Disappearing Atypical Lentiginous Pigmentation of the Desmoplastic Malignant Melanoma

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A 38-year-old man presented with a black pigmented patch overlying his upper lip, a part of the gingiva and the hard palate. An intradermal tumor mass was palpated at the central portion of the pigmented patch of the upper lip.

Diphenylcyclopropenone (DPCP) is a potent contact sensitizer that could stimulate non-specific immunity. We report a case of desmoplastic malignant melanoma (DMM) in which an atypical lentiginous pigmentation disappeared with topical DPCP immunotherapy and the dermal tumor mass was removed by a surgical wedge-shaped excision. Though an atypical lentiginous pigmentation of DMM sometimes undergoes extensive spontaneous regression, in our case it could be attributed to the therapeutic effect of topical DPCP immunotherapy rather than a spontaneous regression. (Ann Dermatol 13(1) 44~47, 2001).

Key Words : Diphenylcyclopropenone, desmoplastic malignant melanoma

In 1971, Conley *et al.* introduced the term *desmoplastic malignant melanoma* to describe a morphologic subtype of malignant melanoma which has a feature of proliferation of spindle cells with pronounced desmoplasia, and it usually arises in pigmented skin lesions on the head and neck region[1]. The concept of desmoplastic malignant melanoma was expanded further by Reed and Reonald[2], and was subclassified into three groups by Jain and Allen[3]; (a) DMM with an atypical intra-epidermal melanocytic component (classical); (b) DMM without an atypical intra-epidermal melanocytic component (de novo); (c) predominantly nerve-centered superficial malignant tumors with or without an atypical intra-epidermal melanocytic component.

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The atypical lentiginous pigmentation of DMM which is histologically represented with an atypical intra-epidermal melanocytic proliferation might undergo extensive spontaneous regression by unidentified causes[3]. Here we report a case of desmoplastic malignant melanoma in which the atypical lentiginous pigmentation has disappeared after topical DCP immunotherapy.

CASE REPORT

In October 1995, a 38-year-old man presented a blackish lentiginous pigmented patch on his upper lip. He had noticed a small pigmented macule on upper gingiva at the age of 20. The pigmentation has spread during the past three years to the entire upper lip, involving a part of the gingiva and hard palate on presentation (Fig. 1). There was no history of trauma. On physical examination, a 0.5×0.8 cm sized, intradermal tumor mass was palpated at the central portion of the lentiginous pigmented patch of the upper lip. The tumor was painless and firm in consistency. Two lymph nodes were palpable in the submandibular and sublingual regions. The outcomes of laboratory studies including blood cell count, urinalysis, blood chemistry, serum carci-

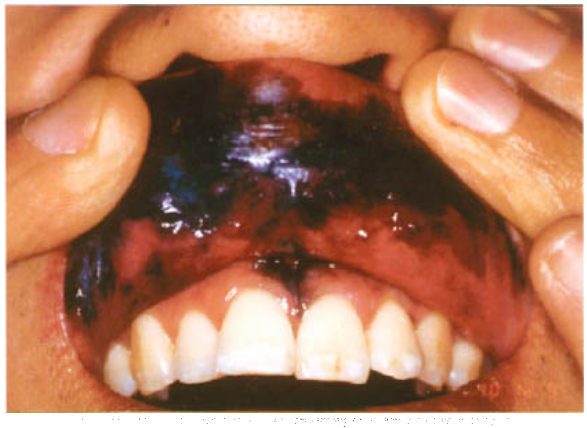

Fig. 1. An atypical lentiginous pigmentation on the upper lip and gingiva at presentation.

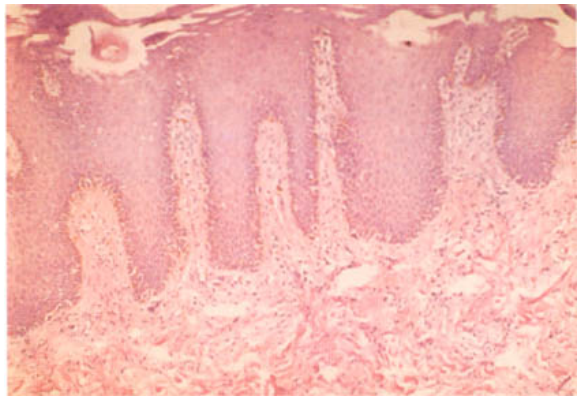

Fig. 2. The overlying pigmented patch on the lip shows marked epidermal lentiginous hyperplasia with atypical melanocytic proliferation (H&E, 100).

noembryonic antigen were within the normal ranges. Roentgenographic examination and computerized tomography also turned out normal. Histopathologic examination on the lentiginous pigmented patch showed marked epidermal lentiginous hyperplasia with atypical melanocytic proliferation (Fig. 2). And the tumor consisted of numerous elongated pigmented spindle cells embedded in a dense fibrous stroma and involved full thickness of the dermis. But there was no discernible histological transition or connection between the pigmented patch and tumor. The cells were pleomorphic, atypical and showed some mitoses. The nerve and vessels are also invaded by tumor cells

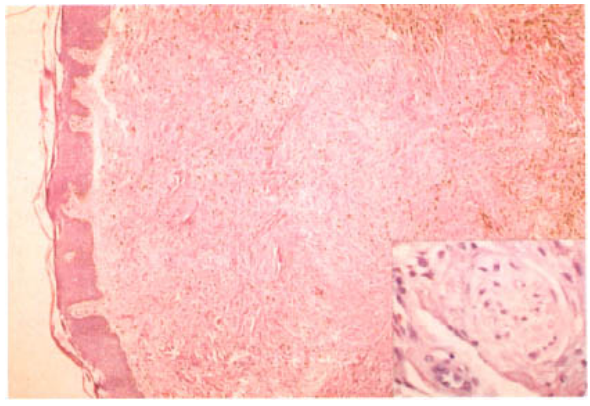

Fig. 3. The tumor consists of numerous elongated spindle cells which are arranged in loose fascicles with a dense fibrous stroma. The cells are pleomorphic, atypical and showed some mitoses (A: H&E, 40). There is neural and vascular involvement (Inset ; H&E, 400).

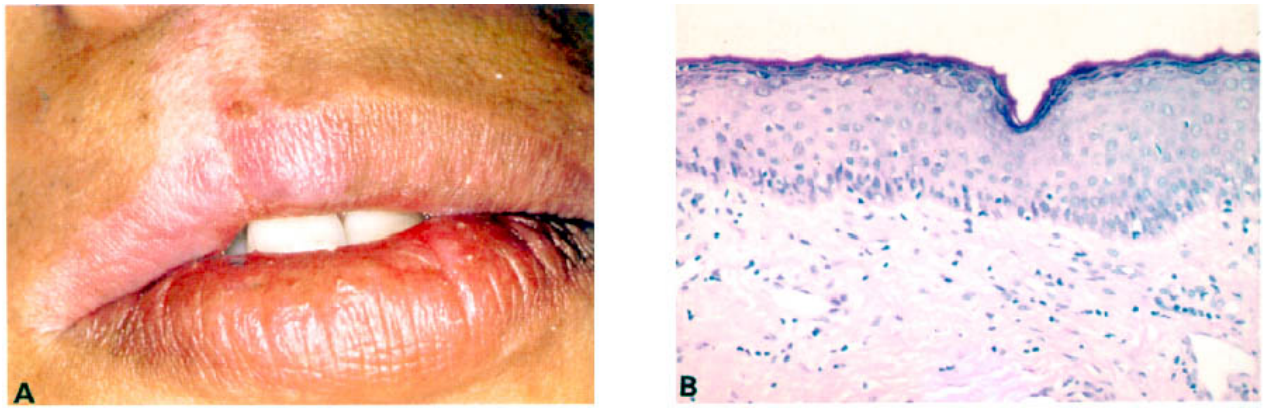

Fig. 4. An atypical lentiginous pigmentation has completely disappeared with continuous topical DPCP immunotherapy for 17 months and hypopigmentation has appeared (A). Histopathologically, the epidermal atypical melanocytic lentiginous hyperplasia disappeared and the treated lesion shows normal epidermis (B: H&E, 200).

(Fig. 3). Immunohistochemical stainings of the tumor were focally positive in S-100 and HMB-45, but negative in cytokeratin, desmin and NSE. The enlarged submandibular lymph node showed no evidence of tumoral invasion by immunohistochemical stain with S-100 and HMB-45 . The clinical association of an atypical lentiginous pigmentation with an apparent fibroblastic spindle cell tumor fulfilled the criteria for diagnosis of desmoplastic malignant melanoma.

The patient had started to receive dacarbazine systemically and interferon-alpha subcutaneously. Additionally the topical contact immunogen, DPCP, was applied epicutaneously to the atypical lentiginous pigmentation of the lip and gingiva at concentrations ranging from 0.01% to 0.1% weekly. After the three months' treatment, we could only continue the topical DPCP immunotherapy due to the leukopenia. The patient was tolerable to topical DPCP immunotherapy, and there were no serious adverse effects except slight numbness and itching of the treated areas. Since the treatment of 5 months, the atypical lentiginous pigmentation began to slowly fade. Finally, after 17 months of continuous DPCP immunotherapy, an atypical lentiginous pigmentation has completely gone but hypopigmentation has appeared. But the size of tumor has not changed during the period of topical DPCP immunotherapy, whereas the atypical lentiginous pigmentation was fading out. The tumor mass was removed by a surgical wedge-shaped excision, including the whole layer of one third of the upper lip (Fig. 4A). The clinical disappearance of the epidermal atypical melanocytic lentiginous hyperplasia was confirmed histopathologically on the treated lesion (Fig. 4B). In contrast to the treated lesions, the untreated lesions of the hard plate showed no changes. After 43 months of treatment, a small tumor mass recurred at the surgical margins. The recurred tumor was excised again. Thereafter we couldn't find any clinical evidence of tumor recurrence or metastasis for 16 months.

DISCUSSION

Desmoplastic malignant melanoma is a special variant of malignant melanoma which usually arises in the sun-exposed skin of the head, neck, and upper part of the trunk, in association with a lentigo maligna in the elderly[4]. The lip also appears to be a favored location for the arising of DMMs from the mucous membrane which is described in the literatures[3,5].

Unfortunately, the biological behavior of the DMMs is not understood as well. Though many investigators dispute the fact that patients with DMM have a better prognosis than those with conventional malignant melanoma of similar depth of the invasion, adequate radical surgery is strongly recommended as with other types of malignant melanoma because the DMMs still have a high recurrence rate and propensity for metastasis[4,6]. Skelton *et al.*[4] reported that the depth of the invasion (Breslow's thickness) is also significantly related to the disease-free survival.

Topical immunotherapy with a contact sensitizer has been used to treat primary and metastatic cutaneous malignant melanoma since 1973[7]. In most of the literatures, dinitrochlorobenzene (DNCB) has been used as a component of immunochemo therapy which combines epifocal applications of DNCB with systemic dacarbazine treatment[8,9]. With the advantages of tolerable side effects and low cost, this immunochemotherapy has been recommended as the effective first line treatment in immunocompetent individuals, even in the patient with concurrent metastases to the skin, visceral organs and brain[9]. In addition, some authors reported their satisfying experience with topical DNCB immunotherapy as a single therapy in primary and metastatic malignant melanoma[10-14]. Illig et al[10,11]. recommended DNCB immunotherapy to spare mutilating surgery especially in superficially growing melanomas, patients with limited operability, or flat melanoma of acral portions. Topical DNCB immunotherapy had also been reported as effective for an immunoprophylaxis or adjuvant therapy in the preoperative or postoperative melanoma patients[13,14].

DPCP is another potent topical contact sensitizer that has been used successfully in clinical ground. Unlike DNCB, it has non-mutagenic properties. We tried DPCP immunotherapy on our patient who was amenable to any other kinds of treatment.

The reason why the atypical lentiginous pigmentation disappeared in our case was somewhat unclear. An atypical lentiginous pigmentation which is histologically represented with atypical intra-epidermal melanocytic proliferation might undergo

extensive spontaneous regression in DMMs[3]. Some investigators have also seen cutaneous hypopigmentation and vitiligo, as with our experience, through DPCP immunotherapy[15,16]. Trucheter *et al.*[17] have assumed that the topical contact sensitizer is melanocytotoxic or works as a non-specific immune stimulator.

We believe that the disappearance of the atypical lentiginous pigmentation of DMM in our case could be attributed to the therapeutic effect of topical DPCP immunotherapy and strongly suggest that topical DPCP immunotherapy might be an effective adjuvant treatment modality for malignant melanoma, especially in non-operable and follow-up cases.

REFERENCES

1. Conley J, Lattes R, Orr W. Desmoplastic malignant melanoma: a rare variant spindle cell melanoma. Cancer 28:914-36, 1971.
2. Reed RJ, Leonard DD. Neurotropic melanoma: a variant of desmoplastic melanoma. Am J Surg Pathol 3:301-11, 1979.
3. Jain S, Allen PW. Desmoplastic malignant melanoma and its variants: a study of 45 cases. Am J Surg Pathol 13:358-73, 1989.
4. Skelton HG, Smith KJ, Laskin WB, et al. Desmoplastic malignant melanoma. J Am Acad Dermatol 32:717-25, 1995.
5. Kilpatrick SE, White WW, Browne JD. Desmoplastic malignant melanoma of the oral mucosa. Am Cancer Society 78:383-9, 1996.
6. Anstey A, Cerio R, Rammarain N, et al. Desmoplastic malignant melanoma: an immunocytochemical study of 25 cases. Am J Dermatopathol 16:14-22, 1994.
7. Malek -Mansour R. Remission of melanoma with DNCB treatment. Lancet I:503-4, 1973.
8. Legha SS. Current therapy for malignant melanoma. Seminars in Oncology 15:34-44, 1989.
9. Strobbe LJA, Hart AAM, R mke PH, Israels SP, Nieweg OC, Kroon BBR. Topical dinitrochlorobenzene combined with systemic dacabazine in the treatment of recurrent melanoma. Melanoma Res 7:507-12, 1997.
10. Illig L, Paul E, B deker RH. Epifocal dinitrochlorobenzene therapy in malignant melanoma (experience during the last eight years). Anticancer Res 4:293-98, 1984.
11. Illig L, Paul E. The nonspecific epifocal Malek-Mansour immunotherapy of malignant cutaneous melanoma using DNCB. Hautarzt 27(12):579-87, 1976.
12. Weidnaer F, Djawari D. Adjuvant DNCB immunotherapy in malignant melanoma. Z Hautkr 54(10):436-43, 1979.
13. Budzanowska E, Pawlicki M. An attempt at topical DNCB immunomodulation in advanced malignant melanoma. Tumori 74(5):519-22, 1988.
14. Lukacs L, Istvan M. Immunosurgical approach to the treatment of malignant melanoma using 2,4-dinitrochlorbenzene. Neoplasma 31(4):437-45, 1984.
15. Van der Steen P, Happle R. Dyschromia in confetti as a side effect of topical immunotherapy with diphenylcyclopropenone. Arch Dermatol 128:518-20, 1992.
16. Hatzis J, Georgiotouo K, Tosca A. Vitiligo as a reaction to topical treatment with diphencyprone. Dermatologica 177:146-8, 1988.
17. Trucheter F, Heid E, Friedel J, Chartier C, Grosshans E. DNCB for malignant melanoma: significance in the treatment strategy. Anticancer Res 9:1531-36, 1989.