Case Report

Acute promyelocytic leukemia with unusual karyotype

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Acute myeloid leukemia (AML-M3) is associated with the translocation t(15;17)(q22;q12-21) which disrupts the retinoic acid receptor alpha (*RARA*) gene on chromosome 17 and the *PML* gene on chromosome 15. We report a two-year-old patient with AML-M3 without the usual translocation t(15;17). Cytogenetic studies demonstrated normal appearance of chromosome 15 while the abnormal 17 homologue was apparently a derivative 17, der(17)(17qter-cen-q21:), the rearrangement distinctly shows deletion at 17q21 band and the morphology corresponding to an iso chromosome i(17q-). This case report is a rare cytogenetic presentation of acute promyelocytic leukemia (APML).

Key words: Acute promyelocytic leukemia, karyotype, *RARA*

Introduction

Acute promyelocytic leukemia (APML) is a subset of AML with characteristic clinical, morphological and genetic features. The disease is very rare in children below 10 years of age. Its incidence gradually increases, reaching a plateau during early adulthood, remaining constant until it diminishes after 60 years of age.[1] The identification of specific chromosomal abnormality plays an important role in determining therapy and prognosis in certain subtypes of AML. Data from the Pediatric Oncology Group have shown that inv(16) / t(16;16), t(8;21), and normal karyotypes are associated with favorable prognostic outcome, whereas poorer outcome was observed in t(15;17) (without all- *trans* retinoic acid (ATRA) treatment), 11q23, and other abnormalities.[2]

AML is heterogeneous at the cytogenetic and molecular levels. Over the years, several specific recurrent chromosome aberrations have been described in AML, both unbalanced and balanced rearrangements.[3] Balanced chromosome rearrangements are detected in approximately 25–30% of adults *with de novo* AML and have attracted a great deal of attention not only because their molecular dissection has led to identification of genes involved in leukemogenesis but also because specific translocations and inversions are associated with clinical features and treatment outcome of patients harboring them.[4-6] In this article, we discuss the case study of a two-year-old child with unbalanced chromosome aberrations involving chromosome 17 with a cytogenetically normal chromosome 15.

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Patient had a history of fever, general weakness and bleeding from the gums. On examination, his general condition was poor, with cervical and axillary lymph nodes. On systemic examination, he had hepatomegaly 2–3 cm, and splenomegaly 1–2 cm. At presentation, hemogram was Hb 69 g/l, total count of 52×10^9/l and platelets 20×10^9/l. Differential count showed neoplastic promyelocytes 80%, neutrophils 12%, lymphocytes 12%, Bone marrow aspiration showed hyper cellular marrow with sheets of neoplastic promyelocytes (70 %).

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Many bilobed and occasional faggot cells were seen [Figure 1a]. Other elements were suppressed. Myeloperoxidase stain was strongly positive [Figure 1b]. Morphological diagnosis of AML-M3 (hyper granular variant) was made.

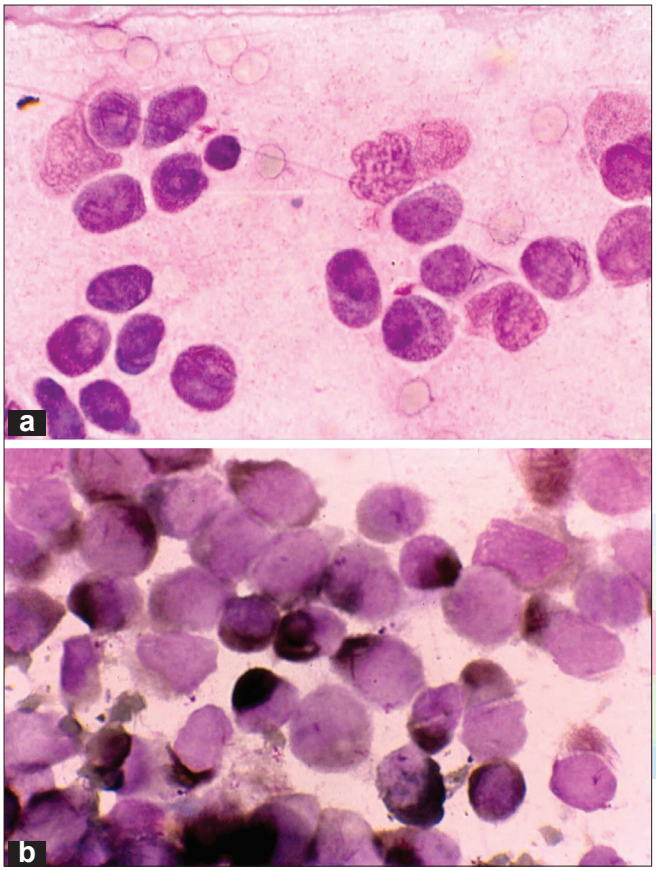

Figure 1: (a) peripheral smear: Auer rods positive, (b) MPO positive

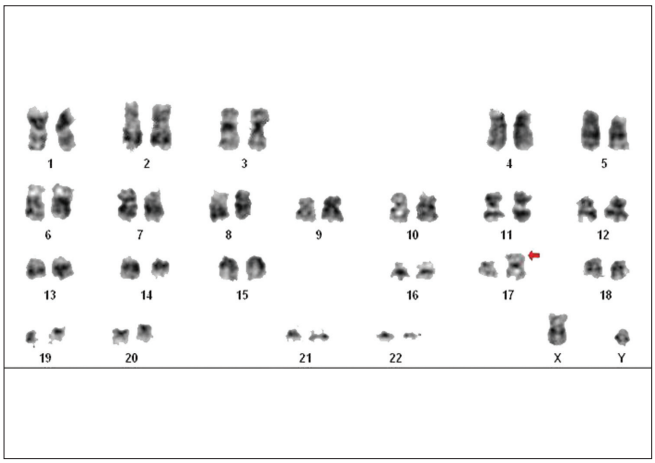

Figure 2: Karyotype: 46XY, -17, +der(17)(17qter-cen-17q21:) Arrow indicates breakpoint

Cytogenetic studies

Cytogenetic study was carried out on cells from bone marrow aspiration. Short-term culture of 24 and 48 h were set up using RPMI 1640 medium supplemented with 20% fetal bovine serum. After 16–18 h, 50 µl of colcemid at a final concentration of 10 µg/ml was added for 30 min followed by hypotonic treatment, fixation in Carnoy's fixative. Giemsa (GTG) banding was performed according to standard protocol. Fifteen metaphases were analyzed which consistently showed 46XY, -17,+der(17)(17qter-cen-17q21:) karyotype [Figure 2].

Discussion

To our knowledge, this is a rare cytogenetic abnormality in a child, involving only chromosome 17. The first report of AML-M3 with normal chromosome 15 with -17, ins(17;?) (q11q21;?) was by Baranger *et al.*,[7] in a 35-year-old female. The present case demonstrated normal appearance of chromosome 15's, while one of the 17 homologues appeared to be an iso (17q), but upon detailed examination showed break on one of the arms at q21 band. The presence of 15q+ and i(17q-) is one of the most frequent abnormalities reported besides the standard translocation,[7] but with an i(17q-) and two normal chromosome 15 is extremely rare. Routinely cytogenetics, fluorescence *in situ* hybridization (FISH), and Polymerase chain reaction (PCR) analysis are employed for the diagnosis and precise localization of the fusion gene. But in our case, FISH could not be performed and even before the cytogenetic results were available the patient died due to disseminated intravascular coagulation. Hence, further molecular studies to establish the type of gene fusion transcript which could have had a prognostic value could not be ascertained.

A small proportion of APML patients do not have t(15;17)/ *PML-RARA* but do have other chromosomal aberrations and gene fusion, all these rearrangements and t(15;17) are very strongly correlated with characteristic marrow morphology in which abnormal promyelocytes predominate (FAB- M3). The present WHO classification recognizes two main morphological subtypes of APML that includes a more frequent hyper granular variant

form featured by abnormal dysplastic promyelocytes with abundant cytoplasmic granules and Auer rods (faggots) and a less frequent micro granular variant of APML characterized by leukemic blast, bilobed nuclei with dusty and minute cytoplasmic granules. The evolution of AML involves leukemogenic events that occur in the stem cell (stem cell origin model) and favors self renewal while disrupting normal hematopoietic cell lineage development.[8-10]

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