A case of B-cell lymphoblastic leukemia cutis flaring following CAR T-cell therapy in a patient with refractory acute lymphoblastic leukemia

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INTRODUCTION

Recent advances in chimeric antigen receptor (CAR) T-cell therapy have demonstrated promising results for diseases ranging from acute lymphoblastic leukemia (ALL) to glioblastoma.[1,2] Leukemia cutis is a rare manifestation of leukemia, in which leukemic cells infiltrate the skin; as such, there is a paucity of literature describing the effects of CAR T-cell therapy in the context of leukemia cutis. Here we present a case of B-cell lymphoblastic leukemia cutis flaring and spontaneously resolving following CAR T-cell therapy.

Abbreviations used:

ALL: acute lymphoblastic leukemia
CAR: chimeric antigen receptor

CASE PRESENTATION

A 21-year-old man with refractory ALL presented with numerous subcutaneous nodules along the scalp, right shoulder, and right forearm. The largest of these included a well-circumscribed, 4-cm, ovoid, raised lesion on the left lower chest wall (Fig 1, *A*). A skin biopsy of this chest wall lesion was performed. Histopathologic examination of the skin biopsy specimen identified a dermal infiltrate of blastic cells positive for CD19, CD20, CD22, CD79a, Pax-5, and TdT. This pattern was consistent with persistence or relapse of B-cell lymphoblastic leukemia.

Further evaluation of his B-cell lymphoblastic leukemia revealed a mass on CT sinus scan, additional extramedullary disease on PET/CT, and 60% blasts on bone marrow biopsy. He underwent apheresis for planned CAR T-cell therapy. While CAR T cells were being engineered, he received bridging radiation therapy to the sinuses and vincristine with pulse dexamethasone, which resulted in substantial improvement in his B-cell lymphoblastic leukemia cutis lesions.

He received an infusion of 2.4E8 CAR-positive viable T cells without any immediate adverse reactions. Within 3 days after infusion, he began developing numerous, slightly pruritic, indurated, red-to-purple nodules along the upper arms, chest, and back (Fig 1, *B, C*). Over the next 6 days, the rash progressed from the anterior upper arms (Fig 2, *A*) down to the upper thighs. During this time period, he also experienced intermittent fevers consistent with cytokine release syndrome.

A skin biopsy was taken from one of the right upper arm nodules. Within the superficial and deep dermis, there was a perivascular and focally nodular infiltrate composed of mononuclear cells with enlarged nuclei positive for CD19, CD20, CD10, CD79a, CD34, Pax-5, and TdT (Fig 3). Abnormal cells were negative for CD3. This was consistent with his known B-cell lymphoblastic leukemia. Treatment included diphenhydramine as needed for his pruritic symptoms and tocilizumab once for cytokine release syndrome. Three weeks following the CAR T-cell infusion, the patient's B-cell lymphoblastic leukemia cutis resolved spontaneously without further intervention (Fig 1, *D*; Fig 2, *B*). The patient's underlying ALL responded to CAR T-cell infusion, with 5 months of clinical remission prior to relapse.

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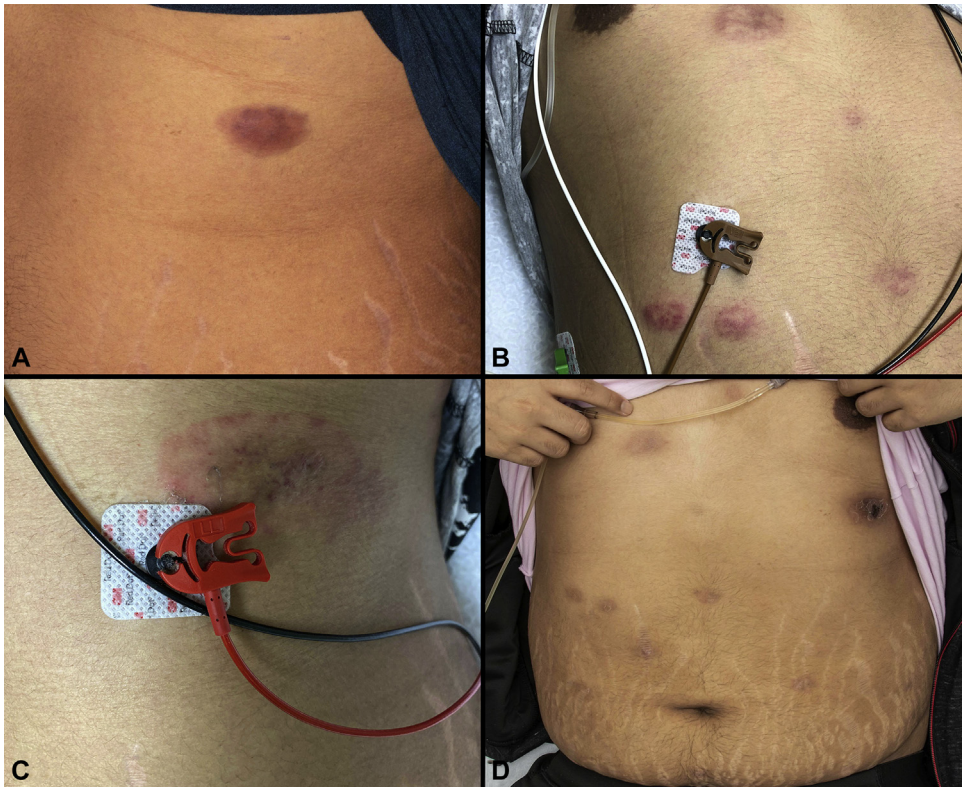

Fig 1. Flaring leukemia cutis with CAR T-cell therapy. **A**, Left chest wall leukemia cutis nodule prior to CAR T-cell therapy. **B**, Leukemia cutis flaring on the right aspect of the chest 5 days post-CAR T-cell initiation. **C**, Left chest wall leukemia cutis nodule flaring 5 days post-CAR T-cell initiation. **D**, Spontaneous resolution of left chest wall leukemia cutis nodules (photo taken 15 days post-CAR T-cell initiation). *CAR*, Chimeric antigen receptor.

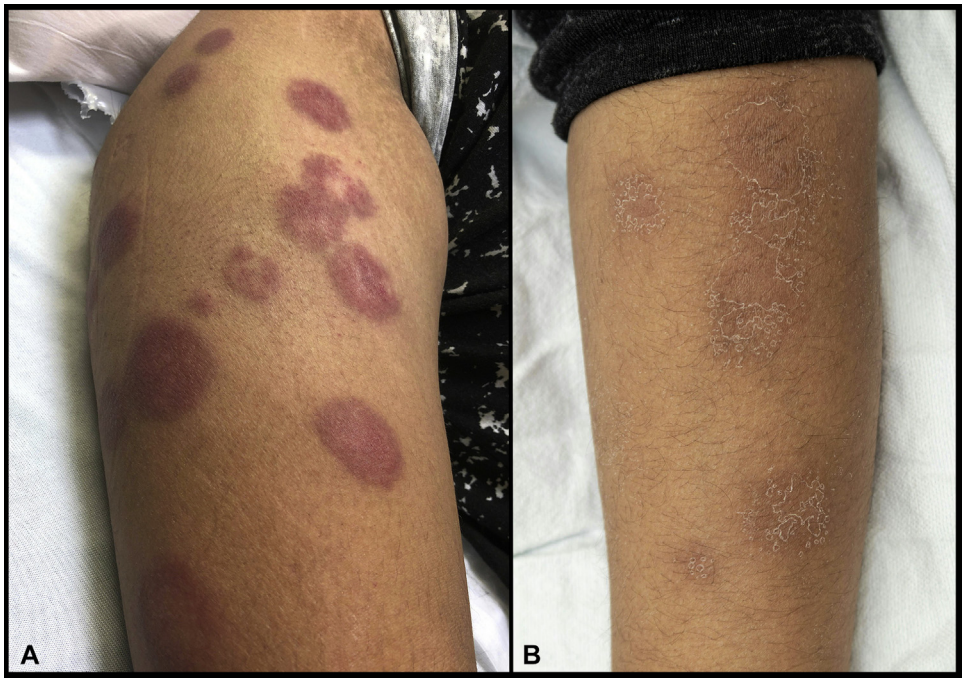

Fig 2. **A**, Leukemia cutis flaring on right upper arm 5 days post-CAR T-cell initiation. **B**, Spontaneous resolution of left forearm leukemia cutis nodules (photo taken 15 days post-CAR T-cell initiation). *CAR*, Chimeric antigen receptor.

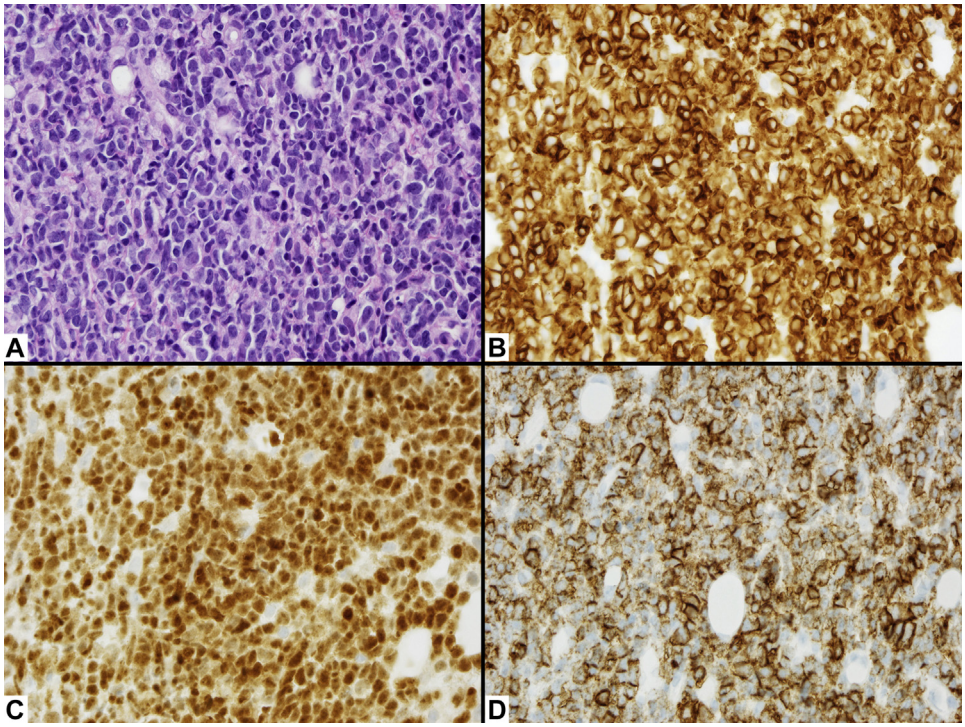

Fig 3. Skin biopsy from a new dermal infiltrate of B-lymphoblastic leukemia on the right arm, occurring 5 days after CAR T-cell therapy. Dense dermal infiltrate of atypical lymphocytes expressing CD79a, TdT, and CD19. (**A**, hematoxylin-eosin; **B**, CD79a; **C**, TdT; **D**, CD19; original magnification: **A**-**D**, ×400 for each.) *CAR*, Chimeric antigen receptor.

DISCUSSION

To the best of our knowledge, this is the first documented case of B-cell lymphoblastic leukemia cutis flaring and spontaneously resolving following CAR T-cell therapy in a patient with ALL. A previous phase I study of CAR T-cell therapy in high-risk acute myeloid leukemia reported a similar presentation in a patient with a previous history of leukemia cutis.[3] This patient developed a transient skin rash 4 days after infusion. The rash resolved in 5 days without any specific management. On day 22 after infusion, the patient developed another rash with infiltration of acute myeloid leukemia blasts with subsequent disease progression. In addition, a previous case series of 5 patients documented dermatologic complications potentially associated with CAR T-cell therapy. Dermatologic complications in this series included 1 patient with Merkel cell carcinoma, 2 patients with unusual mononuclear cell dermal infiltrates, and 2 patients with transient eruptions consistent with "eruption of lymphocyte recovery."[4]

CAR T-cell therapy has revolutionized the treatment landscape for relapsed refractory hematologic malignancies including ALL, though little is known about its effect on leukemia cutis. Our report documents a clear case of flaring disease in the skin, which resolved spontaneously without further intervention after CAR T-cell therapy. This case suggests that disease flare may not be indicative of CAR T-cell therapy failure. In such cases, monitoring the flare with expectant management and symptomatic treatment following CAR T-cell therapy may be a reasonable approach in the short term. Additional case series are needed to determine the natural disease course of individuals with leukemia cutis undergoing CAR T-cell therapy.

Conflicts of interest

None disclosed.

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