakeratosis, epidermal proliferation with focal invagination and cellular infiltrates in the upper dermis. Similar features were also noted in the lesions on the chin. The psoriasis-like lesions disappeared soon after the initiation of chemotherapy of fluorouracil and cisplatin to his aggressive cancer. However, the lesions then reappeared with the recurrence of his colon cancer.

MATERIALS and METHODS

Cytokine studies

Serum cytokine levels of IL-1β, IL-2, IL-6, IL-8 and TNF-α were examined by using an enzyme-linked immunosorbent assay (ELISA) kit. Peripheral blood mononuclear cells (PBMN) were obtained by 60% Percoll solution (Pharmacia), when the psoriasiform eruption worsened. The cells (1×10^6/ml) were plated in 24-well culture plates (Falcon #3074) and cultured for 24 h at 37°C in a humidified 5%-CO_2 atmosphere. Spontaneous IL-6 and IL-8 levels of the supernatants were examined. Controls were obtained from PBMN of 3 healthy volunteers.

Immunoperoxidase staining

Snap-frozen 5-μm tissue sections of psoriasiform lesions were stained with a rabbit antiserum to recombinant human IL-8 (diluted 1:20, in PBS) (ENDOGEN Inc, USA) using ABC technique.

Reverse transcriptase polymerase chain reaction (RT-PCR)

Fifty 5 μm-thick cryostat sections of psoriasiform lesions were isolated from the biopsied specimens and lysed in guanidinium isothiocyanate. Total RNA was isolated using RNA zol (Biotex CS 101) and then reversely transcribed to cDNA by RAV-2 reverse transcriptase. RNA for control amplifications was isolated from normal skin specimens. Polymerase chain reaction (PCR) was performed in a solution containing 20 pmol/l of IL-8 specific primer pairs (5′ ATGACTTCCAAGCTGGCCGTGGCT, 3′ TCTCAGCCCTCTTCAAAACTTCTC) and IL-8 receptor (IL-8R) specific primer pairs (5′ CAGATCCACAGATGTGGGAT, 3′ TCCAGCCATTCACCTTGGAG) (2, 3). We used the following condition of 40 cycles amplification: denaturation at 95°C for 1 min, annealing at 47°C for 1 min, and extension at 72°C for 2 min. Twenty microliters of PCR products was electrophoresed in 1% agarose gel. The gel was stained with 1% ethidium bromide and visualized under ultraviolet light.

RESULTS

Serum and blood monocytes exhibit enhanced IL-8 production

The IL-8 level in the conditioned medium derived from unstimulated cells cultured for 24 h showed 183 pg/ml. That of normal volunteers was 36.5 ± 7.0 pg/ml (mean ± SD). The serum IL-8 level at the time of the exacerbation of cutaneous lesions was 146 pg/ml (normal, < 10 pg/ml). Other serum cytokine levels of IL-1β, IL-2, IL-6, IL-8 and TNF-α were within normal range.

Positive staining for IL-8

Immunohistochemical staining for IL-8 revealed positive staining of the keratinocytes, with predominant staining in the suprabasal keratinocytes (Fig. 1).

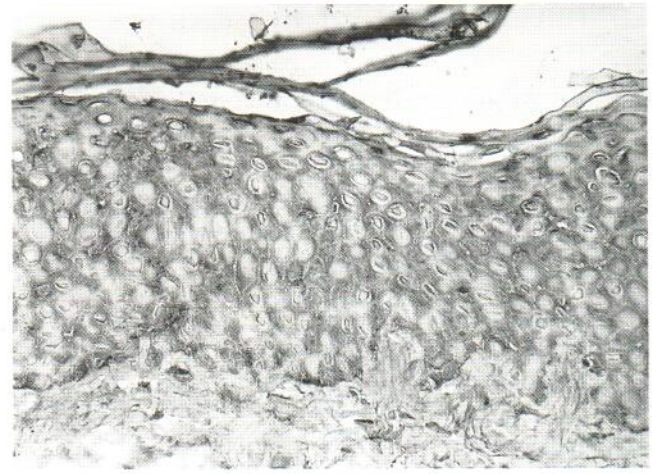

Fig. 1. Prominent IL-8 possibility expressed by keratinocytes, especially in the suprabasal keratinocytes.

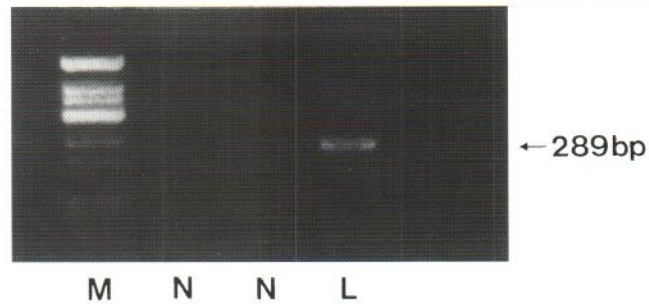

Fig. 2. PCR of IL-8 mRNA (289bp) from normal skin (*N*) and lesional skin (*L*). *Lane M*: marker.

Strong expression of mRNA of IL-8 and IL-8R

IL-8 mRNA was detected only in lesional skin (Fig. 2). IL-8R mRNA was more expressed in lesional skin compared with normal skin (data not shown).

DISCUSSION

It has never been reported that psoriasiform erythematous lesions occur in Torre-Muir syndrome, and it is of note that these lesions appeared in close association with the activity of the colon carcinoma in our case. The sebaceous hyperplasia, on the other hand, did not change either in number or in size.

Recently, IL-8 has been shown to stimulate the proliferation of keratinocytes and reported to be positively stained in the epidermis of psoriasis (4, 5). Abundant NAP-1/IL-8 transcripts are demonstrated only in the upper layers of the lesional psoriatic epidermis by in situ hybridization (6). IL-8 mRNA or IL-8R mRNA is detected in psoriasis (7). In our case, serum and PBMN IL-8 levels were much higher than those in normal volunteers. We also detected positive staining of IL-8 in the keratinocytes of the psoriasis-like lesion and strong expression of both IL-8 and IL-8R mRNA derived from the same lesion. It is suggested that IL-8 is associated with the induction of the psoriasiform lesion in this case. Although the pathogenesis of this syndrome is still obscure, further cases should be compiled and studies are indicated to clarify the stimulus for the development of visceral and cutaneous neoplasias.

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