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CASE REPORT

Ring chromosome 8 and trisomy 8 in a patient with acute myeloid leukemia

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Abstract We describe a child with Acute Myeloid Leukemia (AML M7) with trisomy 8 and ring chromosome 8. Ring chromosome 8 associated with AML is uncommon and is reported to have a poor outcome. The combination of trisomy 8 and ring chromosome 8 has not been previously reported. This 15-month-old girl had presented with a history of fever, weight loss of 1 kg, gum bleeds and pallor. Clinical examinations revealed no nodes or organomegaly. Investigations revealed pancytopenia and elevated serum LDH. Bone marrow aspirate confirmed the presence of myeloid blasts positive only for CD 41 and CD 61 on flow cytometry. Chromosomal analysis from the bone marrow showed 46, XX [13]/ 47, XX, +8[2]/ 47, XX, +r (8) [5]. The child was treated as per UK MRC AML protocol (ADE 10+3+5). Bone marrow on day 21 post-induction was in morphological remission. Repeat karyotyping revealed 46,XX suggesting that the patient was in cytogenetic remission. Cytogenetic sub grouping in AML patients provides guidelines for the choice of optimal treatment strategy. There was no HLA matched family donor and hence an unrelated donor search was commenced as she was in the group with unfavourable cytogenetics. She developed acute myelofibrosis soon after the second cycle of chemotherapy with swinging fever and rapidly enlarging spleen. The marrow showed 11% blasts with intense fibrosis. She went through a stormy period during conditioning for unrelated stem cell transplantation. She passed away on day 11 post transplantation of veno-occlusive disease of liver and multi-organ failure. This case illustrates the poor outcome in paediatric AML with trisomy and ring chromosome 8.

Keywords Acute myeloid leukemia · Trisomy 8 · Ring chromosome 8

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Introduction

Trisomy 8 is the most frequent numerical chromosomal aberration in acute myeloid leukemia (AML), Chronic myeloid leukemia (CML), Myelodysplastic syndromes (MDS) and Myeloproliferative disease (MPD), but rare in Acute lymphoblastic leukemia (ALL) and other lymphoid disorders [1]. We describe a patient suffering from Acute Myeloid Leukemia (AML – M7), in whom cytogenetics analysis revealed trisomy 8 in association with ring chromosome 8. Ring chromosome 8 associated with AML is uncommon and is reported to have a poor outcome. The combination of trisomy 8 and ring chromosome 8 has not been previously reported.

Case report

A 15-months-old girl had presented with a history of fever, weight loss of 1 kg, gum bleeds and pallor. Clinical examination revealed no nodes or organomegaly. Other investigations revealed pancytopenia and elevated serum LDH. CBC count showed Hb: 10 gm/dL, WBC: 3000/cmm and Platelet: 21,000/cmm.

Immunophenotyphic study performed on bone marrow aspirate confirmed the presence of myeloid blasts positive only for CD 41 and CD 61 on flow cytometry.

Cytogenetic study was done with short-term bone marrow culture and overnight colchicine bone marrow

culture. GTG banding was followed. Chromosomes were classified according to the International System for Human Cytogenetic Nomenclature (ISCN 2005). The karyotype is interpreted as 46,XX [13]/47,XX,+8 [2]/ 47,XX,+r(8) [5]

The patient was treated as per UK MRC AML protocol (ADE 10+3+5). Bone Marrow on day 21-post induction was in morphological remission. Repeat karyotyping revealed 46,XX suggesting that the patient was in cytogenetics remission.

She had progressed to acute myelofibrosis soon after the second cycle of chemotherapy. It was decided to perform a high-risk transplantation using unrelated cord blood stem cells. Busulphan, cyclophosphamide and ATG were used for conditioning. She passed away on day 11-post transplantation of veno- occlusive disease of liver and multi organ failure. This case illustrates the poor outcome in pediatrics AML with trisomy 8 and ring chromosome 8.

Discussion

A particularly striking anomaly is produced if a deletion occurs in both arms of the same chromosome and the two ends join together. This produces a ring structure [2].

Occurrence of trisomy 8 as the only chromosome aberration in metaphases of bone marrow or peripheral blood cells is associated with malignant or premalignant conditions of the myeloid hemopoietic system [3].

Trisomy 8 cells might proliferate more or survive longer in male than in female patients. The median survival was found to be 17.1 months. This is shorter than that of the

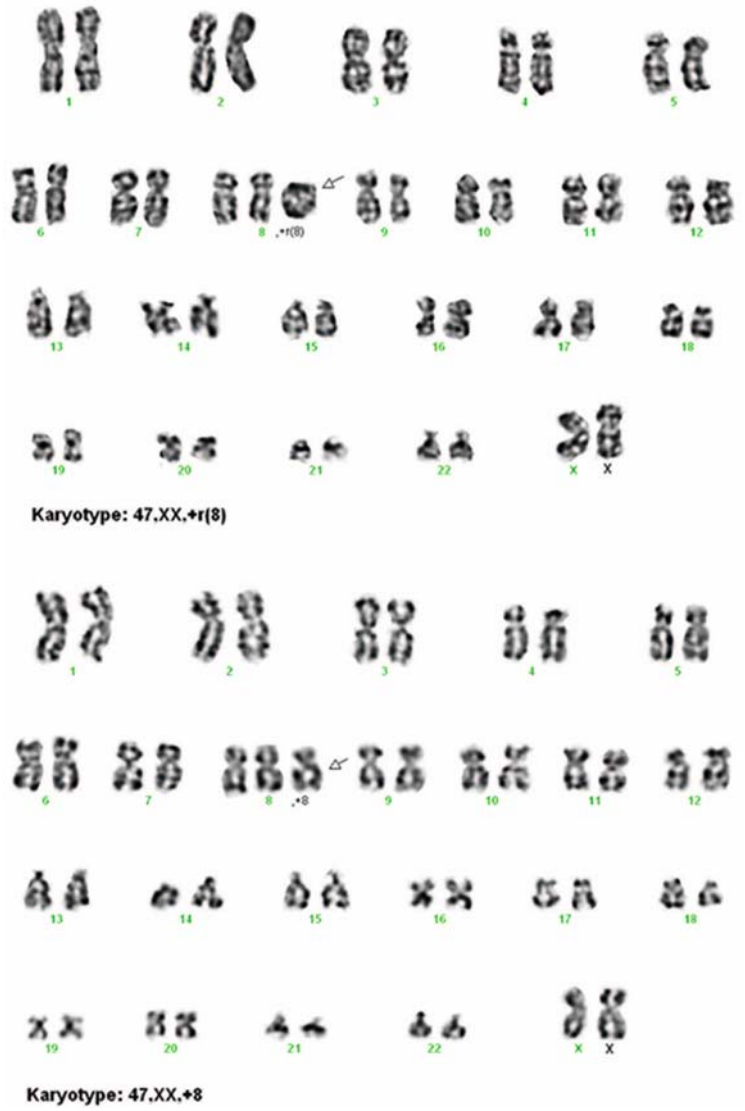

Fig. 1 Bone marrow Karyotype of the patient

5q- syndrome (61 months) [4], equals that of trisomy 4 (17 months) [5], and exceeds those of trisomy 13 and monosomy 7 (6 months) [6, 7], as well as those of 7q- and t(1;7) (11 months) [8, 9].

The situation was more complex in our patient because of the presence of two cytogenetically unrelated clones possibly indicating hematopoietic biclonality. Ring chromosome 8 associated with AML is uncommon and is reported to have a poor outcome. To our knowledge this is the first time to report trisomy 8 along with ring chromosome 8 in AML.

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