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Sezary syndrome manifesting as posttransplant lymphoproliferative disorder

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ABSTRACT

Posttransplant lymphoproliferative disorders (PTLDs) of T-cell orgin are rare biologically heterogeneous diseases of mature lymphoid cells manifesting in immunosuppressed patients. Only a few cases of mycosis fungoides diagnosed post allogeneic hematopoietic cell transplant (alloHSCT) have been described so far. We present a patient with myelodysplastic syndrome (MDS) post matched unrelated donor alloHSCT who was on long-term immunosuppressive therapy due to graft versus host disease. Three years after an alloHSCT, she developed generalized erythroderma and peripheral blood lymphocytosis. Both skin biopsy and peripheral blood flow cytometry revealed atypical CD4+ T-cell population consistent with diagnosis of Sezary syndrome. Chimerism studies revealed 100% donor engraftment. Therapy with extracorporeal photopheresis resulted in complete response in blood and skin.

1. Background

The late complications of alloHSCT include secondary malignancies such as post-transplant lymphoproliferative disorder (PTLD), solid cancers and acute myeloid leukemia/myelodysplastic syndrome (AML/MDS). Among these, PTLD is the most common and typically manifests within six months to one year post-transplant. The majority of PTLDs (>90%) originate from Epstein-Barr virus (EBV) infected B-cells, are donor-derived and occur in the setting of significant immunosuppression leading to decreased immune surveillance of infected B-cells. Other risk factors include the degree of T-cell depleted grafts, host genetic factors, DNA damage secondary to chemotherapy and/or radiation. In contrast, EBV-negative PTLDs typically present more than 1 year after transplant and are non-B-cell in origin [1]. While it has been recognized that up to 15% of PTLDs after solid organ transplant are T-cell in origin, there has only been a handful of reports of T-cell lymphoma and even fewer reports of cutaneous T-cell lymphoma (CTCL) following alloHSCT [2]. Here, we report, a rare case of Sezary syndrome (SS) following alloHSCT from an HLA-matched unrelated donor.

2. Case presentation

Seventy-three year-old female with history of high risk MDS was treated with 5-azacitidine, followed by conditioning with busulfan and fludarabine and alloHSCT from a matched unrelated donor with achievement of complete remission (CR). She was on tacrolimus and sirolimus for immunosuppression. Her post-transplant course was complicated with chronic graft versus host disease (cGVHD).

Approximately three years after alloHSCT, she developed a generalized confluent erythematous rash that was pruritic and continued to worsen. Other than chronic dry eyes and mouth secondary to cGVHD, she was asymptomatic. She was seen by a local dermatologist and underwent skin biopsy. The diagnosis of dermatitis possibly due to drug eruption was made and she was treated with 0.1% triamcinolone cream with minimal improvement. Labs at three months after rash manifestation showed leukocytosis of 12.75 k/uL with 1.66 K/uL atypical lymphocytes, elevated LDH of 261 U/L, hyperglycemia of 258 mg/dL and mildly elevated creatinine of 1.2 mg/dL. Peripheral blood flow cytometry revealed cytologically and phenotypically atypical lymphocytes (Fig. 1A), which prompted additional work up.

Subsequent bone marrow biopsy revealed atypical lymphocytic infiltrate cytologically and phenotypically consistent with mature CD4+ T-cells with decreased expression of CD2, CD3, dim to loss of CD7, loss of CD26 and elevated CD4:CD8 ratio of 19.4 (Fig. 1B, E). Bone marrow was normocellular with trilineage hematopoiesis, and no evidence of recurrent MDS. Sorted CD3(+) and CD33(+) chimerism studies in peripheral blood and unsorted bone marrow chimerism revealed 100% donor engraftment suggesting that malignant T-cell population was

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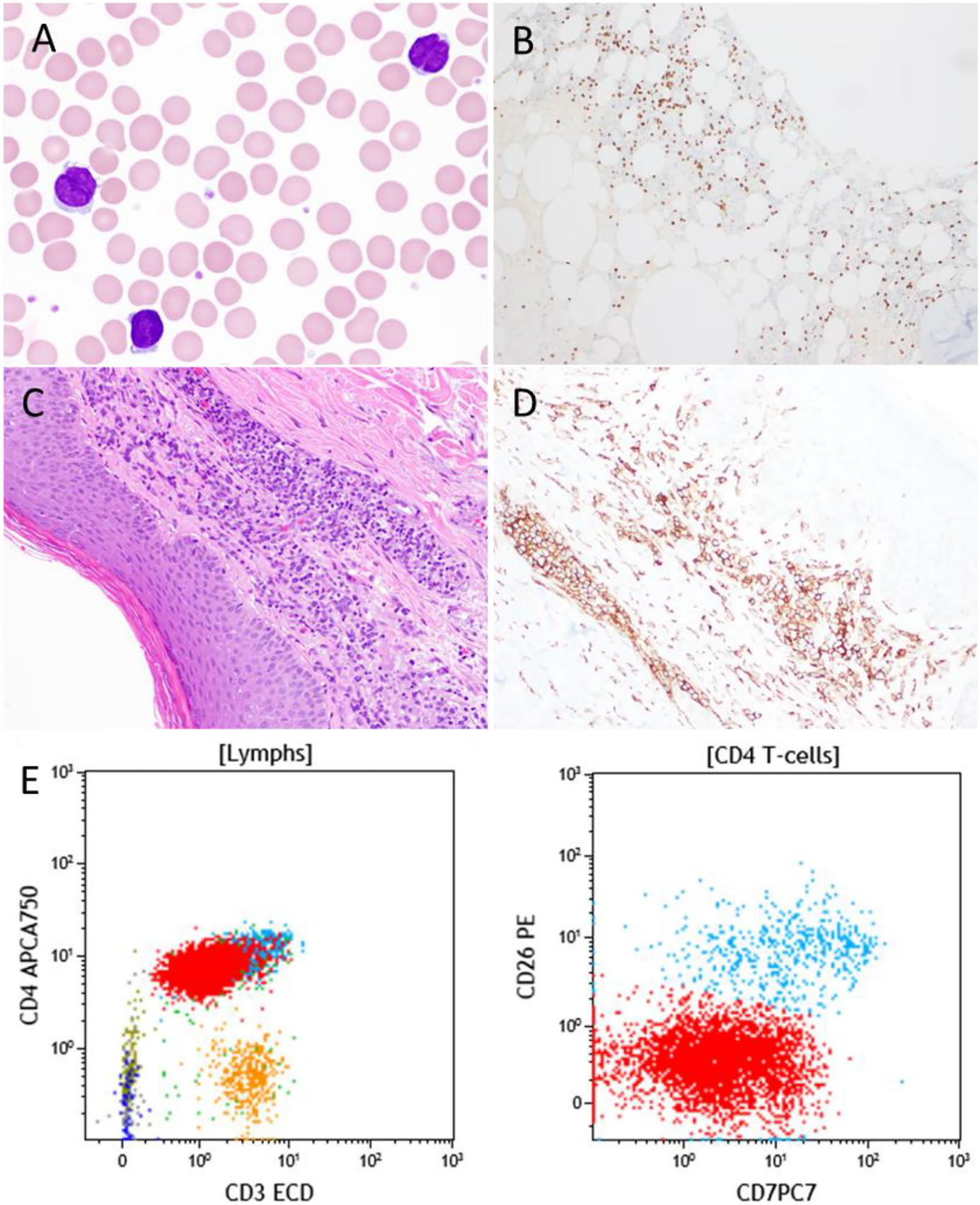

Fig. 1. A. Circulating atypical lymphocytes with irregular nuclear contours in the peripheral blood. 1B. Slightly increased interstitial CD3+ T-cells in the bone marrow biopsy (CD3 immunohistochemical stain, ×100). 1C. Skin biopsy showing superficial dermal atypical lymphocytic infiltrate (H&E stain, ×200). 1D. The dermal atypical lymphocytes are mainly CD4+ cells (CD4 immunohistochemical stain, ×200). 1E. Flow cytometry performed on the peripheral blood showed an atypical CD4+ T-cell population, which decreased CD3 expression, dim CD7 and loss of CD26.