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PB1757 VARIANT PHILADELPHIA CHROMOSOME IN ALL

Topic: 02. Acute lymphoblastic leukemia - Clinical

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Background: The Philadelphia chromosome (Ph) is detected in 10–20% of adult patients with B-cell acute lymphoblastic leukemia (B-ALL). At the cytogenetic level, it usually arises from the balanced (9;22)(q34;q11) translocation. In 50–70% of the Ph-positive ALL patients, the BCR gene breaks between exons 1 and 2, known as m-bcr region. The BCR-ABL chimeric gene encodes the p190 fusion protein. In approximately 5% of these patients, the Ph originates through other rearrangements than the classic t(9;22). These variant translocations involve others chromosomes in addition to chromosomes 9 and 22.

Aims:

To contribute to the description of patients' clinical characteristics and prognosis with variant Ph chromosome-positive leukemia, we report a Ph chromosome-positive ALL characterized by an unusual variant Ph chromosome.

Methods:

A 34-year-old woman with B-ALL was assessed at the genetic level. Cytogenetic and molecular exploration were conducted using bone marrow and blood samples. Cytogenetic analysis was performed on lymphocytes and bone marrow cells. The cells were treated with colchicine and hypotonic KCl solution. The pellet was fixed and washed in methanol-acetic acid (3:1). The cells were resuspended in fixative and dropped onto slides. Chromosome-banding analysis was performed using RHG and GTG banding techniques. Three karyotypes and 25 metaphases were analyzed according to the International System for Human Cytogenetic Nomenclature. Multiplex reverse transcription-PCR (RT-PCR) was used to identify the BCR-ABL transcript. RT-PCR was performed according to European recommendations, as described previously.

Results: Cytogenetic analysis showed 45 chromosomes with a masked variant Ph translocation: 45,XX,der(9)t(9;20;22)(q34;q ?,q11), der(20) t(9;20;22)(q34;q?,q11),-20,-22. At the molecular level, the patient's BCR-ABL fusion gene was confirmed as e1a2 transcript. FISH procedures were performed using an bcr-abl probe that showed a double fused gene signal on interphase nuclei.

Summary/Conclusion:

Unrelatedly to age and breakpoint location, Ph-positive ALL are characterized by poor prognosis. A unique case of similar complex chromosome 9, 20, and 22 rearrangements in acute lymphoblastic leukemia has been reported. This variant Ph chromosome involving three chromosomes was associated with two markers leading to a duplication of BCR and ABL sequences. Further FISH analysis using the whole chromosome 9, 20 and 22 painting probe will be significant to delineate the complex chromosomal rearrangement involved in our B-ALL case.