



The First Case of Acute Myeloid Leukemia With t(10;11)(p13;q21);*PICALM-MLLT10* Rearrangement Presenting With Extensive Skin Involvement

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Dear Editor,

The *PICALM-MLLT10* rearrangement (*PICALM-MLLT10r*) resulting from t(10;11)(p13;q21) can activate the *HOXA* gene cluster [1, 2], which is considered to be the dominant mechanism underlying leukemic transformation [3, 4]. *PICALM-MLLT10r* occurs in ~10% of T-cell lymphoblastic leukemia/lymphoma cases and is rarely reported in B-cell lymphoblastic leukemia/lymphoma, mixed-phenotype acute leukemia, lymphoma, and AML [5-7]. We report a case of AML with *PICALM-MLLT10r* presenting with extensive skin lesions. The Institutional Review Board of Samsung Medical Center, Seoul, Korea approved this report and waived the need for informed consent (2022-06-093).

A 39-year-old man was admitted to our hospital on February 2022 with erythematous patches on his face and trunk. The lesion had appeared on his face three months before, spread to the trunk and upper extremities, and was suspected to have lymphomatous involvement. Positron emission tomography/computed tomography revealed hypermetabolic lesions in the pancreas, anterior mediastinum, and multiple lymph nodes, including the bilateral neck, supraclavicular, axillary, and mediastinal lymph nodes. Initial complete blood count (CBC) was as follows: white blood cells, $16.69 \times 10^9/L$ with 75% blasts; Hb, 173 g/L;

and platelets, $203 \times 10^9/L$. A bone marrow smear showed 83% blasts with hypercellularity (Fig. 1A-F). Flow cytometry analysis revealed that blasts were positive for CD34, cytoplasmic MPO, CD117, CD33, and HLA-DR; weakly positive for CD7, CD64, and CD123; and negative for cytoplasmic and surface CD3, CD19, CD10, cytoplasmic CD22 and CD79a, CD4, and CD56, which was compatible with AML. Leukemic involvement of the skin lesions on the abdomen, back, and flanks in our patient was confirmed via punch biopsy (Fig. 1G-J).

Cytogenetic analysis revealed a complex karyotype: 46,XY,t(10;11)(p13;q21),del(17)(p12)[16]/45,idem,der(12)t(12;17)(p12;q21),-del(17)[4] (Fig. 2A). FISH using the Vysis LSI TP53/CEP17 dual-color probe (Abbott Laboratories, Abbott Park, IL, USA) showed 86.5% of cells with a *TP53* deletion. Reverse transcription-PCR for *PICALM-MLLT10r* was performed using previously reported primers [8]; direct sequencing confirmed the fusion of *PICALM* exon 19 and *MLLT10* exon 3 (Fig. 2B). Targeted next-generation sequencing (NGS) of 46 AML-related genes on NextSeq 550Dx (Illumina, San Diego, CA, USA) identified four mutations: *JAK2* p.Gly402Aspfs*9 (NM_004972.3:c.1202_1-203insCGACATCATTACCTCTGTAAAGAAGTAGCACCTCCAGCCGTGCTTGAAAATATACAAAGCAACTGTCA; variant allele frequency,

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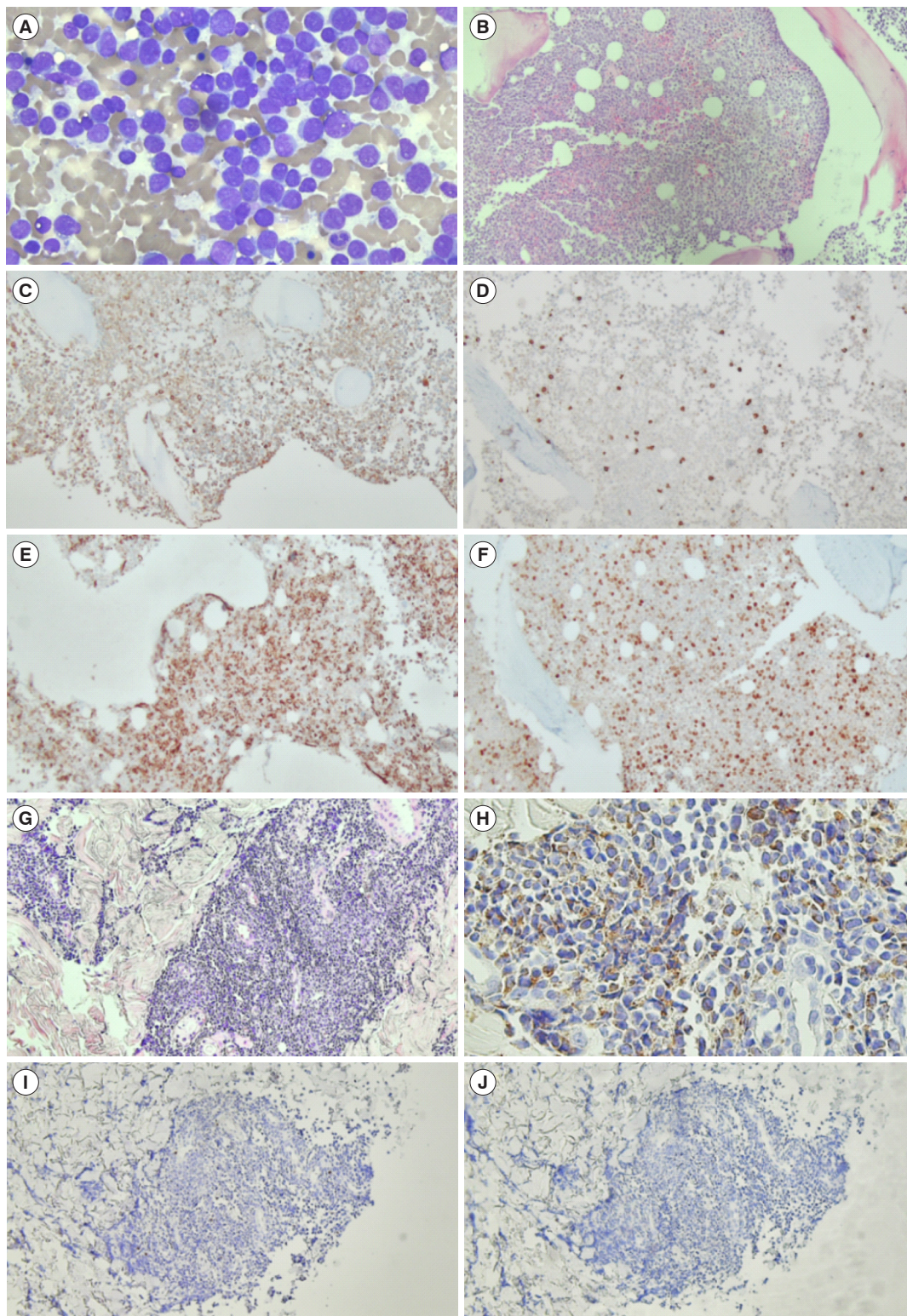


Fig. 1. Bone marrow (BM) aspiration and biopsy. Medium-to-large size leukemic blasts were observed in (A) BM aspiration (Wright-Giemsa stain, $\times 400$) and (B) biopsy (hematoxylin and eosin stain, $\times 100$). In leukemic blasts, (C) myeloperoxidase (MPO) were positive, (D) CD3 were negative, (E) CD34 were positive, and (F) terminal deoxynucleotidyl transferase (TdT) immunostains ($\times 100$) were partially positive. (G-J) Skin biopsy of trunk. (G) Leukemic blasts were observed (hematoxylin and eosin stain, $\times 100$); (H) MPO was positive ($\times 400$) and (I) CD3 and (J) CD20 were negative ($\times 100$).

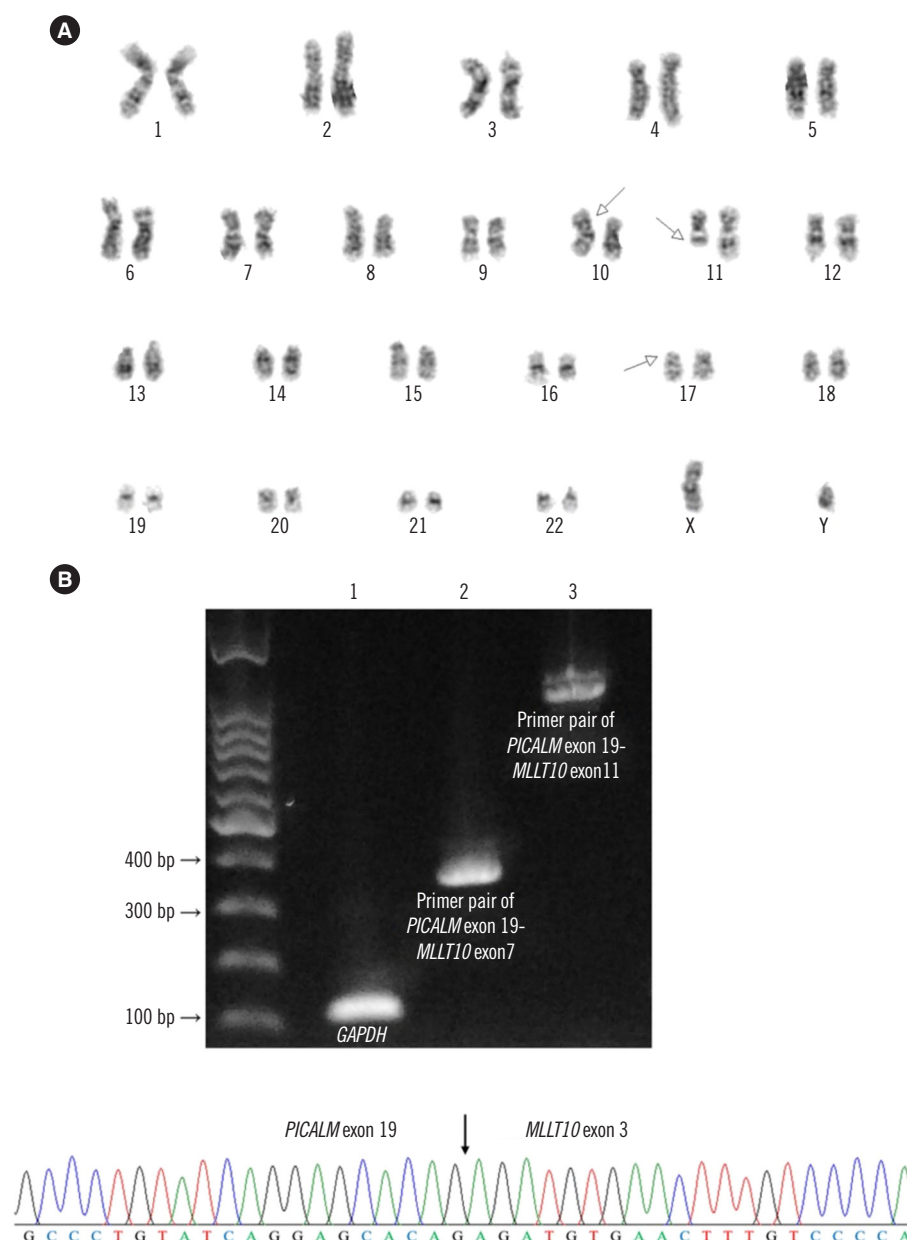


Fig. 2. Cytogenetic and molecular analysis of bone marrow study (A) Chromosomal analysis showed 46,XY,t(10;11)(p13;q21),del(17)(p12). Each arrow indicates the reciprocal translocation between 10p13 and 11q21, and deletion of 17p. (B) The *PICALM-MLLT10* fusion transcript was identified via agarose gel electrophoresis (Lane 1, internal control using *GAPDH* [amplicon size, 131 bp]; lanes 2 and 3, *PICALM-MLLT10* fusion transcripts identified using the *PICALM* exon 19 and *MLLT10* exon 7 primer pair 1 [358 bp] and *PICALM* exon 19 and *MLLT10* exon 11 primer pair 2 [922 bp], respectively) and Sanger sequencing. Chromatogram of Sanger sequencing shows the *PICALM* exon 19-*MLLT10* exon 3 fusion.

22%), *NRAS* p.Gly12Ser (NM_002524.4:c.34G>A; 39%), *PHF6* p.Cys297Arg (NM_032458.2:c.889T>C; 79%), and *TP53* p.Arg248Gln (NM_000546.5:c.743G>A; 67%). After the final diagnosis of AML, the patient received induction chemotherapy with standard-dose cytarabine and idarubicin; however, because of induction failure, re-induction chemotherapy with high-

dose cytarabine and idarubicin was administered. During chemotherapy, the skin lesions showed variable improvement and recurrence. After re-induction, the patient developed neutropenic fever and suspected fungal pneumonia and expired three months after the initial diagnosis while planning for allogeneic hematopoietic stem cell transplantation.

AML with *PICALM-MLLT10*r is very rare and clinically characterized by a young age of onset with frequent extramedullary involvement. To the best of our knowledge, this is the first reported case of AML with *PICALM-MLLT10*r with extensive skin involvement mimicking cutaneous lymphoma. Skin involvement in hematologic malignancies is mainly observed in primary T-cell lymphomas, such as mycosis fungoides, adult T-cell leukemia/lymphoma, and primary cutaneous B-cell lymphoma, but rarely in AML [9]. In particular, blastic plasmacytoid dendritic cell neoplasm, a rare and aggressive hematologic malignancy that frequently invades the skin and bone marrow [5], was strongly suspected clinically in our patient. However, our patient showed a typical AML immunophenotype, except for ectopic CD7 expression, which is recurrently observed in AML with *PICALM-MLLT10*r [2, 6].

The prognostic impact of *PICALM-MLLT10*r in AML is not well established. A few studies have suggested a poor prognosis [2, 6], and our patient indeed showed a very poor prognosis; however, more data are needed. *TP53* is a tumor suppressor gene associated with poor prognosis in AML [10]. In our patient, biallelic *TP53* inactivation identified by targeted NGS and FISH may have contributed to his poor prognosis. At present, there are no reports on the mutation spectrum of AML with *PICALM-MLLT10*r, except for one report of a single *TP53* mutation in an AML patient with *PICALM-MLLT10*r that developed after myeloid sarcoma [11]. More data are needed to evaluate the association between *TP53* mutations and AML with *PICALM-MLLT10*r, which may affect patient prognosis. Additionally, we detected a large (68-bp) insertion mutation in *JAK2* exon 9 causing a frameshift, which may be related to the erythrocytosis observed in the patient's initial CBC. However, there was no morphological evidence of myeloproliferative neoplasms in the bone marrow, and the clinical significance of loss-of-function mutations of *JAK2* is unclear. In conclusion, this is the first reported case of AML with *PICALM-MLLT10*r presenting with extensive skin involvement, showing poor prognosis, with concomitant *TP53* mutation.

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AUTHOR CONTRIBUTIONS

Park MS drafted the manuscript; Kim HY supervised the study and edited the manuscript; Lee JJ and Cho D provided expertise about laboratory data; Jung CW provided clinical informa-

tion; Kim HJ and Kim SH supervised the study.

CONFLICTS OF INTEREST

None declared.

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REFERENCES

1. Dreyling MH, Martinez-Climent JA, Zheng M, Mao J, Rowley JD, Bohlander SK. The t(10;11)(p13;q14) in the U937 cell line results in the fusion of the *AF10* gene and *CALM*, encoding a new member of the AP-3 clathrin assembly protein family. *Proc Natl Acad Sci U S A* 1996;93:4804-9.
2. Savage NM, Kota V, Manaloor EJ, Kulharya AS, Pierini V, Mecucci C, et al. Acute leukemia with *PICALM-MLLT10* fusion gene: diagnostic and treatment struggle. *Cancer Genet Cytogenet* 2010;202:129-32.
3. De Braekeleer E, Douet-Guilbert N, Basinko A, Le Bris MJ, Morel F, De Braekeleer M. *Hox* gene dysregulation in acute myeloid leukemia. *Future Oncol* 2014;10:475-95.
4. Lim HJ, Lee JH, Lee YE, Baek HJ, Kook H, Park JH, et al. The First Korean Case of *NUP98-NSD1* and a Novel *SNRK-ETV6* Fusion in a Pediatric Therapy-related Acute Myeloid Leukemia Patient Detected by Targeted RNA Sequencing. *Ann Lab Med* 2021;41:443-6.
5. Swerdlow SH, Campo E, et al., eds. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Lyon: International Agency for Research on Cancer (IARC), 2017:173-209.
6. Borel C, Dastugue N, Cances-Lauwers V, Mozziconacci MJ, Prebet T, Vey N, et al. *PICALM-MLLT10* acute myeloid leukemia: a French cohort of 18 patients. *Leuk Res* 2012;36:1365-9.
7. Krzisch D, Zduniak A, Veresezan EL, Daliphard S, Contentin N, Penther D, et al. Successful treatment of T/myeloid mixed-phenotype acute leukemia with the translocation (10;11)(p13;q14) *PICALM/AF10* with 3 + 7 myeloid standard treatment: a case report. *Clin Case Rep* 2021;9:1507-13.
8. Laforêt MP, Turlure P, Lippert E, Cornillet-Lefebvre P, Pigneux A, Pradeau R, et al. Design and feasibility of a novel, rapid, and simple fluorescence 26-plex rt-PCR assay for simultaneous detection of 24 fusion transcripts in adult acute myeloid leukemia. *J Mol Diagn* 2013;15:186-95.
9. Han JH, Ko YH, Kang YK, Kim WS, Kim YJ, Kim I, et al. Characteristics

- of cutaneous lymphomas in Korea according to the New WHO-EORTC classification: report of a nationwide study. *Korean J Pathol* 2014;48:126-32.
10. Short NJ, Montalban-Bravo G, Hwang H, Ning J, Franquiz MJ, Kanagal-Shamanna R, et al. Prognostic and therapeutic impacts of mutant *TP53* variant allelic frequency in newly diagnosed acute myeloid leukemia. *Blood Adv* 2020;4:5681-9.
11. Naesens L, Devos H, Nollet F, Michaux L, Selleslag D. Mediastinal myeloid sarcoma with *TP53* mutation preceding acute myeloid leukemia with a *PICALM-MLLT10* fusion gene. *Acta Haematol* 2018;140:97-104.