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LETTER TO THE EDITOR

Spontaneous remission of congenital AML with skin involvement and t(1;11)(p32;q23)

Congenital/infant acute myeloid leukemia (AML) has poor outcome despite aggressive therapy with rare instances of spontaneous remission. The two well-known entities with spontaneous remission are transient myeloproliferative disorder (TMD) seen in Down syndrome newborns and infant AML with t(8;16)(p11;p13). While most TMD cases resolve spontaneously, 20–30% would present with AML later.[1] Leukemia cutis is common in spontaneously regressing infant AML with t(8;16)(p11;p13); among seven infants reported, four relapsed with a median of 17 months.[2–4] Here, we report a congenital AML case with t(1;11)(p32;q23) involving the *Mixed lineage leukemia* (*MLL*) gene with sustained spontaneous remission.

A 2-month-old female with an uneventful prenatal history presented with skin lesions first seen at 1-month of age (Fig. 1A). There were fading skin lesions, otherwise physical exam was unremarkable. Complete blood count (CBC) and lactate dehydrogenase were within normal limits. Skin biopsy revealed CD4/CD56-positive and myeloperoxidase-negative infiltrating monotonous cells with irregular folded and indented nuclei. Bone marrow morphology and flow cytometry findings were consistent with AML (Figs. 1B and 1C). Cytogenetic study revealed t(1;11)(p32;q23); fluorescence in situ hybridization analysis showed *MLL* gene rearrangement, which was negative in the peripheral blood. Cerebrospinal fluid analysis was negative for leukemia cells. Positron emission tomography did not indicate extramedullary site involvement. Peripheral blood natural killer lymphocytes were higher than age-normal range.

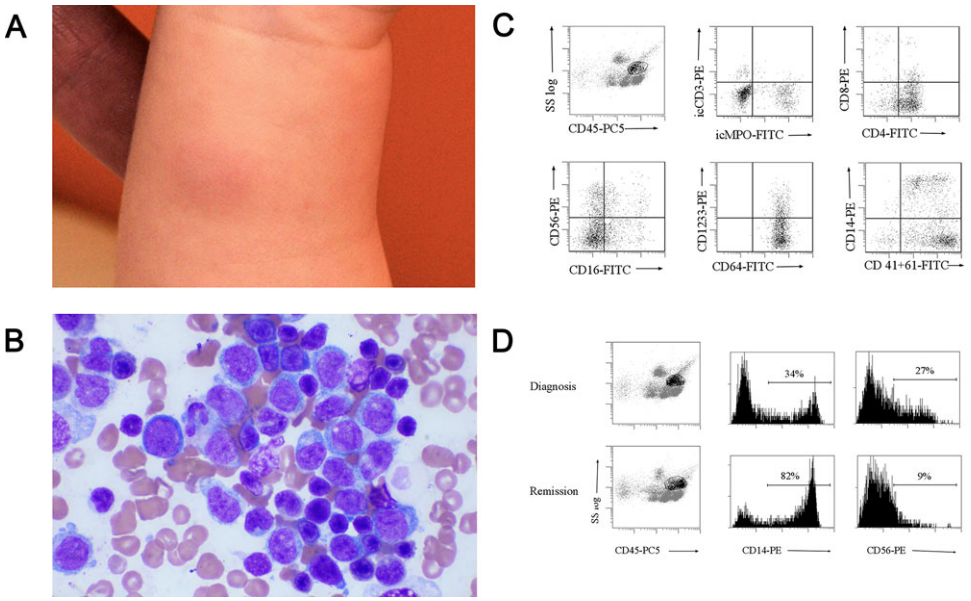

FIGURE 1 Clinical and laboratory findings. (A) Raised skin lesions were red/purple in color and spread over time, then started to fade slowly leaving mild hyperpigmentation behind. (B) Bone marrow aspiration showed patchy infiltration with immature large cells making up to 12% of the cellularity, despite overall well-preserved trilineage hematopoiesis with increased megakaryocytes and no dysplastic changes. Abnormal cells had bean-shaped and folded nuclei and —two to three nucleoli resembling immature monocytic cells accompanied by several mitotic and apoptotic figures. In addition to the occasional immature cells among the normal marrow elements, there were sheets of immature monocytic cells on the aspirate constituting as high as 85% of cellularity in the respective areas. (C) Flow cytometric analysis did not reveal a distinct CD45-dim/negative clonal leukemia population on side scatter/CD45 histogram; however, gating on the wider monocyte population showed a subpopulation of immature cells that were largely myeloperoxidase-negative, similar to what was observed in the leukemia cells that infiltrated the skin. Abnormal monocytic cells expressed CD4 and partial CD14 and CD56, but were largely negative for CD123. (D) Six weeks from her presentation, bone marrow flow cytometric study showed the maturation of these immature monocytic cells with increasing expression of CD14 and loss of CD56 expression.

Due to already regressing skin lesions, normal CBC, absence of clinical findings and unusual flow cytometric findings, and following discussions with her parents, a decision for close monitoring was made. She achieved remission by morphology, cytogenetic, and flow cytometric studies in 6 weeks (Fig. 1D). Her skin lesions completely resolved and

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CBC, complete blood count; TMD, transient myeloproliferative disorder

natural killer lymphocytes decreased to normal range. She continues to be in complete remission 2 years from diagnosis.

Eight percent of congenital AML, many with monocytic phenotype, undergo spontaneous complete remission.[4] While AML with the t(1;11)(q21;q23) has 100% overall survival rate in childhood, the prognosis of t(1;11)(p32;q23) AML was dismal with a median survival of 15 months. Thirty-eight percent of reported leukemia patients with t(1;11)(p32;q23) were infants equally distributed between acute lymphoblastic leukemia (ALL) and AML.[5,6] This translocation was also seen in monozygotic twins with ALL and therapy-related ALL.[7,8] No cases of spontaneously resolving leukemia with t(1;11)(p32;q23) have been reported.

Leukemia cutis is noted frequently at the onset of disease; rare cases preceding diagnosis were reported, likely at the aleukemic phase.[9,10] Skin involvement was reported in congenital AML with t(1;11)(p32;q23).[11] In our case, initial bone marrow involvement pattern was reminiscent of a metastatic disease; whether leukemic process started in the skin remains unknown. Leukemia cell maturation at diagnosis points at in utero initiation of the process.

Our patient with unique features of leukemia cutis, normal CBC, bone marrow infiltration pattern, lack of CD45-dim clonal cells with maturation in abnormal cells, presence of t(1;11)(p32;q23) with *MLL* gene rearrangement, and the achievement of sustained spontaneous remission raises the possibility of similar cases achieving spontaneous remission that might go unrecognized, with or without the resurgence of AML. Further molecular analysis would potentially shed light on the mechanism of spontaneous remission in this otherwise high-risk AML type.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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