Effective Control of Rush Progression of CD8+ Mycosis Fungoides with Pegylated Interferon

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Sir,

Peripheral T-cell lymphomas frequently involve the skin either as a primary or secondary target (1, 2). The WHO-EORTC (European Organization for the Research and Treatment of Cancer) has proposed that primary cutaneous T-cell lymphomas (CTCLs) be classified into mycosis fungoides (MF), Sezary syndrome, a group of primary cutaneous CD30+ lymphoproliferations, and subcutaneous panniculitis-like T-cell lymphomas as distinct, well-defined entities (2). CD8+ MF, a rare type of MF, has an indolent clinical course with slow progression, similar to CD4+ MF. However, tumour-stage MF sometimes has an aggressive course, irrespective of the CD4/8 expression (3). We describe a patient with CD8+ MF that developed from parapsoriasis en plaque, whose aggressive progression was successfully blocked by pegylated interferon (PEG-IFN) treatment.

CASE REPORT

A 72-year-old Japanese woman visited us with a 2-month history of numerous asymptomatic tumours developing on her trunk and extremities. She had a history of parapsoriasis en plaque from 10 years before. Physical examination disclosed multiple erosive plaques and partly confluent tumours on almost her whole body (Fig. 1A). Moreover, she had lymph node swelling in her inguinal, axillary and cervical regions. A full blood count and biochemical profile revealed slight anaemia (Hb 11.2 mg/dl) and high levels of serum IL-2R (2,454 U). Histopathologically, there were atypical large lymphocytes densely infiltrating with plasma cells and eosinophils in the whole dermis and subcutis (Fig. 2A, B). This image was different from the parapsoriasis en plaque 10 years before that showed a slight epidermotropism of a mixture of CD4+ and CD8+ T cells together with a perivascular infiltration of lymphocytes in the upper dermis. Flow cytometry of the infiltrating lymphocytes revealed cellular characteristics as follows: CD2+, CD3 +, CD4-, CD7 +, CD8 +, CD20-, CD30-, CD45+, CD56- TIA+ and Granzyme B+. From the above data, we diagnosed this patient as having CD8+ MF. The histology of the enlarged inguinal lymph node was dermatopathic lymphadenopathy. There was no evidence of visceral involvement.

We performed total body electron beam therapy (TBEBT) (31.5 Gy), after which her tumours slowly regressed, almost disappearing 2 months later without any additional therapy. However, 3 months after treatment, tumour recurrence was observed in the palmar lesions. These tumours responded well to treatment with PEG-IFN, a derivative of recombinant interferon alpha-2a. She received 180 mg of PEG-IFN subcutaneously every week, and her tumours began to regress gradually. Because of a moderate increase in the serum alanine aminotransferase (ALT) (165 IU/ l) levels, we discontinued the PEG-IFN after 6 weeks. About 1 week after the discontinuation of the PEG-IFN administration, tumour recurrence occurred rapidly. Therefore, after normalization of her serum ALT, we re-started the treatment with 180 mg of PEG-IFN once every week, which suppressed the tumour recurrence that resulted from the discontinuation of therapy (Fig. 1B).

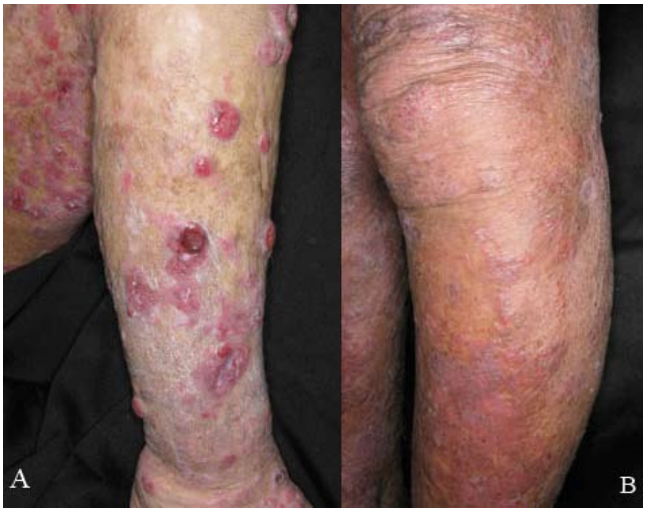

Fig. 1. Multiple red erosive plaques and tumours with confluence on the patient's extremities (A). After treatment with total body electron beam therapy followed by pegylated interferon, the tumours disappeared (B).

DISCUSSION

We describe here a woman with CD8+ MF developing from parapsoriasis en plaque. According to the WHO-EORTC classification for cutaneous lymphoma (2), our case was CD8+ mycosis fungoides (MF), rather than primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, which was separated as a provisionally distinct entity. Primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma has an aggressive clinical course without long-standing precursor lesions, differing from MF (2). Her previous eruption slowly progressed from parapsoriasis en plaque to MF over years, as is commonly seen in usual MF. However, the recent tumour formation had the rush progression, for which PEG-IFN together with total body electron beam therapy was proven to be effective.

As described here, our patient had an aggressive clinical course. Following the guidelines of the Dutch Cutaneous Lymphoma Group, most patients with multi-

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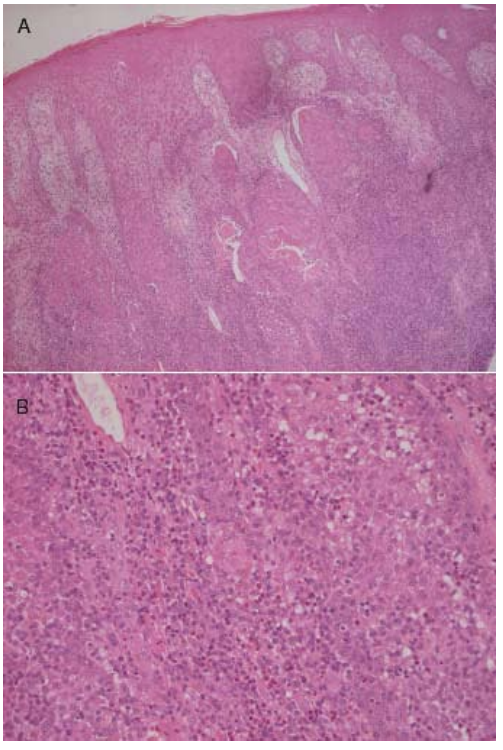

Fig. 2. Biopsied skin specimen showed dense infiltrates of atypical large lymphocytes in the whole dermis and subcutis associated with prominent exocytosis into the epidermis (H&E stain: A, 640; B, 6200; original magnification).

focal skin lesions of peripheral T-cell lymphoma are generally treated with doxorubicin-based chemotherapy (CHOP [cyclophosphamide, doxorubicin, vincristine and prednisolone] or CHOP-like courses) (4). However, doxorubicin-based or other chemotherapies were reported to be ineffective for CD8+ MF (1, 3), although previous cases may have included primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma. Thus, we were required to employ other therapeutic modalities against the rapid enlargement of her tumours.

Recently, it was reported that both IFN-α and -γ are effective for cutaneous T-cell lymphoma through their cytotoxic and immunological effects on tumorous T cells (5–7). However, we selected IFN-α for this patient rather than IFN-γ, which is mainly effective for type 2 helper T cells (5). Although the combination of IFN with PUVA therapy is usually effective for the early stage of CTCL (5, 6), we chose total body electron beam therapy because the lymphoma cells showed an expansion into the subcutaneous tissues. It has been reported that initial radiotherapy resulted in a complete remission in 71% of patients, but that these complete remissions were only short-lived (1). From this point of view, we thought that INF should be used with radiotherapy.

We used PEG-IFN, which allowed once-weekly dosing, thereby potentially increasing the tolerability. PEG-IFN has been found to exert an effect at least equal to that of regular interferon alpha against other malignancies (7). In our present case, the recurrent tumours disappeared after administering PEG-IFN. Because there has been no other effective therapy for CD8+ MF, PEG-IFN may be considered useful to suppress CD8+ MF.

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