-7/del(7q) in adults

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Identity

Note
-7/del(7q) in childhood blood malignancies exhibits a specific pattern of pathogenesis; chromosome 7 anomalies are not rare in acute lymphocytic leukaemia (ALL); they occur in balanced translocations involving 7p15 or 7q34 in T lineage and 7q22 or 7q32 in B proliferations; monosomy 7 is present in 5 to 6 % of ALL, most often as a secondary anomaly of the t(9;22); the association t(9;22), -7 is present in 16 % of the Ph1+ ALL, i.e. in 3% of ALL as a whole; we will hereunder focus on -7/del(7q) in adult myeloproliferations.

Phenotype/cell stem origin
MDS cases : found in 30% of RAEB/RAEB-T, 20% of CMML, and only 5% of RA with an abnormal karyotype;
ANLL most often M4 or M6 ;
Monosomy 7 and these deletions does not seem a specific feature of the dysplastic clone in the MDS, they are secondary events contributing to the leucogenesis.

Epidemiology
-7 is the most frequent abnormality in secondary myeloid disorders, found in 51% of the cases in a series of 246 cases, while del(7q) was found in 7%, and a partial monosomy 7 as a result of an unbalanced translocation in 8% of cases; in contrast, -7/del(7q) is found in 10% of de novo myeloid disorders; the sex ratio is 1.5 male for 1 female; the proportion of adults with a -7 myeloid disorder grows dramatically after 60 years.

Clinics
Characterized by infectious susceptibility, quick aggravation, and treatment resistance.

Prognosis
Monosomy 7 is classified as a poor prognostic criterium by the International Prognostic Scoring System; the actuarial relapse rate at one year is 82 %, and the 7-yr actuarial event-free survival is 6 %; after an allogeneic bone marrow transplantation, -7 is predictive of an unfavorable outcome.

Cytogenetics

Cytogenetics morphological
Deletion (7q) is always interstitial; cluster of breakpoints in 7q11 to 7q36, is a with two common minimal zones in q22 and in q32-34.
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Cytogenetics molecular

Using loss of heterozygocity (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 7q221: marker D7S658, through D7S2494, YAC H5C7E441 to HSC7E572; 7q33-34: D7S498 to D7S505; near-centromeric probes of chromosome 7 and 7q31 probes are produced by commercial companies.

Additional anomalies

-5/del(5q), found in 40 to 60 % of the secondary MDS cases; 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 not only frequent in secondary MDS or ANLL, but 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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