

Leukaemia Section

Mini Review

+21 or trisomy 21

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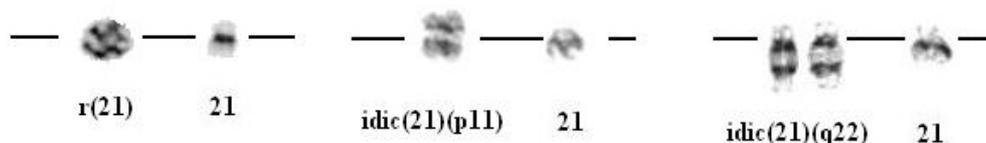
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Identity

Note

Acquired trisomy 21 is not to be confused with constitutional trisomy 21 (Down syndrome, DS) which is a factor of predisposition to childhood acute leukemia but whose significance and clinical context are quite different.



Ring(21) and dicentric(21) chromosomes, G-banding - Courtesy Elise Labis.

Clinics and pathology

Disease

Acute non lymphocytic leukemia (ANLL) / myelodysplastic syndromes (MDS)

Phenotype/cell stem origin

No specific phenotype but possibly a slight higher incidence in monocytic phenotypes (ANLL-M4 and -M5, chronic myelomonocytic leukemia (CMML)). ANLL-M7 with acquired +21 is exceptional, whereas ANLL-M7 is frequent in Down Syndrome.

Epidemiology

+21 is the second more frequent acquired trisomy, after trisomy 8, in adult ANLL/MDS. It is rarely observed as the sole abnormality. According to large series, +21 was observed in 3% to 7% of cases, out of which 0.3-0.4% of cases with +21 as the only abnormality.

The more frequent association is with -5/5q- and -7/7q-, followed by trisomy 8 and structural rearrangements t(8;21), t(15;17) and inv(16).

Alternatively to +21 and in the same clinical context, tetrasomy or pentasomy 21 can be observed, as well as single or multiple copies of a structurally rearranged

chromosome 21, such as i(21q), psu dic(21q) or r(21). In some of these der(21), a chromosome 21 segment can be tandemly amplified as homogeneous staining region (HSR).

Prognosis

+21 as sole abnormality has an unfavorable prognosis, none of the published patients could achieve a long-term disease-free survival.

When associated with other recurrent chromosome changes, it does not modify the prognosis of these abnormalities.

Disease

Acute lymphocytic leukemia (ALL).

Phenotype/cell stem origin

Essentially B-cell lineage.

Epidemiology

+21 is the more frequent aneuploidy observed in both adult and childhood ALL. Its overall incidence would be around 15% of cases.

As the sole clonal abnormality (excepting DS patients), +21 accounts for 2% of pediatric and less than 1% of adult ALL cases.

In childhood ALL, the incidence of +21 is approximately of 40% and of 80%, respectively, in the 47-50 chromosomes and in the >50 chromosomes ploidy groups.

The main association is with t(12;21)(p13;q22) in childhood (15% of cases at diagnosis), followed by 6q abnormalities. Association also with t(1;19)(q23;p13), t(4;11)(q21;q23) and 14q abnormalities.

The main association with a second aneuploidy is with +X, +16 or -20.

In adults, +21 is associated the most frequently with t(9;22)(q34;q11): about 50% of cases.

Prognosis

+21 as sole abnormality has a favorable prognosis.

In the group 47-50 chromosomes, + 21 has a rather good prognosis in children, when it is not associated with a bad prognosis structural rearrangement. In the same ploidy group, +21 has no prognostic impact in adults.

Genetics

Note

Gene(s) involved in trisomy 21 associated leukemia is (are) unknown.

The 21q22 region seems crucial. Der(21) containing an HSR have constantly multiple copies tandemly amplified of the AML1 gene, both in ANLL and in ALL, but there is no proof that this gene is directly implicated.

The overexpression of cystathionine-b-synthetase (CBS; 21q22.3) would be linked to increased sensitivity of myeloblasts to ara-C and daunorubicin in DS ANLL patients. This has not been confirmed in acquired trisomy 21.

References

- Dewald GW, Diez-Martin JL, Steffen SL, Jenkins RB, Stupca PJ, Burgert EO Jr. Hematologic disorders in 13 patients with acquired trisomy 21 and 13 individuals with Down syndrome. *Am J Med Genet Suppl.* 1990;7:247-50
- Mitelman F, Heim S, Mandahl N. Trisomy 21 in neoplastic cells. *Am J Med Genet Suppl.* 1990;7:262-6
- Raimondi SC, Pui CH, Head D, Behm F, Privitera E, Roberson PK, Rivera GK, Williams DL. Trisomy 21 as the sole acquired chromosomal abnormality in children with acute lymphoblastic leukemia. *Leukemia.* 1992 Mar;6(3):171-5
- Watson MS, Carroll AJ, Shuster JJ, Steuber CP, Borowitz MJ, Behm FG, Pullen DJ, Land VJ. Trisomy 21 in childhood acute lymphoblastic leukemia: a Pediatric Oncology Group study (8602). *Blood.* 1993 Nov 15;82(10):3098-102
- Cortes JE, Kantarjian H, O'Brien S, Keating M, Pierce S, Freireich EJ, Estey E. Clinical and prognostic significance of trisomy 21 in adult patients with acute myelogenous leukemia and myelodysplastic syndromes. *Leukemia.* 1995 Jan;9(1):115-7
- Wei CH, Yu IT, Tzeng CH, Fan FS, Hsieh RK, Chiou TJ, Liu JH, Chen PM. Trisomy 21 in acute myeloid leukemia. *Cancer Genet Cytogenet.* 1996 Feb;86(2):177-80
- Berger R. Acute lymphoblastic leukemia and chromosome 21. *Cancer Genet Cytogenet.* 1997 Mar;94(1):8-12
- Loncarevic IF, Roitzheim B, Ritterbach J, Viehmann S, Borkhardt A, Lampert F, Harbott J. Trisomy 21 is a recurrent secondary aberration in childhood acute lymphoblastic leukemia with TEL/AML1 gene fusion. *Genes Chromosomes Cancer.* 1999 Mar;24(3):272-7
- Wan TS, Au WY, Chan JC, Chan LC, Ma SK. Trisomy 21 as the sole acquired karyotypic abnormality in acute myeloid leukemia and myelodysplastic syndrome. *Leuk Res.* 1999 Nov;23(11):1079-83

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