Iraqi Journal of Cancer and Medical Genetics

# Acute Lymphoblastic Leukemia with a novel dic (11;11) (q24;q24) : A case report

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## Abstract:

Cytogenetic study was performed on a case of acute lymphoblastic leukemia . The chromosomal analysis for bone marrow cells by using G- banding technique showed A novel dic (11;11)(q24;q24) in 5 metaphases (15%) of 32 total metaphases studied , which has not been described previously in this leukemia type . Different abnormalities involving chromosome 11q have been reported as well . Novel rearrangement of 11q may reflect the heterogeneity of the genetic change which possibly refers to the differences in environmental and genetic factors of the Iraqi patients in comparison with other patients in another countries, which may contributes in the pathogenesis of acute lymphoblastic leukemia .

***Keywords:*** *Acute Lymphoblastic Leukemia , dic (11;11)(q24;q24) , chromosome 11q , Novel rearrangement .*

## Introduction:

Acute lymphoblastic leukemia (ALL) is characterized by the clonal proliferation and accumulation of malignant blast cells in the bone marrow and peripheral blood (1) . It is regarded as a childhood disease with a peak at 2-5 years of age (2) . The frequency of ALL in adults ( >15 years of age) is one-third of that of children , producing a second peak of incidence at 50 years , which rises steadily with increasing age (3).

It has been frequently reported that acquired chromosomal abnormalities in the leukaemic blasts of patients with ALL are closely associated with the biology of the disease and indicate the genes involved in leukemogenesis (4) . In this role they also define patient sub-groups and have important prognostic implications (5,6) . In fact, it has been known that the karyotype is an important predictor of outcome in ALL (7, 8). As a result cytogenetics plays a vital role in diagnosis and patient management and has become a requirement for entry of patients to ALL treatment trials (9) .

Numerical or Structural Chromosomal abnormalities can be seen in ALL (10) . Structural abnormalities include translocations, deletions, inversions and other rearrangements involving genes with oncogeneic potential, which lead to disruption of specific differentiation or proliferative pathways and the progression of leukemogenesis (11) . Numerical chromosomal changes lead to clones with too many or too few copies of one or more chromosomes and are classified into groups according to the chromosome number ( 12 ) .

The 11q rearrangements, particularly 11q23 translocations are a frequent cytogenetic abnormalities found in 7–10% of Acute Lymphoblastic Leukemia (ALL), 60–70% of all Acute Leukemias in infants, and in most patients with t-AML/ t-ALL secondary to therapy that is targeting topoisomerase II (13) .

Most of these abnormalities involve the Mixed Lineage Leukemia gene ( MLL gene ) , which is also known as ALL-1, HRX, and HTRX1 (14) . That gene plays a key role in developmental regulation of gene expression including HOX genes in normal hematopoiesis and in leukemia this function is subverted by breakage, recombination and chimeric fusion with various partner genes (15) . To date, no case of ALL has been reported to have the dic (11;11)(q24;q24) aberration .

**Case Report :**

A 15-year old male was diagnosed in January (2008) as acute lymphoblastic leukemia in Baghdad Teaching Hospital . At diagnosis , hematological data were as follow : in the peripheral blood , 160 x109/ L leukocytes with 40% blast cells , 91×109/L platelets and a hemoglobin level of 7.2g/dL . bone

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marrow was hyper cellular with 89% blasts .

After two months of treatment with Adriamycin , Vincristine , and Prednisolone , Cytogenetic study on bone marrow cells was performed by using direct and short term culture technique (16) in Iraqi center for cancer and medical genetics research . Briefly, Unstimulated bone marrow cells were cultured for 30 minute (direct culture technique ) and for 24 , 48 hour (short term culture technique ) at 37 °C . cells were exposed to colcemid (0.2 µg/ml) in last 25 minute of culturing time at 37 °C and harvested for chromosome analysis on G-banded metaphases.

Karyotype designation followed the International System for Human Cytogenetic Nomenclature (ISCN, 1995 ) (17) . showed: 45XY , dic (11;11)(q24;q24)[5] / 46XY[27] . The number of cells that were analyzed is given in square brackets after the karyotype .

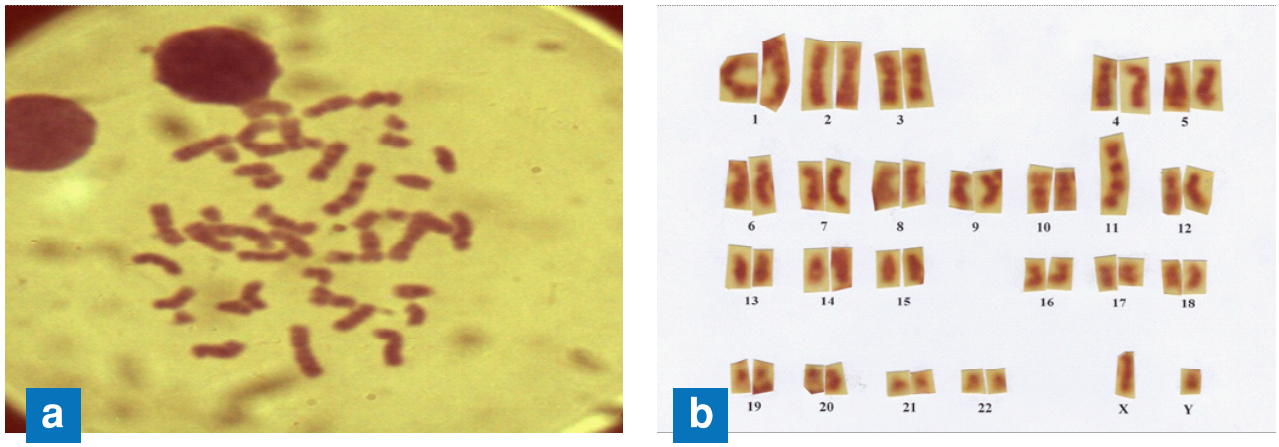


*Figure (1) (a) G-banding metaphase cell of the bone marrow revealed chromosomal abnormality : dic (11;11) (q24;q24) ( ⟶ ) , under ( 1000X ) magnification . (b) karyotype of the bone marrow cell : 45XY , dic (11;11)(q24;q24) .*

## Discussion :

In this case of ALL the karyotype of the patient revealed a novel dic (11;11)(q24;q24) as a sole chromosomal abnormality which suggests that this may be early or primary event in leukemogenesis . The dic (11;11)(q24;q24) has never been described before , even though 11q rearrangements , particularly 11q23 translocations are among the most common cytogenetic abnormalities in patients with ALL (18-20) . Most of these abnormalities involve the Mixed Lineage Leukemia gene ( MLL gene ) , which is also known as ALL-1, HRX , and HTRX1(21) . That gene plays a key role in developmental regulation of gene expression including HOX genes in normal hematopoiesis and in leukemia this function is subverted by breakage, recombination and chimeric fusion with various partner genes (15) . The functional outcome of the aberration suggesting loss of genetic material rather than a consistent gene rearrangement . The immediate effect of this rearrangement is the haploinsufficiency of the genes located in the 11q24 and it is reasonable to assume that the loss of one copy of 11q24 is an ALL-causing event in this case . Deletions involving 11q are relatively common cytogenetic alterations in a number of hematological malignancies (22) and solid tumors (23-25) .These data suggest that alterations of putative tumor suppressor genes on 11q are important events in development of these malignancies .

Novel or new chromosomal rearrangements of the 11q , which had not been recorded in previous studies , which refers to the differences in environmental and genetic factors of the Iraqi patients in comparison with other patients in another countries , which could contributes in the pathogenesis of ALL . This case may add a new anomaly to the list of chromosomal aberration involving the long arm of chromosome 11 . Its prognostic significance in ALL is currently unknown . We recommend that karyotypic analysis always be complemented by molecular or FISH methods to unravel cryptic MLL rearrangements (26) .

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# كروموسوم ثنائي المركز جديد (11;11)(dic q24;q24) في ابيضاض الدم اللمفاوي الحاد: تقرير حالة

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## الخلاصة :

تم اجرء دراسة وراثية خلوية لحالة ابيضاض دم لمفاوي حاد عولجت بالعقاقير : prednisolone , vincristine Adriamycin لمدة شهرين بعد تشخيصها . أظهر التحليل الكروموسومي لخلايا نخاع العظم , باستخدام طريقة التحزيم بالكمزا , كروموسوم ثنائي المركز جديد (11;11)(dic q24;q24) في 5 خلايا في الطور الاستوائي ( 15% ) من مجموع 32 خلية تم دراستها , والذي لم يسجل سابقا في هذا النوع من ابيضاض الدم . مختلف التغيرات التي تشمل الكروموسوم 11q تم تسجيلها ايضا . التغيرات الجديدة لكروموسوم 11q تعكس التباين في التغيير الجيني الذي يشير إلى الاختلافات في العوامل البيئية والجينية للمرضى العراقيين بالمقارنة مع المرضى الآخرين في بلدان أخرى، الأمر الذي من الممكن ان يسهم في امراضية ابيضاض الدم اللمفاوي الحاد .