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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 frequents 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 month; 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 heterogygocity (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 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.

References

Daghistani D, Toledano SR, Curless R. Monosomy 7 syndrome. Clinical heterogeneity in children and adolescents. Cancer Genet Cytogenet. 1990 Feb;44(2):263-9

Rubin CM, Arthur DC, Woods WG, Lange BJ, Nowell PC, Rowley JD, Nachman J, Bostrom B, Baum ES, Suarez CR. Therapy-related myelodysplastic syndrome and acute myeloid leukemia in children: correlation between chromosomal abnormalities and prior therapy. Blood. 1991 Dec 1;78(11):2982-8

Luna-Fineman S, Shannon KM, Lange BJ. Childhood monosomy 7: epidemiology, biology, and mechanistic implications. Blood. 1995 Apr 15;85(8):1985-99

Marie JP, Simonin G, Legrand O, Delmer A, Faussat AM, Lewis AD, Sikic BI, Zittoun R. Glutathione-S-transferases pi, alpha, mu and mdr1 mRNA expression in normal lymphocytes and chronic lymphocytic leukemia. Leukemia. 1995 Oct;9(10):1742-7

Passmore SJ, Hann IM, Stiller CA, Ramani P, Swansbury GJ, Gibbons B, Reeves BR, Chessells JM. Pediatric myelodysplasia: a study of 68 children and a new prognostic scoring system. Blood. 1995 Apr 1;85(7):1742-50

Johnson EJ, Scherer SW, Osborne L, Tsui LC, Oscier D, Mould S, Cotter FE. Molecular definition of a narrow interval at 7q22.1 associated with myelodysplasia. Blood. 1996 May 1;87(9):3579-86

Le Beau MM, Espinosa R 3rd, Davis EM, Eisenbart JD, Larson RA, Green ED. Cytogenetic and molecular delineation of a region of chromosome 7 commonly deleted in malignant myeloid diseases. Blood. 1996 Sep 15;88(6):1930-5

Stephenson J, Czepulkowski B, Hirst W, Mufti GJ. Deletion of the acetylcholinesterase locus at 7q22 associated with myelodysplastic syndromes (MDS) and acute myeloid leukaemia (AML). Leuk Res. 1996 Mar;20(3):235-41

Groupe Français de Cytogénétique Hématologique. Forty-four cases of childhood myelodysplasia with cytogenetics, documented by the Groupe Français de Cytogénétique Hématologique. Leukemia. 1997 Sep;11(9):1478-85

Kiuru - Kuhlefelt S, Kristo P, Ruutu T, Knuutila S, Kere J. Evidence for two molecular steps in the pathogenesis of myeloid disorders associated with deletion of chromosome 7 long arm. Leukemia 1997;11:2097 - 2104. (Review)

Fischer K, Fröhling S, Scherer SW, McAllister Brown J, Scholl C, Stilgenbauer S, Tsui LC, Lichter P, Döhner H. Molecular cytogenetic delineation of deletions and translocations involving chromosome band 7q22 in myeloid leukemias. Blood. 1997 Mar 15;89(6):2036-41

Liang H, Fairman J, Claxton DF, Nowell PC, Green ED, Nagarajan L. Molecular anatomy of chromosome 7q deletions in myeloid neoplasms: evidence for multiple critical loci. Proc Natl Acad Sci U S A. 1998 Mar 31;95(7):3781-5

Nevill TJ, Fung HC, Shepherd JD, Horsman DE, Nantel SH, Klingemann HG, Forrest DL, Toze CL, Sutherland HJ, Hogge DE, Naiman SC, Le A, Brockington DA, Barnett MJ. Cytogenetic abnormalities in primary myelodysplastic syndrome are highly predictive of outcome after allogeneic bone marrow transplantation. Blood. 1998 Sep 15;92(6):1910-7

Hasle H et al. for the European Working Group on MDS In Childhood. Monosomy 7 has different prognostic significance in childhood MDS and AML. 5th International Symposium on Myelodysplastic Syndromes. Prague, Czech Republic, 21-24 April 1999. Abstracts. Leuk Res. 1999 Apr;23 Suppl 1:S1-87

Hast R, Eriksson M, Widell S, Arvidsson I, Bemell P. Neutrophil dysplasia is not a specific feature of the abnormal chromosomal clone in myelodysplastic syndromes. Leuk Res. 1999 Jun;23(6):579-84

Koike M, Tasaka T, Spira S, Tsuruoka N, Koeffler HP. Allelotyping of acute myelogenous leukemia: loss of heterozygosity at 7q31.1 (D7S486) and q33-34 (D7S498, D7S505). Leuk Res. 1999 Mar;23(3):307-10

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