Our Dermatology Online

Case Report

Pegylated interferon α-2a in the management of cutaneous T-cell lymphoma

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ABSTRACT

Advanced primary cutaneous T-cell lymphomas often represent a therapeutic challenge regarding the uncertain efficiency of therapies and their poor tolerance. Interferon alpha in combination with phototherapy is part of the therapeutic arsenal of this heterogeneous group of lymphoproliferative diseases, which is mainly dominated by mycosis fungoides. However, its short half-life and poor tolerance by patients often lead us to reconsider this therapeutic option. Herein, we report four cases of our experience with pegylated interferon alpha 2a, its better tolerance profile, and longer half-life.

Key words: Cutaneous T-cell lymphoma, Mycosis fungoides, Pegylated interferon α-2a, Interferon α-2a

INTRODUCTION

Cutaneous T-cell lymphomas (CTCL) are due to the proliferation of activated T-cells in the skin. They form a heterogeneous group of malignant lymphoproliferative disorders (LPD), among which mycosis fungoides (MF), known for its slow and indolent progression, is by far the most common subtype.

Recombinant human interferon-alpha 2A (IFNα-2a), usually combined with PUVA therapy, is among the standard therapeutics for cutaneous T-cell lymphomas. However, its quite short plasma half-life requires administration at least three times a week, with poor tolerance by patients. Pegylated IFNα-2a (PEG-IFNα-2a) is a modified form of IFNα-2a resulting from the non-covalent binding of a methoxy polyethylene moiety. PEG-IFNα-2a has a longer half-life and lower clearance, providing the same or even greater efficacy with fewer side effects. In this paper, we report four cases of cutaneous T-cell lymphoma treated with PEG-IFNα-2a.

CASE REPORT

Case 1

A 63-year-old male patient with no medical history presented mycosis fungoides evolving since 2013, initially diagnosed at the plaque stage, which later evolved to the erythroderma stage (T4N0M0B0), successively treated with methotrexate, RePUVA therapy and IFNα-2a, with only transient improvement. Since his progression to the T3N0M0B0 stage in August 2020 (Fig. 1a), the patient was initiated on PEG-IFNα-2a at a weekly dose of 180 µg subcutaneously combined with PUVA therapy. A three-month outcome revealed a satisfactory response with good tolerance. After nineteen months of treatment, all lesions disappeared, and no new lesions appeared (Fig. 1b).

Case 2

A 71-year-old male had a history of non-metastatic gastric adenocarcinoma treated in 2006 by subtotal

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gastrectomy, in complete remission. Since 2019, he had presented CD30-positive cutaneous pleomorphic large T-cell lymphoma (Fig. 2), treated for eleven months with PEG-IFNα-2a at a weekly dose of 180 µg without improvement. The patient died due to tumor lysis syndrome.

Cases 3 and 4

Two male patients, aged 74 and 77 years, respectively, presented with chemotherapy-refractory mycosis fungoides (Figs. 3a and 3b) that has not responded to methotrexate, CHOP (doxorubicin + vincristine + prednisone), gemcitabine, and DHAP (dexamethasone + cytarabine + cisplatin) protocols. In both patients, the histological examination of skin biopsies found mycosis fungoides with CD30-positive large cell lymphoma transformation and mild pilotropism without follicular mucinosis. Staging assessment revealed IIB (T3N0M0B1a) and IB (T2bN0M0B0) stages, respectively.

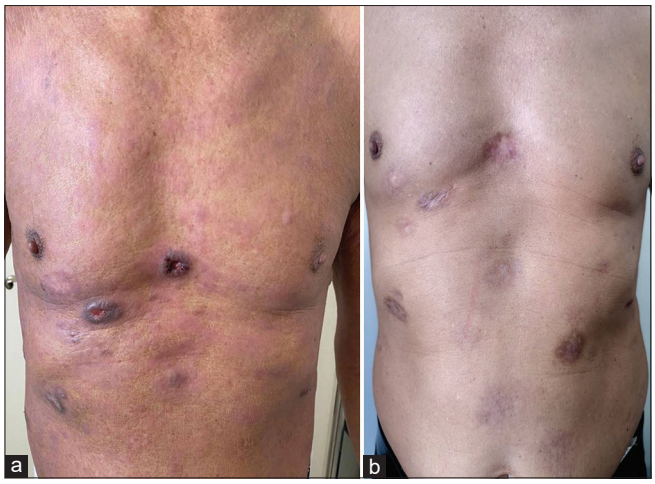

Figure 1: (a) Ulcerated tumor lesions on the trunk. (b) Scar damage after nineteen months of treatment with pegylated Interferon α-2a combined with PUVA therapy.

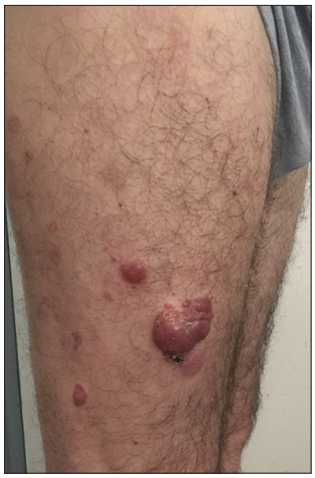

Figure 2: Erythematous tumor lesions of cutaneous pleomorphic CD30+ large cell lymphoma on the thigh.

A treatment with PEG-IFNα-2a was then initiated as follows:

- For the first patient: 135 µg per week for six months, then once every two weeks;
- For the second patient: 180 µg per week for twelve cycles, then one cycle every two weeks, then one every three weeks.

Follow-up showed good clinical and biological tolerance and a satisfactory clinical response in four cycles (Figs. 3c and 3d).

DISCUSSION

Cutaneous T-cell lymphoma is characterized by clonal accumulation T cells in the skin microenvironment. Malignant T-cell populations are made of highly differentiated mature cells that still have the ability to regulate their immune functions. These are memory T-helper cells that mainly present TH2 cytokines, such as interleukin 10, resulting in a local and, then, systemic imbalance of the TH1/TH2 system [1].

Most of these lymphomas are indolent neoplasias with a widely varying clinical presentation. In the early stages, they mainly affect the quality of life through pruritus and clinically visible skin lesions. In the advanced stages, the skin lesions are associated with systemic disorders of the immune response, which lead to an increased risk of infections and secondary malignancies that may be life-threatening [2,3].

Lymphomas usually occur in patients of advanced age, most often with multiple comorbidities. Since there is still no cure, the realistic goal for the management of cutaneous T-cell lymphoma is to achieve long-term remissions with therapies that may be employed safely with no long-term toxicity [4].

Based on this concept, new therapies are being constantly investigated, in particular, pegylated interferon α-2a which has both immunomodulatory and antiproliferative actions. It would be an interesting option in the advanced stages of the disease failing to respond to standard treatments [5]. In addition, its long half-life allows a weekly administration, which is more convenient than a three-weekly dose of INF α-2a [6].

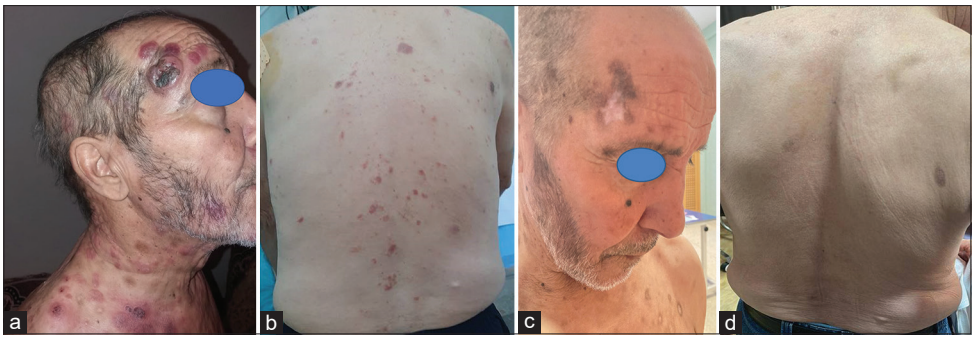

Figure 3: (a) Papulous nodules and erythematous tumors on the cephalic extremity in the first patient. (b) Infiltrated and spread erythematous macules on the back of the second patient. (c) Evolution of the lesions 4 cycles after the beginning of treatment in the first patient.(d) Evolution of the lesions 4 cycles after the beginning of treatment in the second patient.

Schiller et al. reported that PEG-IFNα-2a was generally well tolerated in a series of fourteen patients with mycosis fungoides. The most common side effects were fatigue, acute flu-like symptoms, and hepatic cytolysis. The latter, occurring in one patient receiving a weekly dose of 270 μg, was the only adverse event warranting dose limitation. A response rate after twelve weeks of treatment was 50% in the 180 μg group (OR: 50%; PR: 0%), 83% in the 270 μg group (OR: 67%; PR:17%), and 66% in the 360 μg group (OR: 33%; PR: 33%) [7].

Lype conducted a study on a group of twelve patients with cutaneous T-cell lymphoma treated with PEG-IFN α-2a. All patients were initially treated with a weekly dose of 135 μg with a good clinical response, except for two patients, in whom the weekly dose was escalated to 180 μg. The median response time was 42 days. The duration of treatment ranged from 1 to 17 months, with six patients still undergoing treatment. Pegylated interferon was well tolerated, and no patients interrupted treatment because of toxicity [8].

In four of our patients, PEG-IFNα-2a was also well tolerated, with no side effects. The weekly dose prescribed was 180 μg in three patients and 135μg in one. A good clinical response was noted in three of our patients with mycosis fungoides or transformed MF (T-MF) after twelve, sixteen, and twenty-four weeks of treatment. The patient with CD30-positive large cell pleomorphic lymphoma was in therapeutic failure despite weekly treatment for eleven months.

The duration of PEG-IFNα-2a treatment is not well established in the literature. In fact, the therapeutic protocol of PEG-IFNα-2a in cutaneous T-cell lymphomas is not well defined. In addition, there is insufficient evidence of long-term tolerance.

CONCLUSION

In view of its safety and efficacy, even at high doses reaching up to 360 μg per week, PEG-IFNα-2a could be an advantageous option for patients with progressive cutaneous T-cell lymphomas unable to tolerate standard IFN-α. Nevertheless, in order to assess the comparability between standard IFN-α and PEG-IFN, larger clinical trials are required, studying IFNs alone and in combination with oral photochemotherapy (PUVA).

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published, and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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