

IMAGENS EM HEMATOLOGIA/IMAGES IN HEMATOLOGY

Morphologic, cytogenetic and molecular analyses in the identification of acute promyelocytic leukaemia

Análise morfológica, citogenética e molecular na identificação da leucemia promielocítica aguda

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The association of an exaggerated haemorrhagic syndrome with certain leukaemias was described by Croizat & Favre-Gilli in 1949,¹ and in 1957 Hillstad² bestowed the appellation acute promyelocytic leukaemia (APL) upon this morphologic-clinical syndrome of acute myelogenous leukaemia (AML). This variant is called M3 in the FAB classification, and is characterised by the infiltration of bone marrow by promyelocytes. The haemorrhagic manifestations result, particularly, from procoagulant release by promyelocytes, and frequently determine fatal evolutions for these patients.

A translocation between chromosomes 15 and 17 $t(15;17)(q22;q11-21)$ is present in most, maybe all, cases

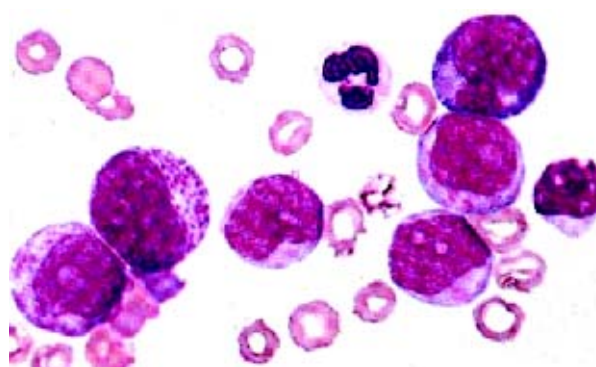


Fig. 1 – Bone marrow smear obtained from the acute promyelocytic leukaemia at diagnosis predominantly showing promyelocytes (Romanovsky, 1000x)

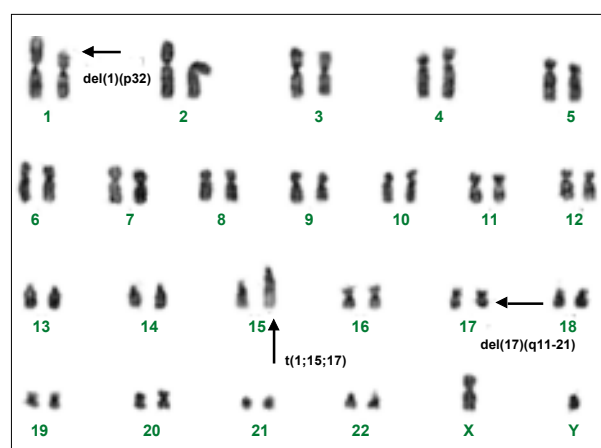


Fig. 2 – G-banded karyotype obtained from the acute promyelocytic leukaemia patient at diagnosis: 46,XY,t(1;15;17)(p32;q22;q11-21). The arrows show the chromosomal abnormalities

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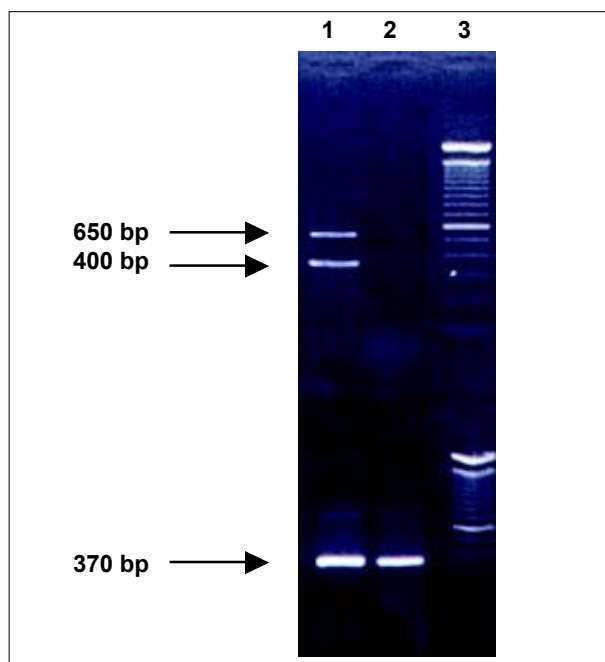


Fig. 3 – Ethidium bromide-stained 2% agarose gel showing reverse transcriptase-polymerase chain reaction (RT-PCR) products of detection of PML/RARA fusion in the acute promyelocytic leukaemia patient. Fragments of 650 bp and 400 bp (Lane 1) expressing fusion mRNAs with breakpoints PML/RARA transcript and fragments of 370 bp corresponding to the control microglobulin b2. Lane 2 shows negative control and Lane 3 shows DNA size markers Ladder 100 bp

of APL³ but this is not found in other AML subtypes. In addition, several descriptions exist of patients with seemingly classic APL but with variant translocations between 15q, 17q and a third chromosome.^{3,4}

As a result of the translocation t(15;17) or its variants, the retinoic acid receptor gene (RARA) from chromosome 17 is moved to chromosome 15, where it is fused with a gene called PML to give rise to a new PML/RARA hybrid gene.³⁻⁶

A clinically intriguing correlate of the molecular genetic detection of a PML/RARA rearrangement in APL is the remarkable, albeit temporary, response to all-trans retinoic acid (ATRA) treatment. After an initial transient proliferation, the APL cells differentiate senesce and die. In consequence, a decrease in mortality by hemorrhagic manifestations has been seen in treated patients.

Herein, we present, for educational purposes, the images obtained from morphologic (Figure 1), cytogenetic (Figure 2), and molecular (Figure 3) analyses of a APL case seen at the Haematology and Haemotherapy Centre of the State University of Campinas.

It is important to comment that the patient was initially treated with ATRA attaining haematologic remission without significant haemorrhagic episodes. Another finding to be mentioned was the presence of the PML-RARA rearrangement in the variant translocation found in the case.

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