21q22 rearrangements in treatment related leukemia

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Identity

Note: This data is extracted from a very large study from an International Workshop on treatment related leukemias - restricted to balanced chromosome aberrations (i.e.: -5/del(5q) and -7/del(7q) not taken into account per see), published in Genes, Chromosomes and Cancer in 2002.

Clinics and pathology

Disease

Treatment related myelodysplasia (t-MDS) or acute non lymphocytic leukemias (t-ANLL).

Note

The study included 79 cases; t-MDS without progression to ANLL accounted for 15%, t-MDS progressing to ANLL for the remaining 67%; there was no case of acute lymphoblastic leukemia.

Phenotype/cell stem origin

MDS cases were frequently refractory anemia with excess of blasts cases; 58% of ANLL cases were M2 ANLL.

Etiology

Frequent antracyclin exposure.

Epidemiology

21q22 rearrangements were found in 15% of t-MDS/t-ANLL; 1M to 1F sex ratio

Clinics

Age at diagnosis of the primary disease was 47 yrs (range 2-75); age at diagnosis of the t-MDS/t-ANLL was 51 yrs (11-77) and median interval was 39 mths (6-306). Primary disease was a solid tumor in 56% of cases (mainly: breast, lung, sarcoma/ PNET, colon cancer) and an hematologic malignancy in 43%. Treatment of the primary disease included radiotherapy (in 6%), chemotherapy (46%) or both (48%). 75% of patients with a 21q22 rearrangement had previously received topoisoromerase II inhibitors, a higher proportion than other subgroups of treatment related leukemia, except 11q23 patients, who were 84% to have been exposed to topoisoromerase II inhibitors; alkylating agents exposure was higher than in patients with t(15;17) or inv(16).

Treatment

Patients who received bone marrow transplantation had a higher median survival (31 mths).

Prognosis

Median survival was 14 mths, there was 58% of patients surviving 1 yr, 33% 2 yrs, and 18% 5 yrs., a better outcome than patients with 11q23 rearrangement, 3q21q26 rearrangement, 12p13 rearrangement, t(9;22), or t(8;16) and a worse outcome than those with t(15;17) or inv(16) treatment related leukemias. By th 21q22 group, patients with a t(8;21) had a better outcome, and those with a t(3;21) had a worse outcome.

Cytogenetics

Cytogenetics morphological

t(8;21)(q22;q22) (ETO / AML1) was found in 56% of cases, t(3;21)(q26;q22) (MDS-EVI1 / AML1 in 20 %, t(16;21)(q24;q22) (CBFA2T3 / AML1) in 5%. Rare recurrent anomalies were: t(1;21)(p36;q22),
t(9;21)(p22;q22), t(10;21)(p12;q22), t(15;21)(q21-q22), t(17;21)(q12;q22), and t(20;21)(q11;q22).

Additional anomalies
-7/del(7q) in 23% of cases (especially in cases with alkylating agents exposure), +8 in 11%, -5/del(5q) rarely found; complex karyotypes in 28% of cases (more frequently than in treatment related leukemias with a 11q23 rearrangement or a t(15;17)).

Genes involved and proteins

AML1 partner

Result of the chromosomal anomaly

Hybrid gene
Description
5' AML1 - 3' partner.

References

This article should be referenced as such: