Acute lymphoblastic leukemia and a complex karyotype in a 6-year-old patient

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INTRODUCTION

The translocation t(12;21) ETV6/RUNX1 is one of the most common rearrangements in pediatric acute B-cell lymphoblastic leukemia (B-ALL) (25–30%) and it is usually associated with a favorable prognosis with a cure rate of 90% (Levine *et al*, 2016). Herein we report a pediatric B-ALL case with t(12;21) within the context of a complex karyotype.

CLINICAL REPORT

The patient is a 6-year-old girl who was referred to a tertiary referral hospital by the general practitioner with the diagnosis of thrombocytopenia. The child had fallen ill 3 days prior to referral with a febrile fever up to 39,8 °C. She also complained of ear ache and had developed a petechial rash on her arm a week before she fell ill with a fever. Upon hospitalization her blood tests showed a marked anemia (69 g/l), thrombocytopenia (22 x 10/9 l) and neutropenia (0 x 10/9 l). In addition she had a marked elevation of C-reactive protein (223 mg/l), erythrocyte sedimentation rate (74 mm/h) and lactate dehydrogenase (957 U/l). The bone marrow biopsy revealed hypercellular marrow containing >90% blasts. The bone marrow morphological findings were consistent with the diagnosis of acute B-cell lymphoblastic leukemia. A lumbar punction showed no central nervous system involvement.

INVESTIGATIONS AND RESULTS

Flow cytometry showed 91% of cells expressing CD 19+, CD38+, CD45dim, CD34+, CD10+, CD99+, TdT+/dim, CD20 heterogenous, CD79a+, CD22+, CD58+, HLA DR+, consistent with B-cell lymphoblastic leukemia.

Hemavision mRNA panel showed presence of translocation t(12;21).

Conventional cytogenetics showed a karyotype with multiple abnormalities: del(3)(p21), del(8)(q21), del(11)(q14q23), derivative 12 and derivative 19 (fig 1).

FISH studies identified t(12;21) ETV6/RUNX1 with a loss of one ETV6 copy (fig 2). FISH panel also included t(9;22) BCR/ABL, t(1;19) TCF3/PBX1, dic(9;20) and 11q23 KMT2A break which were found negative.

In order to better understand the complex changes, mFISH and a chromosomal microarray analysis (CMA) were additionally carried out.

mFISH revealed translocations t(8;12;21) and t(3;19) (fig 3).

Chromosomal microarray analysis using HumanCytoSNP-12 BeadChip (Illumina Inc., San Diego, CA) revealed more duplications and deletions and determined breakpoints of the deletions more accurately. Deletions were seen near the breakpoints of the translocations (fig 4). In addition, mosaic monosomy X (15-20%) was found.

With the help of all of the above mentioned approaches **the karyotype** was characterized as 46,XX,del(3)(p21.31),?t(3;19),del(8)(q21.12),t(8;12;21),del(11)(q14.1q23.3),del(12)(p13.31p12.3),del(12)(q21.33),del(16)(q22.1),del(19)(q13.32),del(20)(q13.12q13.13).

Treatment was started in accordance with the NOPHO ALL-2008 non-high risk protocol. On day 15 of treatment the bone marrow was assessed for residual disease which showed 0,2% of blast cells by flow cytometry. On day 29 another bone marrow assessment was done which showed 0,002% of blast cells. With the exception of one episode of severe stomach ache and constipation she has tolerated the treatment reasonably well.

DISCUSSION

The present case highlights the importance of the combination of approaches, i.e., standard karyotyping, FISH, mFISH and chromosomal microarray analysis for the detection of complex translocations t(8;12;21) and t(3;19).

Precise determination of all rearrangements in complex karyotypes brings important information about the chromosomes, regions, and genes involved in these rearrangements and leads to a better understanding of their clinical and biological importance and its role in leukemogenesis.

References

Levine, S. *et al*. Challenges faced in the treatment of acute lymphoblastic leukemia in adolescents and young adults. Clinical Oncology in Adolescents and Young Adults 2016:6 11–20

The authors declare no conflict of interest.

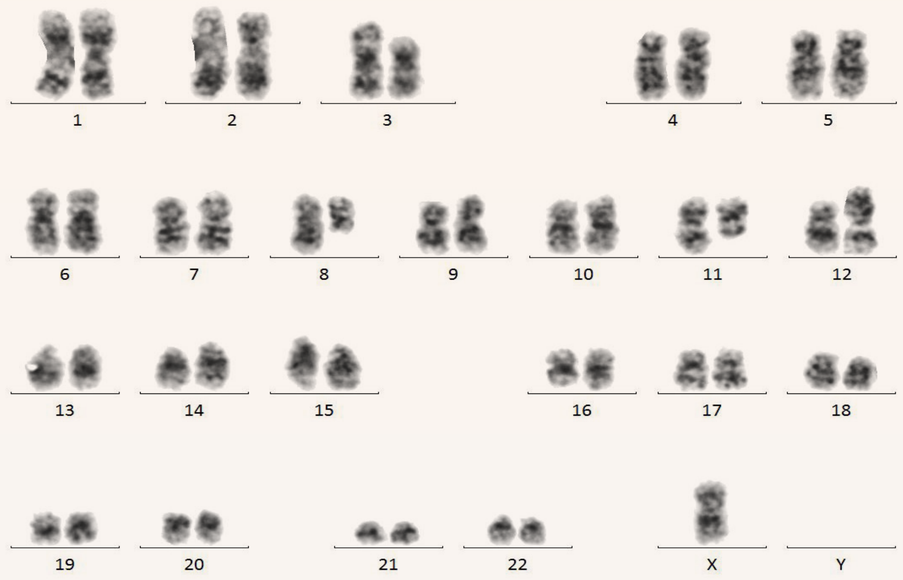

Fig 1. G-banded metaphase. Karyotype: 45,X,-X,?t(3;19),?t(8;12;21),del(11)(q14q23). *Note that the final karyotype was reported as follows 46,XX,?t(3;19),?t(8;12;21),del(11)(q14q23)[20].*

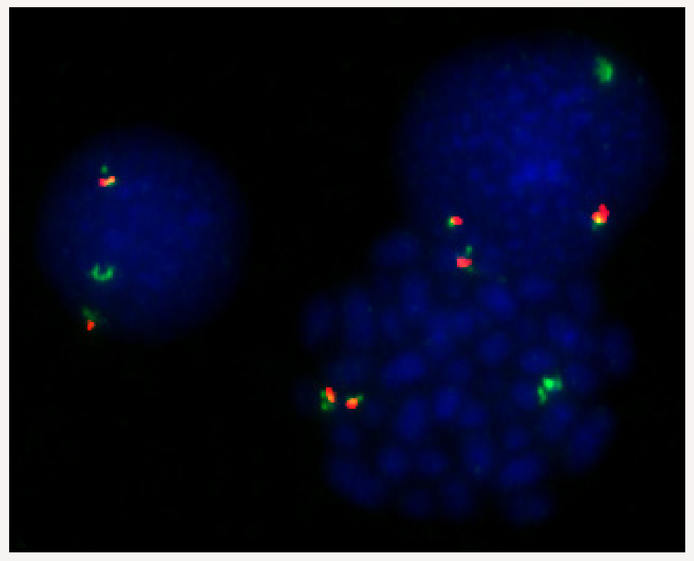

Fig 2. FISH analysis of ETV6/RUNX1 t(12;21), using Kreatech™ ETV6/RUNX1 t(12;21) Fusion FISH probe. ETV6 (12p13) – red, RUNX1 (21q22) – green. The reciprocal translocation is splitting the red and green signals, resulting in two fusion signals on the relevant chromosomes. One red loci is deleted.

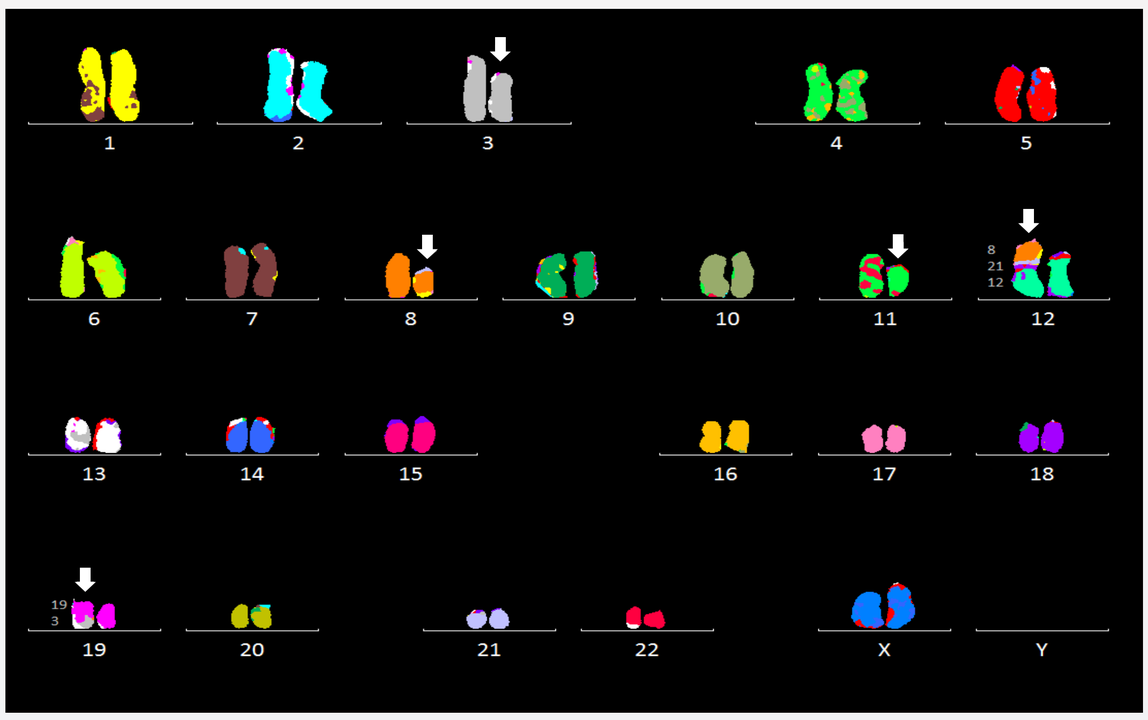

Fig 3. mFISH analysis. Multicolor FISH analysis confirmed the deletion on chromosome 3p, revealed the unbalanced translocation t(8;12;21) and a suspected unbalanced translocation t(3;19), confirmed additionally the deletion on chromosome 8q and on chromosome 11q.

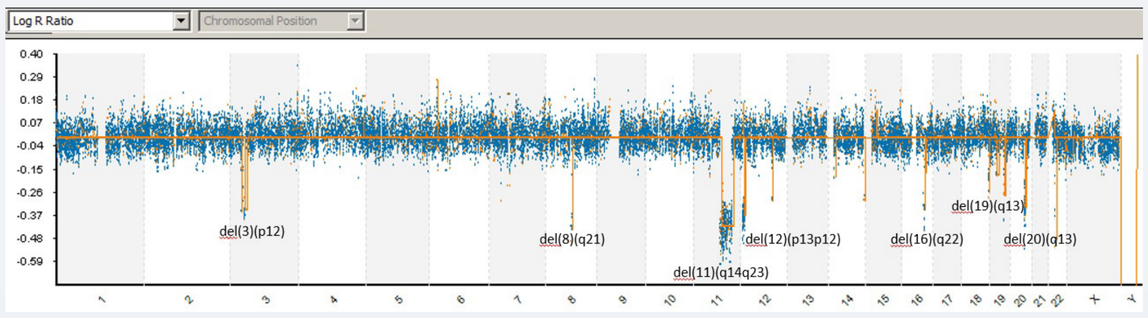

Fig 4. Illumina SNP-array result showing all chromosomes. CMA analysis showed deletions of breakpoints of the translocations [del(3)(p21), del(8)(q21), del(12)(p13p12), del(19)(q13.32)] and additional deletions [del(11)(q14q23), del(12)(q21), del(16)(q22), del(20)(q13)] (BlueFuse™ Multi Analysis Software, Illumina Inc., San Diego, USA).