

Leukaemia Section

Mini Review

-7/del(7q) in childhood

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Identity

Note

-7/del(7q) is a more common entity of blood malignancies in the adults.



del(7q) G- banding - Courtesy Jean-Luc Lai and Alain Vanderhaegen.

Clinics and pathology

Disease

Myelodysplastic syndromes (MDS) and acute non lymphocytic leukemia (ANLL); may occur:

- 1- de novo,
- 2- be secondary to treatments with alkylating agents, or
- 3- in patients with predisposing leukemia syndromes: Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome, Neurofibromatosis type I, Down syndrome, familial monosomy 7.

Phenotype/cell stem origin

MDS cases : more often RAEB/RAEB-T, CMML, or the following specific childhood presentations : juvenile chronic leukemia (JCML), and monosomy 7 syndrome; ANLL most often M4 or M6.

Epidemiology

the most frequent abnormality in childhood myeloid disorders; found in 30% of the MDS and in 4% of the ANLL; sex/age: 90% of the children with this anomaly are younger than 5 years; before 5 years, there is a majority of boys (3M/2F), with -7 as the sole cytogenetic abnormality; after 5 years, girls are in majority, and the -7/del(7q) is then often associated with additional anomalies.

Clinics

Several clinical forms: the most frequent are JCML and the monosomy 7 syndrome; these disorders have some common features:

- JCML is defined by clinical and cytological observations; 6 to 24% of JCML
- children show monosomy 7 in the bone marrow;
- monosomy 7 syndrome is a cytogenetic-defined entity.

The therapy related cases of monosomy 7 had been exposed to alkylating agents, they have a myelodysplastic phase preceding acute leukemia with multilineage bone marrow dysplasia. In opposite, therapy including anti-topoisomerase drug induce myelodysplastic syndromes and leukemias with 11q23 abnormalities

Cytology

Before 5 years, the disease presents as a specific myeloid leukemia characterized by leucocytosis with monocytosis but thrombopenia, anemia in blood and hyperplasia of the bone marrow; for some authors, the diagnosis of monosomy 7 syndrome should be made in any FAB class (principally CMML), whereas the diagnosis of JCML applies to cases of CMML with fetal hemoglobin > 10 %, and with no monosomy 7; the remaining CMML are diagnosed as CMML; for others,

a - 7 does not exclude the diagnosis of JCML; however, cases of JCML without visible monosomy 7 appear to have no loss of heterozygosity on chromosome 7.

After 5 years, the disease presents as a MDS with cytopenia in blood and hypodysplasia of bone marrow, like in adults.

Prognosis

Slow evolution of the ANLL in infants before 6 months; for children older than 1 year, the survival is less than 2 years; the European Working Group on MDS in Childhood noted a superior survival for children with MDS having a - 7 alone than for those with other anomalies (3 year survival of 56% vs 24%); but this was the reverse in children with ANLL.

Cytogenetics

Cytogenetics morphological

Deletion (7q): cluster of breakpoints in 7q11 to 7q36, is a with two common minimal zones in q22 and in q32-34.

Cytogenetics molecular

Using loss of heterozygosity (LOH) studies and YAC libraries, a 2 to 3 Mb segment in 7q22 has been designated as the proximal common deleted area; the 7q33-34 zone is the consensual area for the distal deletion; LOH studies suggest that a specific mechanism, such as mitotic recombination in bone marrow stem cell leading to homozygosity in both granulocytes and lymphocytes, may be implicated.

Probes

Chromosomal band 7q22: marker D7S658, through D7S2494, YAC HSC7E441 to HSC7E572; 7q33-34: D7S498 to D7S505; near-centromeric probes of chromosome 7 and 7q31 probes are produced by commercial companies.

Additional anomalies

7 alone is observed in 75% of MDS cases and in 32% of ANLL; the specific additional anomalies are - 5/del(5q), and trisomy 8.

Variants

The balanced translocation t(1;7)(q10;p10), and many unbalanced translocation, having for consequence a partial monosomy 7 of the 7q22 to 7q34 bands may, in a way, be considered as variants.

Genes involved and proteins

Note

-7/del(7q) is frequent in secondary MDS or ANLL, and also in leukemias occurring in individuals with constitutional syndromes including predisposition to myeloid disorders; these findings suggest the presence of a putative myeloid leukemia suppressor gene in the commonly deleted genomic segment 7q22 and even multiple genes in 7q22 -31.1 that are playing a role in

leukemogenesis; candidate genes are : ASNS (asparagine synthetase gene) in 7q21.3-q22.1; ACHE (acetyl cholinesterase), EPO (erythropoietin), PLANH1 (plasminogen activator inhibitor 1) in 7q22; and MET in 7q31.2-31.3.

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