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Case report:

SPECTRAL KARYOTYPING REVEALS A COMPREHENSIVE KARYOTYPE IN AN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA

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ABSTRACT

Cytogenetic abnormalities are frequently detected in patients with acute lymphoblastic leukemia (ALL). Comprehensive karyotype was related to poor prognosis frequently in ALL. We present a comprehensive karyotype in an adult ALL by spectral karyotyping (SKY) and R-banding. SKY not only confirmed the abnormalities previously seen by R-banding but also improved comprehensive karyotype analysis with the following result 47,XY,+9, ins(1;5)(q23;q23q34) t(6;7)(q23;p13). Our report demonstrated that SKY is able to provide more information accurately for prediction of disease prognosis in adult ALL with comprehensive karyotype.

Keywords: SKY, comprehensive karyotype, acute lymphoblastic leukemia

INTRODUCTION

Cytogenetic abnormalities are frequently detected in patients with acute lymphoblastic leukemia (ALL). Comprehensive karyotype was related to poor prognosis frequently in ALL (Lu et al., 2002). SKY can simultaneously and unambiguously display human and rat ALL chromosomes in 24 different colours without a priori knowledge of any abnormalities (Schröck et al., 1996). SKY has been shown to provide additional chromosome information by improving the characterization of marker chromosomes, cryptic translocations, and complex chromosomal rearrangements that cannot be fully defined by conventional cytogenetics (Betts et al., 2008; Cohen et al., 2004; Karst et al., 2006; Mrózek et al., 2002). In this report, we demonstrate the role of SKY in resolving complex cytogenetic abnormalities in an adult ALL with comprehensive karyotype.

CASE REPORT

A 33-year-old man was admitted to General Hospital of People's Liberation Army of China, because of fever and cough for 10 days. The clinical laboratory findings are summarized as follows: hemoglobin was 44 g/L, white blood cells were 1.9×10^9/L with 33 % blast cells, and a platelets were 103×10^9/L. Bone marrow examination found hypercellularity with 92 % cells, and chemical staining revealed POX (peroxidase) (-), a periodic acid Schiff (PAS) positive rate of 87 %, and an α-naphthyl acetate esterase (ANAE) positive rate of 35 %. Immunophenotyping studies with flow cytometry indicated that the blasts expressed the following antigens: CD19, CD22, CD7, CD33, CD14 and HLA-DR, and part cells expressed CD5, CD3, and CD84. The diagnosis of T/B double expression lymphoblastic leukemia was established according to the World Health Organization classification. R-band cytoge-

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netic analysis on bone marrow aspirates was performed by using standard methods. Karyotypic analysis was made in accordance with ISCN 1995 (Shaffer and Tommerup, 2005).

Slides for SKY analysis were prepared from fixed suspension material stored at -20 ℃. The SKY kit probe cocktail (Applied Spectral Imaging, USA) was hybridized to metaphase slides according to the manufacturer's protocol. After hybridization, chromosomes were counterstained with DAPI. Image acquisition was performed with an SKY View 1.6 system of Nikon E600 microscope. Automatic identification of chromosomes was based on the measurement of the spectrum for each chromosome.

Cytogenetic analysis of bone marrow cells revealed a 47, XY, t(1;5)(q32;q21),7p-,+mar1 karyotype in 20 metaphases analyzed (Figure 1A). SKY analysis confirmed the abnormalities previously seen by R-banding. SKY analysis also showed a complex karyotype involving chromosomes 1, 5, 6, 7 and 9 together with the 47,XY,+9, ins(1;5)(q23;q23q34) t(6;7)(q23;p13) (Figure 1B).

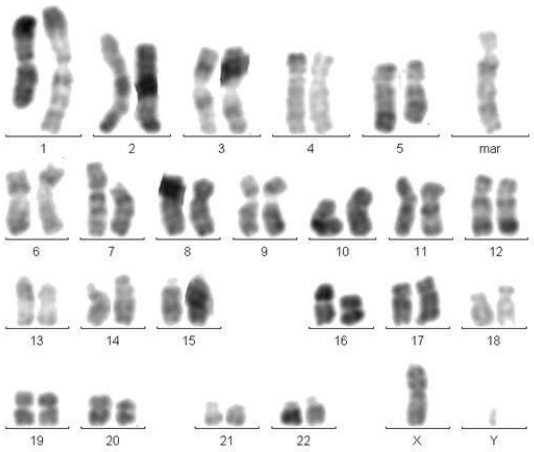

Figure 1A: R-band karyotype showing 47,XY,t(1;5)(?q32;?q21),7p-,+mar1

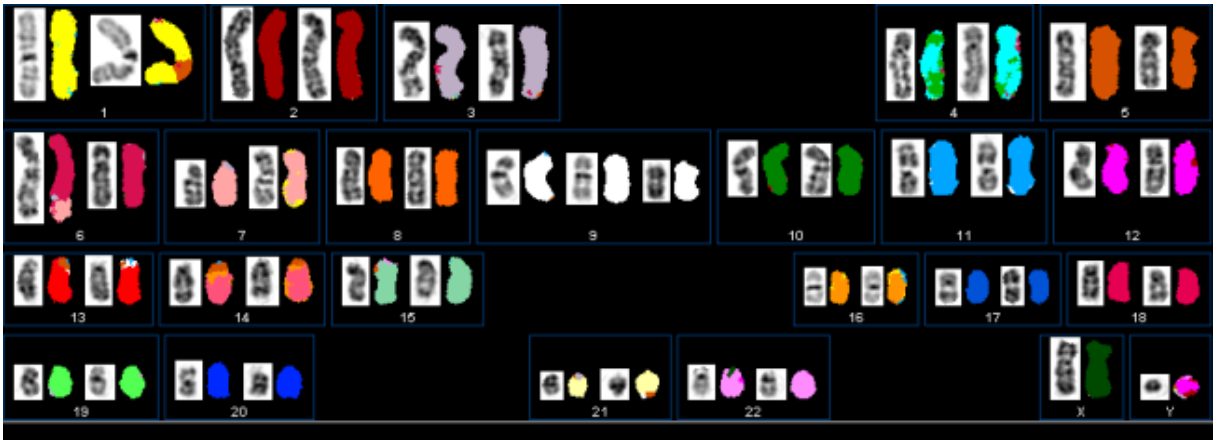

Figure 1B: SKY karyotype from a leukemia cell at the time of diagnosis showing the inverted DAPI (left) and the classified (right) profiles for each chromosome. Translocation t(6;7) (q23;p13), insertion (1;5)(q23;q23q34), and the chromosome 9 are trisome.

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DISCUSSION

The accurate detection of chromosome 6q aberrations by R-banding presents a major challenge to the cytogeneticist. The main reason is that the chromosome arm lacks major landmarks, and it is difficult to make exact breakpoint determination. A problem of the frequent poor morphology in ALL metaphases is further accentuated (Karst et al., 2006; Lu et al., 2002; Stanchescu et al. 2009).

In this case, conventional karyotype was applied and results showed translocation between chromosomes 1 and 5, 7p deletion. In addition, marker chromosome was indicated. Moreover, SKY exactly identified the aberration as insertion between chromosomes number 1 and 5. The supernumerary marker chromosome was identified by SKY as chromosome number 9 based on the colour specificity. Thus, reorganization and abnormalities of chromosomes and their origin can be demonstrated by SKY

R-banding detected 7p- but not the aberration in chromosome number 6 while SKY indicated the karyotype as t(6;7)(q23;p13). It can be concluded that SKY identified the breakpoints in marker chromosomes which cannot be characterized by R-banding, as well as cryptic rearrangements missed by R-banding.

Abnormalities with chromosome 47, XY, +9, ins(1;5) (q23;q23q34), t(6;7) (q23;p13) were rarely observed by conventional cytogenetic technique. In adult ALL, del 6q occurs somewhat less frequently than in children and seems to preferentially correlate with a T cell phenotype; this abnormality does not appear to be associated with an unfavorable prognosis (Betts et al., 2008; Burkhardt et al., 2006; Mancini et al., 2002). It has been proposed that a tumor suppressor gene may be located in this region, whose absence through deletion may contribute to malignant transformation or proliferation reference (Crowley et al., 2005).

In this report, SKY revealed unbalanced translocations. The patient's comprehensive karyotype indicated poor prognosis, which was in accordance with the clinical status. The patient received DOLP regimen (Daunorubicin 40 mg, d1-3, Vincristine 2 mg, d1, 8, L-asparaginase 1wu, d6-16, Prednisone 60 mg, d1-28), without remission, and died after 20 days. From our study, SKY revealed the accurate identification of cytogenetic breakpoints, which is prone to be missed by conventional cytogenetics. It is suggested to use SKY for improving the diagnostic quality of conventional banding to gain more accurate karyotypes.

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