Pediatric Acute Erythroid Leukemia with Monocytic Antigen Expression and Novel Chromosomal Translocation

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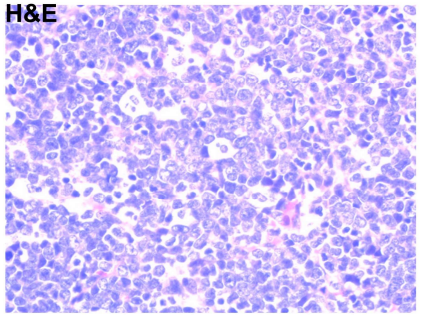
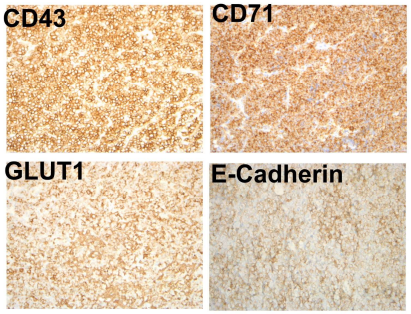
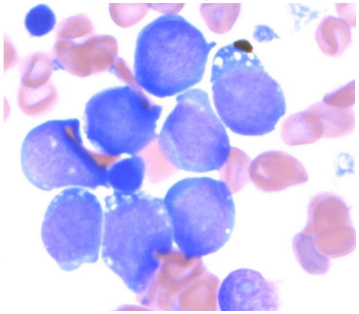
BACKGROUND Acute erythroid leukemia (AEL) is a rare subtype of pediatric acute myeloid leukemia (AML). Previous genomic studies of adult and pediatric AELs identified enrichment of NUP98-rearrangement and a wide spectrum of somatic mutations. Recent study from Children Oncology Group reports recurrent NUP98-rearrangements in approximately one third of patients, but majority lack recurrent genetic abnormalities. Moreover, this study reported AEL with variable antigen expression and subclassified AELs into erythroid/myeloid and pure erythroid subtypes, with the latter subtype associated with a worse prognosis. Such that, further studies on genetic abnormalities and immunophenotypes are warranted. Here we report two unusual AELs.

CASE REPORT Our first patient was a 2-month-old male with past medical history of sickle cell trait, who presented a right shoulder mass, with the biopsy showing a diffuse infiltrate of atypical tumor cells; they are positive for CD43, CD71, GLUT1 and E-Cadherin immunostains; while negative for CD1a, CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD20, CD30, CD34, CD56, CD61, CD79a, CD117, CD163, TdT, myeloperoxidase, ALK1, PAX5, glycophorin A; CK-OSCAR, AE1/AE3, EMA, desmin, SALL4, synaptophysin, chromogranin, CD99, and S100. The bone marrow aspirate shows numerous tumor cells, morphologically compatible with erythroblasts. The concurrent flow cytometry confirmed the diagnosis of acute erythroid leukemia with variable monocytic antigen expression. Peripheral blood contained approximately 13% blasts. The bone marrow biopsy showed approximately 81% blasts and no dysplasia in the background. Flow Cytometry showed blast population expressing CD13, CD43, CD71, and CD235 (partial), and variable monocytic antigen CD14. A fusion gene of CIC-NUT2MA was detected by next generation sequencing. Patient received the induction chemotherapy per standard arm of AAML 1831 protocol and his end of induction flow cytometry MRD on bone marrow was negative. The MRI imaging at the end of induction showed a marked response of the extramedullary disease burden. However, patient's disease progressed shortly and deceased 3 months after the diagnosis.

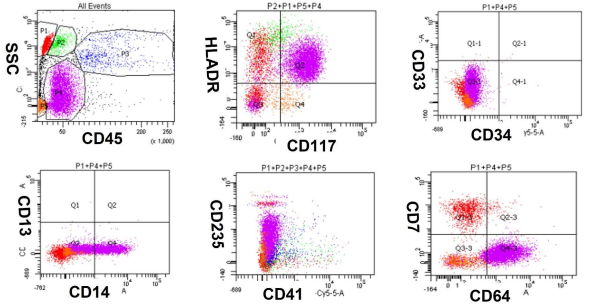




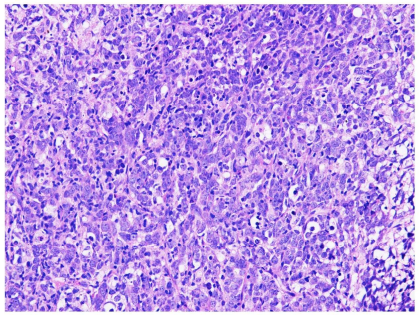
Bone marrow aspirate



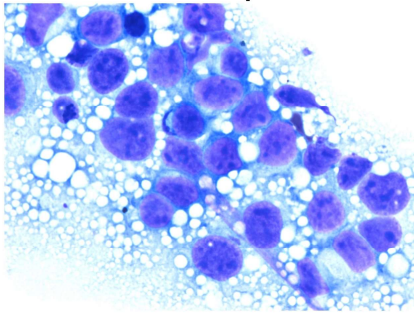
Our second patient was a 2-year-old female with no significant past medical history, who presented with pancytopenia. Bone marrow biopsy identified up to 76% of blasts on aspirate smear, with a morphology compatible with erythroblasts. Flow Cytometry identified abnormal blasts with erythroid and monocytic differentiation, expressing CD71, CD117, HLA-DR, CD64 (dim), CD14 (partial), CD2 (partial/dim), CD235 (partial). The cytogenetic karyotyping showed 48,XX,t(1;8)(p34;q22),del(3)(p13p21),+6,+19 [13]/ 46,XX. FISH studies were negative for recurrent genetic abnormalities of our myeloid neoplasm panel. A fusion gene of NFIA-RUNX1T1 was detected by next generation sequencing. Patient received an induction chemotherapy with a complete response and negative MRD; but relapsed 3 months later. The flow cytometry immunophenotype of the relapsed leukemia showed surface antigen expression of CD117, CD71, CD235a (dim), CD36; while negative for HLADR, CD64, CD14, CD56, CD34, and CD123. The cytogenetic karyotyping showed 48,XX,t(1;8)(p34;q22),del(3)(p13p21),+6,+19 [1]/ 48,idem, t(17;22)(q21;q11.2) [9]/46,XX[10].



Bone marrow core biopsy, H&E



Bone marrow touch print



DISCUSSION & CONCLUSION we show two pediatric AELs with monocytic antigen expression, and unusual genetic translocations. Our data suggest that AEL is an immunophenotypically and genetically heterogeneous disease, which needs further studies. An interesting observation from our two patients is that both patients originally responded to the induction chemotherapy and achieved the morphological and flow cytometric remission. However, both patients relapsed relatively quickly, and the relapsed leukemia appears to have poor or no response to salvage chemotherapy.