Two Cases of Basal Cell Carcinoma Treated with Recombinant Alpha-2 Interferon

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Two patients with basal cell carcinoma (BCC) were treated with recombinant alpha-2 interferon. One patient was a 48-year-old man who had a 8×5cm sized ulcer with an elevated border on the face for 10 years, which revealed BCC of the solid type, histopathologically. He received intralesional injections of recombinant alpha-2 interferon (total dose: 51×10^6 IU) for 11 weeks. The biopsy specimen after completion of injections showed a remaining small tumor cell nest in the lesion despite clinical remission.

The other patient was a 75-year-old female, who had 1.2×1.2 cm-sized, darkly pigmented, nodular BCC of the solid type on the nose for 3 years. She also received intralesional injections of recombinant alpha-2 interferon (total dose: 18×10^6 IU) for 8 weeks. The biopsy specimen after completion of injections did not show any tumor cells.

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The interferons are a group of naturally occuring glycoproteins which have antiviral, antiproliferative, antitumoral and immunomodulatory activities.[1] Interferons are divded into three types: alpha or leukocyte interferon, beta or fibroblast interferon and gamma or immune interferon. Recombinant alpha-2 interferon is commercially available, and is produced in bacteria using a recombinant technique.[2] Recombinant alpha-2 interferon has been used as an antineoplastic agent in a number of studies for cutaneous neoplasms including cutaneous T cell lymphoma, malignant melanoma, and Kaposi's sarcoma.[3]

We report herein two cases of basal cell carcinoma (BCC) on the face treated with intralesional injections of recombinant alpha-2 interferon.

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REPORT OF CASES

Case 1: A 48-year-old man visited our department on February 14, 1989 with a large ulcer on the left preauricular area. A single erythematous papule on the left preauricular area developed 10 years ago, and then gradually enlarged with central ulceration. The skin lesion showed a 8×5cm, hemorrhagic, crusted ulcer with a peripheral elevated border (Fig. 1).

Laboratory examinations including complete blood count and liver function test were within normal limits.

The skin biopsy from the lesion showed many tumor cell nests composed of basalioma cells with a peripheral palisading arrangement of nuclei in the dermis (Fig. 2).

At first we treated him with topical application of 5-fluorouracil for 4 weeks without improvement. So we performed intralesional injections of recombinant alpha-2 interferon. One vial (3×10^6 IU) of freeze-dried recombinant alpha-2 interferon was diluted with 1 ml sterile water. The lesion was in-

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jected two times a week with 1 ml (3×10^6 IU) by a 25-gauge needle on a tuberculin syringe for the first 4 weeks, two times a week with 2×10^6 IU for the next 3 weeks, and then once a week with 2×10^6 IU for 3 weeks. The lesion was injected with a total of 51×10^6 IU by 20 injections over 11 weeks. The lesion improved gradually, and healed with depigmentation and central telangiectases after 10 weeks of treatment (Fig. 3).

A second skin biopsy was done 3 months after completion of treatment. The histopathologic findings showed atrophy of the epidermis and small tumor cell nests were found in the margin of the upper dermis although it appeared to be healed (Fig. 4).

Case 2: A 75-year-old female visited our department on December 26, 1989 due to a single, 1.2×1.2 cm, darkly pigmented tumor with a rolled border of 3 years duration on the right side of the nose (Fig. 5).

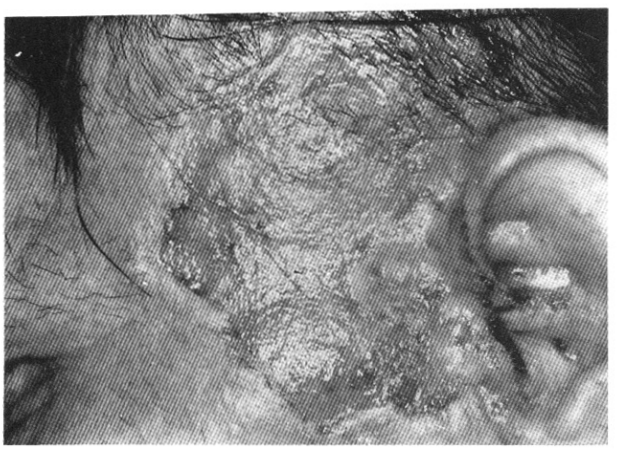

Fig. 1. An 8×15 cm-sized, hemorrhagic crusted ulcer with a peripheral elevated border.

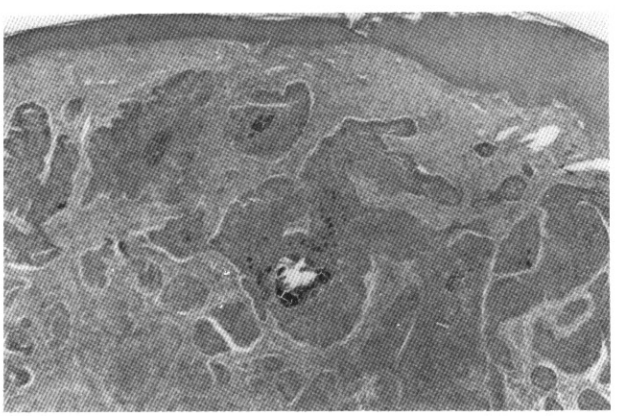

Fig. 2. Many tumor cell nests composed of basalioma cells with peripheral palisading arrangement of nuclei in the dermis (H & E stain, ×40)

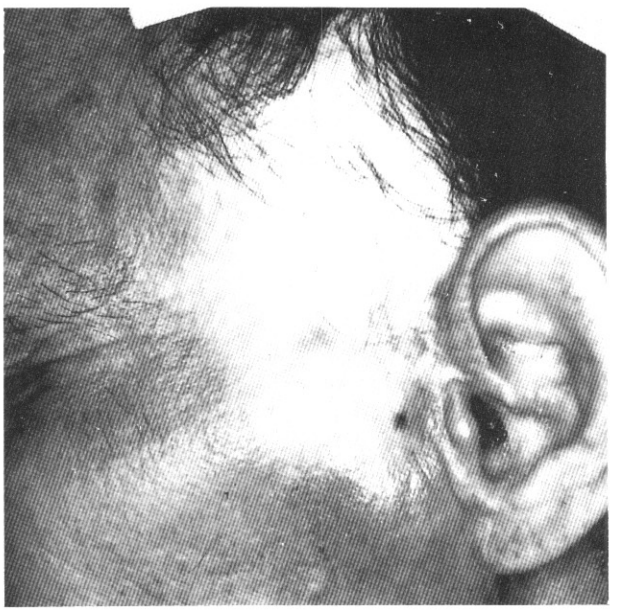

Fig. 3. Depigmented and atrophic patch with central telangiectases at the previous lesional site after 11 weeks of treatment.

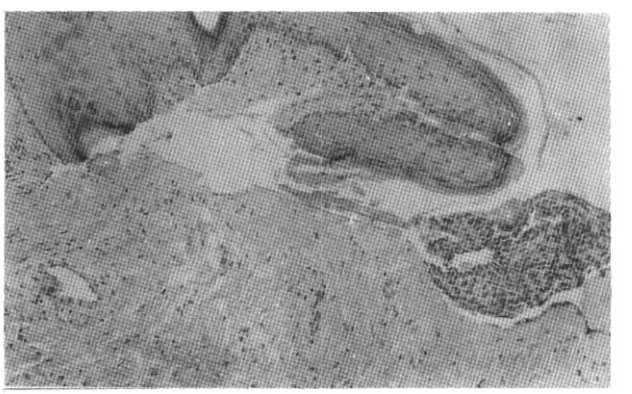

Fig. 4. A small tumor cell nest is seen in the right margin of the upper dermis (H & E stain, ×100)

Laboratory examinations including chest roentgenogram, electrocardiography, urinalysis and liver function test were within normal limits with the exception of 18,200/mm^3 of WBC with 26% eosinophils on complete blood count. Histopathologic findings of the tumor showed tumor cell nests composed of basalioma cells with a peripheral palisading arrangement of nuclei in the dermis (Fig. 6).

We treated her with intralesional injections of

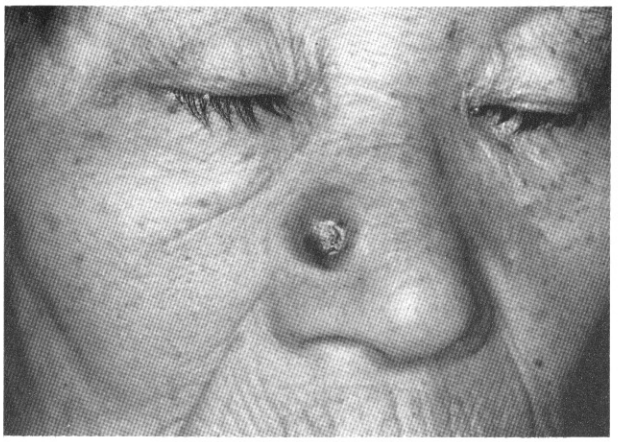

Fig. 5. A 1.2×1.2 cm-sized, darkly pigmented tumor with a rolled border on the right side of the nose.

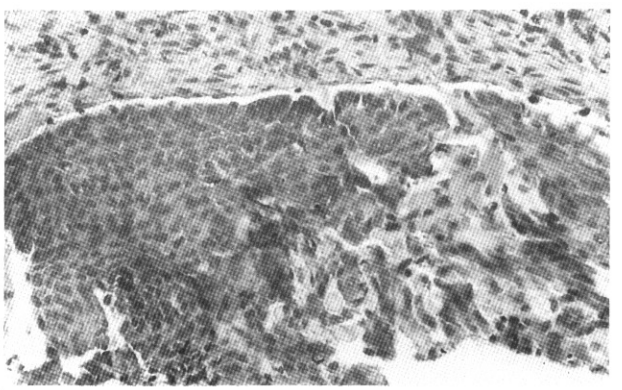

Fig. 6. Tumor cell nests composed of basalioma cells with a peripheral palisading arrangement of nuclei in the dermis (H & E stain, ×400).

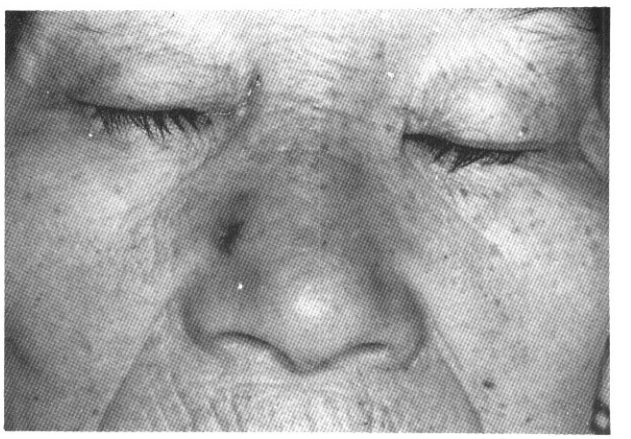

Fig. 7. Flattened lesion with decrease in size after 8 weeks of treatment.

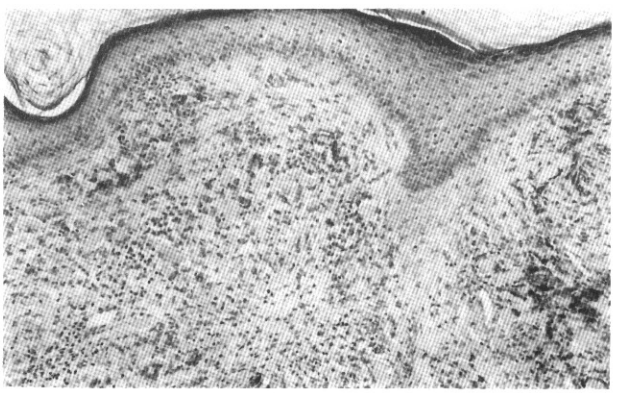

Fig. 8. No tumor cells in the dermis (H & E stain, ×100)

recombinant alpha-2 interferon. One vial of freeze-dried recombinant alpha-2 interferon was diluted with 0.5 ml sterile water. The lesion was injected three times with 0.5 ml (1×10^6 IU) of recombinant alpha-2 interferon by a 25-gauge needle on a tuberculin syringe for the first 3 weeks and two times a week with the same dose for next 5 weeks. The lesion received a total of 18×10^6 IU by 18 injections over 8 weeks. Histopathologic findings in the second biopsy specimen, performed 1 month after the completion of treatment (Fig. 7), showed that it was free of tumor cells (Fig. 8).

DISCUSSION

The interferons have been utilized in the dermatologic field in a number of studies for viral dermatoses (condyloma acuminata, common warts, epidermodysplasia verruciformis, herpes simplex virus infection, varicella zoster virus infection), dermato-oncology (Kaposi's sarcoma with acquired immune deficiency syndrome patient, cutaneous T cell lymphomas, malignant melanoma, actinic keratosis, BCC) and inflammatory dermatoses (Behcet's syndrome, psoriatic arthropathy).[4]

Alpha interferon is a naturally occurring mixture identified by recombinant deoxyribonucleic acid (DNA) technics: its production can be virally induced in peripheral blood leukocytes or cultured lymphoblastoid cells and alpha-2 interferon can be produced in bacteria using recombinant technics.[3]

BCC is a malignant skin of varying clinical pat-

terns, arising from basal cells of the epidermis and its appendages. In spite of the frequency of BCC and remarkable capacity for local destruction, metastasis is distinctly unusual.[5,6] Several clinical types of BCC occur: (1) nodulo-ulcerative type, (2) pigmented type (3) morphea-like or fibrosing type, (4) superficial type, and(5) fibroepithelioma. In addition, there are three clinical syndromes: (1) the nevoid basal cell epithelioma syndrome (2) the linear unilateral basal cell nevus, and (3) the Bazex syndrome.[7] We considered our two cases to be the nodulo-ulcerative type.

The various therapeutic modalities include surgical methods, such as excision curettage, cryosurgery, electrosurgery, Mohs' surgery, and nonsurgical methods such as ionizing radiation therapy, topical application of 5-fluorouracil, laser therapy, and intralesional injection of interferon.[8] Nonsurgical methods are not only desirable but may have advantages, especially in cases of multiple BCC, recurrent BCC, and BCC that are difficult to excise because of their location. Recently, Greenway et al.[3] performed a very interesting pilot clinical trial to treat BCC with intralesional injection of recombinant alpha-2 interferon, and reported a favorable result. But Wickramasinghe et al.[9] observed no histologic improvement although the lesions were clinically flattened. Recently Edward et al.[2] evaluated the effects of intralesional interferon gamma on BCC in 29 patients. The result showed a 50% cure rate with a high dose of interferon gamma. But Tank et al.[10] reported no antitumor response in 7 cases of BCC treated with low dose recombinant interferon gamma.

The mechanism of action by which interferon acts on BCC is partially known. Perhaps as a biologic response modifier, interferon acts primarily by changing the host's cells rather than directly destroying the tumor.[11] Interferon binds to specific receptors on the cell surface, thereby resulting in prolongation of all phases of the mitotic cycle and an ultimate antiproliferative effect. Immune enhancing properties include the activation of natural killer cells and macrophages and the enhancement of both class I and class II major histocompatibility antigen expression on the surface of various cells.[12,13]

The side effects of interferon therapy are mild or moderate, transient and reversible which include flu-like symptoms (fever, chill, headache, myalgia, fatigue), leukocytopenia and thrombocytopenia.

The effect of recombinant alpha-2 interferon injection in our case 1 is controversial because of the microscopic evidence of tumor cells which remained in the posttreatment biopsy specimen despite complete clinical healing. But case 2 showed no microscopic evidence of tumor cells with clinical flattening. The reasons for the unsatisfactory result in case 1 may be due to the large size of the lesion, long duration, the irregular interval of injection, and inadequate distribution of interferon within the lesion. Although we experienced only two cases, our results suggest that intralesional injection of recombinant alpha-2 interferon is a safe and effective therapeutic method for BCC under the condition where non-surgical theraphy is desired.

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