Complete response of refractory mycosis fungoides to treatment of pancreatic cancer with combination gemcitabine and nab-paclitaxel: A possible new regimen for the treatment of advanced cutaneous T-cell lymphoma

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INTRODUCTION

Mycosis fungoides is a cutaneous T-cell lymphoma that typically has an indolent, relapsing, and remitting course. Patients with mycosis fungoides often require lifelong treatment with stepwise or concurrent use of multiple therapies, and therefore agents with lower toxicity and immunosuppressive potential are preferred. In general, mycosis fungoides has a good prognosis, but up to 25% of patients can develop progressive disease.[1]

Treatment of advanced mycosis fungoides requires an interdisciplinary approach involving dermatologists, medical oncologists, and radiation oncologists. The main goal of therapy is long-term disease control, which can be especially challenging in patients who present with aggressive lesions.

In cases of early and localized mycosis fungoides, skin-directed therapies are preferred, including topical corticosteroids and nitrogen mustard, as well as phototherapy and local electron beam therapy.[2,3] In advanced or refractory cases progressing toward tumors, these therapies often need to be combined with systemic medications, total skin electron beam therapy, or both.[2,3] Although there is no consensus on the optimal therapy for advanced disease, many clinicians prefer to start with retinoids (including bexarotene), low-dose methotrexate, or both, followed by interferon alfa, before considering additional therapies such as biologics (eg, brentuximab vedotin) and histone deacetylase inhibitors (eg, romidepsin).[3] Extracorporeal photopheresis can be an effective treatment for patients with Sézary syndrome.[4] Patients with lymph node or visceral involvement often require single or multiagent chemotherapy. A minority of patients are candidates for curative-intent allogeneic hematopoietic cell transplants, but morbidity and early mortality remain high in these cases.[5]

Abbreviation used:

UV: ultraviolet

In general, systemic chemotherapies yield variable short-lived response rates and are therefore reserved for refractory or palliative cases. Although many of the regimens used for other types of non-Hodgkin lymphoma have been used in the treatment of advanced mycosis fungoides, there is no consensus on optimal choice.[2,6,7] There are several studies that support the use of single-agent gemcitabine in the treatment of mycosis fungoides,[8-10] but to our knowledge, this is the first reported case of combination treatment with gemcitabine and nab-paclitaxel.

CASE REPORT

A 56-year-old white man with a medical history of type 2 diabetes, hyperlipidemia, hypertension, and smoking presented in 2010 to a community

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dermatologist with widespread, erythematous, scaly, indurated plaques and patches on his trunk. Skin biopsy confirmed the clinical suspicion of mycosis fungoides (stage Ib, NCCN [TNMB]). Flow cytometry result was negative for Sézary syndrome, and there was no lymphadenopathy or hepatosplenomegaly. The patient was treated with narrowband ultraviolet (UV) B phototherapy 5 times weekly in addition to potent topical corticosteroids, but despite 6 months of therapy (97 treatments) his disease continued to progress. He was transitioned to psoralen plus UV A therapy with the bath method. When this was ineffective, he began receiving systemic psoralen plus UV A in combination with acitretin 25 mg/d. After initial improvement and stabilization, his disease continued to progress after approximately 1 year (90 treatments; 299.3 J). He was then treated with topical nitrogen mustard application continuously for 2 years before further disease progression. Systemic psoralen plus UV A was restarted, and the patient received 200 treatments between July 2013 and January 2016 (401.2 J). Alitretinoin 30 mg by mouth daily and bleach baths twice weekly were started in November 2014. Nevertheless, his disease continued to progress with the development of tumors (stage IIb) and he required localized radiotherapy on his face, eyelids, and trunk. The result for systemic evaluation in 2016, including flow cytometry, was negative for peripheralized lymphoma, and repeated skin biopsy result was negative for large cell transformation. Methotrexate 30 mg by mouth weekly was added to his regimen, followed by interferon alfa 3 million units subcutaneously 3 times weekly from February to June 2017. He had minimal response to these therapies, and after several months of worsening abdominal pain and weight loss, an abdominal computed tomographic scan in July 2017 identified a pancreatic mass consistent with locally advanced pancreatic adenocarcinoma. Diagnosis was confirmed on biopsy, and the tumor was unresectable. The decision was made to start palliative combination gemcitabine and nab-paclitaxel chemotherapy in October 2017. Improvement in mycosis fungoides lesions was observed during the first cycle, and complete remission by 3 months of treatment, with stable pancreatic disease (Fig. 1). As of April 2020, the patient had received 32 cycles during 30 months and is still in remission.

DISCUSSION

In general, single-agent chemotherapies are preferred in the treatment of advanced mycosis fungoides to limit toxicity.[2,3] Commonly used single agents include pegylated liposomal doxorubicin, gemcitabine, pralatrexate, and purine analogues (eg, fludarabine).[6,7] Unfortunately, response to chemotherapy is generally short-lived, and there is no evidence that early aggressive treatment of mycosis fungoides is superior to more conservative management.[11]

Gemcitabine has been shown to be an effective treatment for advanced mycosis fungoides. In 2000,

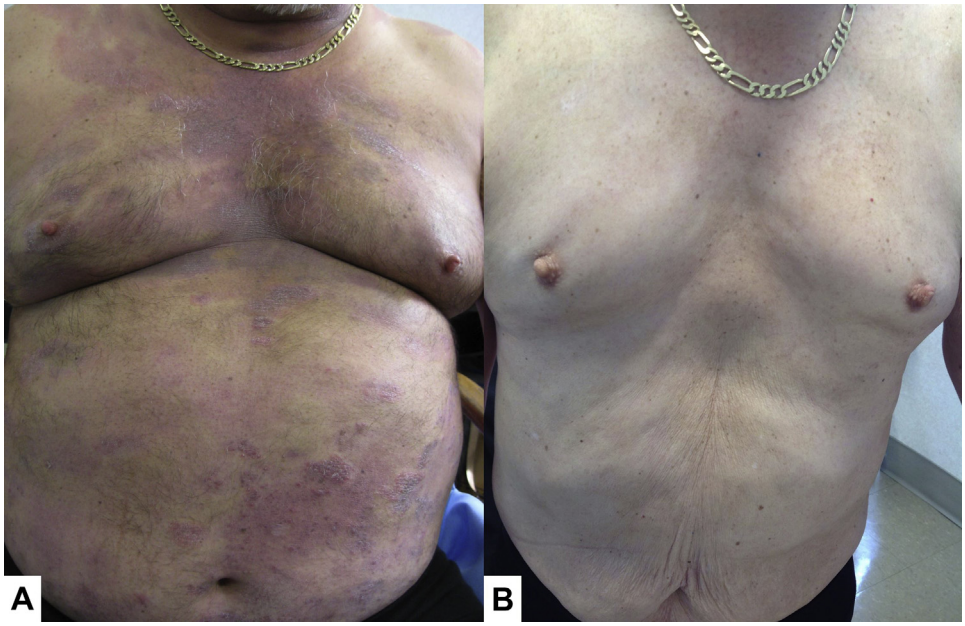

Fig 1. Complete remission of mycosis fungoides. Before **(A)** and after **(B)** treatment with combination gemcitabine and nab-paclitaxel.

44 previously treated patients with mycosis fungoides (n = 30) or cutaneous peripheral T-cell lymphoma unspecified (n = 14) were administered three 28-day cycles of gemcitabine. Five patients (11.5%) achieved complete response and 26 (59%) achieved partial response, with median durations of 15 and 10 months, respectively.[8] In an open-label trial performed in 2006, 25 patients with mycosis fungoides or $CD30^+$ anaplastic large T-cell lymphoma received a minimum of 6 cycles, with an overall response rate of 68% (complete response = 2). Stages ranged from Ib to IVb.[9] In a 2010 study, 19 patients with pretreated mycosis fungoides (all T3-4, N0, M0) received 3 to 6 cycles of gemcitabine monotherapy, and 48% responded (complete response = 3). Of the complete-response patients, 1 relapsed after 10 months and the other 2 were disease free at publication in 2010, with ongoing remission periods of 18 and 120 months, respectively.[10] In general, single-agent gemcitabine is relatively well tolerated, although more common adverse effects reported in these studies included fever, flulike symptoms, nausea and vomiting, peripheral neuropathy, and myelosuppression.[8-10]

To our knowledge, this case represents the first report of a patient with advanced mycosis fungoides treated with combination gemcitabine and nab-paclitaxel. Despite having an aggressive and very refractory clinical course, the patient achieved complete remission of his mycosis fungoides. Combination gemcitabine and nab-paclitaxel was shown in 2013 to be superior to single-agent gemcitabine in the treatment of advanced pancreatic cancer and has become first-line standard of care in recent years for that disease.[12] Although combination therapy is more toxic than single-agent gemcitabine, it is still fairly well tolerated, as evidenced by this patient who has received an extended course with few adverse effects. Reported studies show response rates of approximately 50% to 70% for single-agent gemcitabine for cutaneous T-cell lymphoma; however, the rate of complete response is much lower.[7-10] Given the complete and sustained response of our patient to combination gemcitabine and nab-paclitaxel, we believe this combination should be investigated as a possible option for advanced mycosis fungoides.

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