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Case Report

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Durable Remission after Allogeneic Hematopoietic Stem Cell Transplantation (Allo-HSCT) for Refractory Mycosis Fungoides: A Case Report

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ABSTRACT

Mycosis fungoides (MF) is the most common subtype of cutaneous T-cell lymphoma (CTCL) and is characterized by a heterogeneous clinical course and variant stage involvement. Indolent disease is usually observed in its early stages. However, the treatment options for patients with advanced MF are limited and have poor outcomes. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potential curative treatment for refractory cases. Here, we describe the case of a 34-year-old man who was diagnosed with MF at an advanced stage. Eight months before allo-HSCT, the patient received six courses of polychemotherapy based on cyclophosphamide, doxorubicin, vincristine, and prednisolone, which were administered every three weeks. A partial response was obtained.

He underwent allo-HSCT after a myeloablative conditioning regimen and remained in complete remission (CR) for 26 months posttransplantation. Our findings confirm that allo-HSCT can be a curative option for refractory MF**.**

Keywords: Mycosis Fungoides; Allogeneic stem cell transplantation; Refractory

INTRODUCTION

Cutaneous T-cell lymphomas (CTCLs) are a rare heterogeneous group of skin neoplasms. Mycosis fungoides (MF) represents the most frequent subtype, characterized by an initial clinical presentation with plaque lesions and a possible progressive evolution over years to tumor-stage disease. Patients in the early stages generally have an indolent clinical course and long-term survival. However, patients with advanced-stage disease have a poor prognosis with the currently available treatments[1]. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potential curative treatment for patients with advanced/refractory disease due to the graft-versus-lymphoma (GVL) effect[2–4]. Here, we report a patient with advanced MF who received two lines of therapy and achieved complete remission within 3 months after allo-HSCT.

Case presentation

A 34-year-old patient who had a history of erythematous-hyperchromic plaques starting in the abdomen. A skin biopsy was not performed at that time. He initially received topical corticosteroids. Clinical features are characterized by the progressive extension of plaques over 8 years and the appearance of new plaques with multiple erythematous hyperchromic and desquamative lesions that involve approximately 75% of the skin surface with no tumor or palpable adenopathy. He was then referred to the dermatology department. A skin biopsy confirmed the diagnosis of MF. An immunochemical study revealed positive CD3 and CD4 expression, with negative CD30 expression. The full blood count was normal, with no aberrant T-cell populations (in particular sezary cells) detected via flow cytometry in the peripheral blood. A computed

tomography (CT) scan revealed no enlarged nodes or organ involvement. The patient was diagnosed with MF 1B in the early stage (TII N0 M0 B0), according to the updated classification of the International Society for Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) classification of mycosis fungoides and Sezary syndrome.

He received a low dose of oral methotrexate (15 mg) once a week for four consecutive weeks without significant clinical improvement. PUVA therapy was proposed to the patient, but he refused it and was then lost to follow-up.

One year later, he experienced progressive disease with extensive skin involvement characterized by multiple large plaques and the appearance of numerous tumors on the scalp, measuring 1 to 3 cm in the major axis, with alopecia plaques and infracentimetric cervical lymph nodes (Figure 1). A repeat skin biopsy (scalp) confirmed the disease progression of MF without transformation. The peripheral blood smear revealed no Sezary cells. The patient was classified as stage IV A2 (TIIINIIIM0B0). A second-line therapy with CHOP protocol (cyclophosphamide, doxorubicin, vincristine, and prednisolone) was administered every 3 weeks. After 6 cycles, the patient achieved a partial response (reduction of 50% of the skin lesions). He did not receive any other drugs, in particular brentuximab until allo-HSCT.

Prior to allo-HSCT, the patient achieved a partial response, and CT revealed no lymph node or organ involvement. He underwent allo-HSCT from an HLA-matched sibling donor (43-year-old brother) after a myeloablative conditioning regimen (thiotepa 5 mg/kg/d for 2 days, fludarabine 50 mg/m2/d for 3 days, and melphalan 70 mg/m2/d for 2 days), followed by a peripheral blood stem cell infusion (total 5.15 × 10^6 CD34+ cell count/kg).Granulocyte growth factor was used for the mobilization. Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine and a short course of methotrexate. Neutrophil recovery was observed at D+13. At 3 months following allo-HSCT, the patient achieved a complete response on CT and clinical evaluations. He did not develop GVHD or CMV reactivation. Molecular chimerism was not performed.

At 26 months after allo-HSCT, the patient experienced localized relapse, with the appearance of small plaques initially at the elbow and then at other sites (Figure 2). Skin biopsy confirmed MF relapse. He was diagnosed with early-stage IA and received topical corticosteroids with localized radiation (8 Gy). At the last follow-up (6 years after allo-HSCT), the patient was alive without evidence of progressive disease.

The patient's treatment course is summarized in Figure 3.

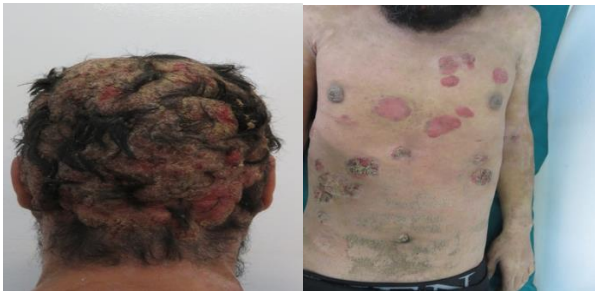

Figure 1. Skin involvement in progressive disease

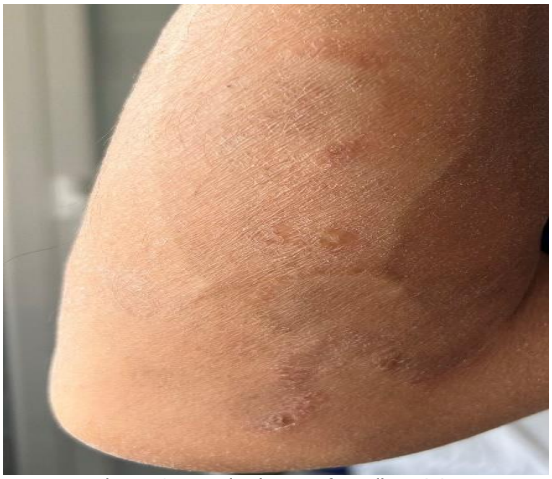

Figure 2. Local relapse after allo-HSCT

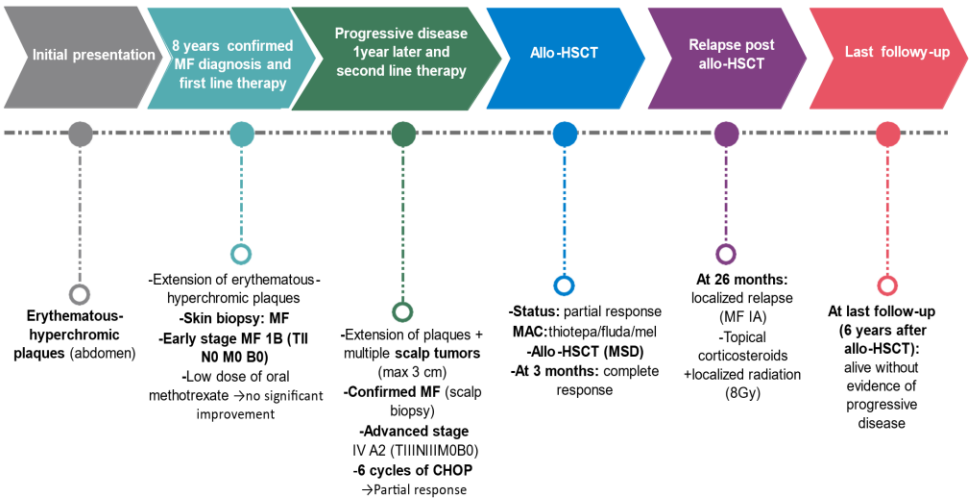

Figure 3. Summary of the chronological diagnosis and treatment course of mycosis fungoides

DISCUSSION

Mycosis fungoides is an epidermotropic lymphoma and the most common type of CTCL; it preferentially affects adults and older patients. The diagnosis of MF is challenging. It is often delayed due to the resemblance of skin lesions to eczema, chronic dermatitis, and psoriasis, which typically appear in non exposed areas[5].

Late diagnosis can lead to disease progression to the disseminated plaque phase, as observed in our case, as the diagnosis was made after eight years until the patient was referred to the dermatology department. The diagnosis is confirmed by skin biopsy, histopathology and immune-histochemical analysis. The classic histopathological features of MF include atypical monoclonal CD4+ lymphocytes with convoluted nuclear contours, Pautrier's microabscesses, and papillary dermal fibrosis[6]. Disease staging is classified according to the later revised ISL/EORTC classification on the basis of the pattern of skin involvement, lymph node and organ involvement and extension to peripheral blood[7].

Treatment depends on whether the disease is in its early or advanced stages. Conventional treatments for skin-limited disease include topical chemotherapy, such as carmustine, PUVA therapy, and electron beam therapy[8]. In our patient, initial treatment with methotrexate resulted in nonsignificant improvement of the lesions. The combination with PUVA therapy could have potentially enhanced the response, but the patient refused this option. Maintaining remission in MF is challenging, as conventional therapy shows limited durability. However, Gregoriou et al reported rapid and durable complete remission with bexarotene, which was achieved and sustained after 6 months of treatment[9]. Unfortunately, this treatment is not available in our country.

The advanced stages of MF are associated with a poor prognosis and short remission with conventional therapy [10,11], as observed in our patient who received the CHOP protocol. Allo-HSCT is a potential treatment option for these patients. However, it is restricted to eligible patients without major comorbidities[12]. Additionally, the optimal conditioning regimen for allo-HSCT remains unclear, as different regimens impact the balance between therapeutic benefit and nonrelapse mortality.

Reduced-intensity conditioning (RIC) is preferred over myeloablative regimens (MACs) in advanced MF because it results in lower nonrelapse mortality and GVL with promising results[13–16]. Our patient received the MAC regimen with a combination of thiotepa, fludarabine and melphalan. He did not develop GVHD or major infectious complications. The choice between MAC and RIC should be carefully considered on the basis of patient comorbidities and disease status prior to allo-HSCT.

Posttransplant relapse remains the major cause of failure in patients with MF, occurring in nearly 50% of cases, mainly in the first year post-transplant and impacting survival rates, with estimated 5-year overall survival (OS) and relapse-free survival (RFS) rates of 50% and 25%, respectively[14,16–18]. The time interval between diagnosis and transplantation, disease status, and performance status at the time of transplant significantly influence both OS and progression-free survival rates. Patients who achieved a very good partial response or complete response and who underwent transplantation within three years from the time of diagnosis had the best OS and RFS rates[12,14,18–20].

Our patient achieved a complete response at 3 months post-transplantation, which was maintained for 26 months. Relapses posttransplant are usually less aggressive and are generally managed with local therapy, as observed in our patient, who remains in remission following local relapse treatment.

Owing to its GVL effect, donor lymphocyte infusion can also be a treatment option for posttransplant relapse in MF, but it can only be proposed for patients without GVHD [21].

In conclusion, the diagnosis and treatment of MF are still challenging. Allo-HSCT is the current potential treatment for advanced stages, allowing prolonged remission and improved survival rates. However, the timing of transplantation and the optimal conditions remain to be established. The emergence of novel treatment options, including targeted immunotherapies such as brentuximab and mogamulizumab, is promising in this setting[22–24]. Further investigations are needed to establish a standard of care for patients with advanced-stage MF.

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