Cutaneous refractory T-cell lymphoma treated with allogeneic hematopoietic stem cell transplantation

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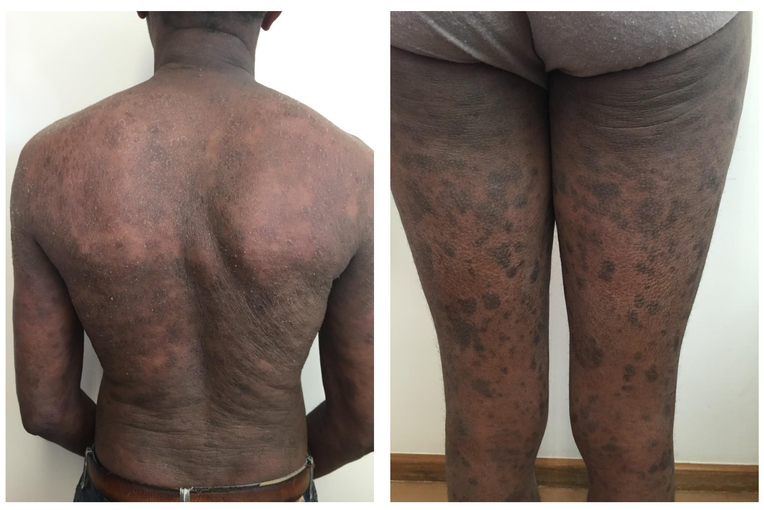
INTRODUCTION

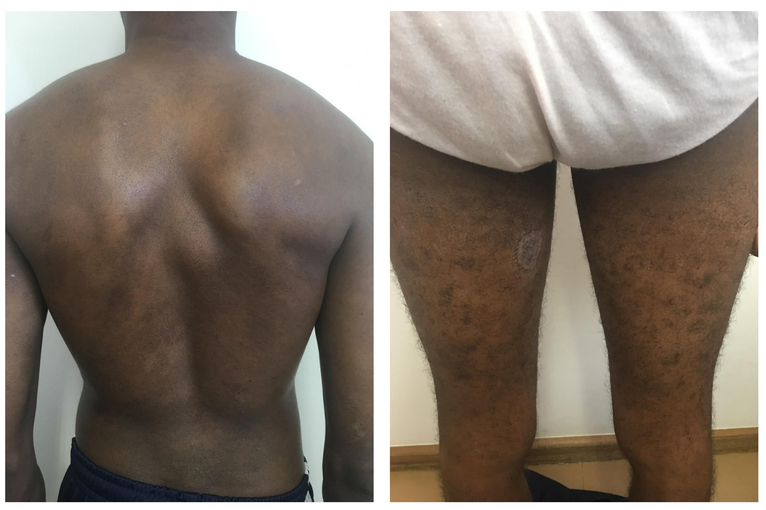
Folliculotropic mycosis fungoides (fMF) is an aggressive clinical course variant of cutaneous T-cell lymphoma (CTCL) - classic mycosis fungoides (MF)[1], with distinct clinical and pathological characteristics, and it is less responsive to skin-directed therapies. For diseases in advanced stages, chemotherapy, autologous hematopoietic stem cell transplantation (HSCT) or immunomodulatory drugs may provide remissions with limited duration and the treatment remains substantially palliative[2]. These dismal results have induced to explore the therapeutical approach with allogeneic hematopoietic stem cell transplantation (HSCT) in such patients. Early studies have shown encouraging results also in patients with advanced disease, suggesting a major clinical role played by the graft versus lymphoma (GVL) effect[3].

CASE REPORT

A 31-year-old male patient with refractory subtype B fMF T-cell lymphoma[4], diagnosed in 2007, clinically characterized by exfoliative erythroderma, widespread plaques on the trunk and limbs, solitary tumor on the right shoulder, pruritus and bilateral inguinal lymphadenomegaly. After failing to seven conventional treatment lines(methotrexate; COP -cyclophosphamide, vincristin and prednisone; gemcitabine; PUVA; interferon; acitretin and extracorporeal photopheresis) , allogeneic HSCT from an identical related HLA donor was indicated. The non-myeloablative conditioning consisted of fludarabine (200mg / m2) D-6 to D-2, cyclophosphamide (50mg / kg) D-7 and total body irradiation(TBI) (400cGy) D-2. Prophylaxis of graft versus host disease (GVHD) was performed with cyclosporine (3mg / kg) and mycophenolate mofetil (30mg/kg). After conditioning, there was improvement of pruritus and involution of the skin involvement. Bone marrow infusion occurred on 2/9/2018 (D0). On D+ 83 it was noticed recurrence of fMF skin lesions . Donor lymphocyte infusion (DLI) was performed (1 x 10^7 CD3 + cells / kg / receptor). Oral lichen and diarrhea presented respectively as manifestations of GVHD on D+ 104 and D + 112. As infectious intercurrence, hemorrhagic cystitis by BK virus appeared 3 months after the first DLI and conservative treatment was performed and the patient remained without systemic immunosuppression. Nine months after HSCT, a second DLI (5 X 10^7 CD3 + cells / Kg / receptor) was performed and until now the patient has no clinical manifestations of fMF or GVHD.



fMF B pre HSCT



fMF B post HSCT

DISCUSSION

The first report[5] of the use of autologous HSCT after TBI for the treatment of MF occurred in 1991, with complete remission in five out of six patients and early relapse in three responders. The case reports that described frequent relapses of the disease led to the abandonment of the use of autologous HSCT. However, with allogeneic HSCT, long-term remissions of CTCLs were observed and remained the only therapeutic option with a curative intent. A review study[6] was recently published where myeloablative conditioning (MAC) regimen and reduced-intensity conditioning (RIC) regimen were used with similar efficacy and with reduced non-relapse-related mortality. The incidence of GVHD was lower in those who used RIC. We used the RIC scheme and rapid response of pruritus and dermatological clinical picture was obtained. Because of early relapse in less than 100 days after HSCT, DLI was used in an attempt to induce the GVL effect, since this seems to be important in inducing and maintaining remission of CTCL[7]. The patient presented moderate GVHD in oral and intestinal mucosa after first DLI without indication of systemic treatment. This case reported a young patient, with no tumor burden in the blood (only on the skin), refractory to various therapies at the time of HSCT, as described in the literature, which are risk factors for progression of CTCL and worse prognosis[7].

CONCLUSION

The clinical response of the presented case confirms what has been reported in the literature. CTCLs appear to be particularly susceptible to GVL, what turns HSCT into a potential cure for advanced CTCLs in eligible patients. The timing to perform HSCT in the clinical course of the disease remains a matter to be settled.

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