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Leukaemia Section
Mini Review

del(5q) in myeloid malignancies

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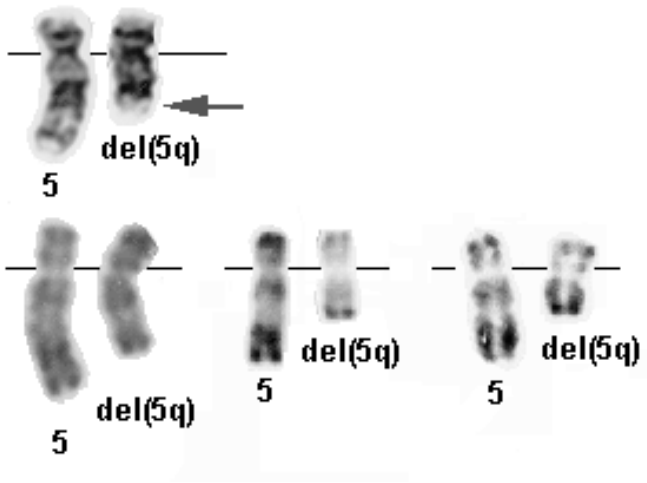
Identity



del(5q) G-banding (top) - Jean-Luc Lai; R-banding (bottom), Courtesy Christiane Charrin (2 and 3), Editor (1).

Note: Interstitial del(5q) was first described in refractory anaemia; it is also the most common structural rearrangement in myelodysplastic syndromes (MDS) and in acute myeloid leukemias (ANLL); del(5q) is accompanied with given clinical and haematological features; we herein summarize these three pictures as:
1- 'the 5q- syndrome', with del(5q) as the sole karyotypic anomaly,
2- MDS with del(5q) and additional karyotypic anomalies, and
3- ANLL with del(5q) (solely or not).

Clinics and pathology

Disease

The 5q-syndrome is a myelodysplastic syndrome.

Phenotype / cell stem origin

Classified as refractory anemia (RA) in 75% of cases, RA with excess blasts (RAEB) in 15%.

Etiology

Possibility of a toxic agent in the environment.

Epidemiology

Mean age 65-70 yrs; sex ratio: 1M/3F.

Clinics

Blood data: macrocytic anemia, minor leukopenia, normal or high thrombocytosis.

Cytology

Bone marrow erythroid hypoplasia (50%) and characteristic hypolobulated megakaryocytes (95%).

Treatment

Supportive treatment requiring regular blood transfusions for years, leading patients to develop clinical symptoms of iron overload.

Prognosis

Favorable, with a low risk of transformation in acute leukemia (15%); median survival is 5 yrs.

Disease

MDS with del(5q) and additional karyotypic anomalies are de novo and therapy-related MDS.

Phenotype / cell stem origin

Classified as RAEB or RAEB in leukemic transformation (RAEBT), chronic myelomonocytic leukemia (CMML) in transformation (rare).

Etiology

Of therapy-related MDS: prior exposure to alkylating agents with or without radiotherapy.

Epidemiology

10-15% of MDS; female preponderance is less characteristic than in above; mean age 65 yrs.

Clinics

Blood data: macrocytic anemia, leukopenia and low platelet count (50%).

Prognosis

Unfavorable; median survival: 10-12 mths.

Disease

ANLL with del(5q) solely (in 20-25% of cases) or not.

Phenotype / cell stem origin

De novo and therapy-related ANLL; all FAB subgroups, mainly M2 ANLL.

Etiology

Represents 15% of therapy-related AML with prior exposure to alkylating agents with or without radiotherapy.

Epidemiology

10-25% of ANLL; mean age 65 years; sex ratio: 1M/1F.

Clinics

Blood data: anaemia, leukopenia or hyperleucocytosis (blasts) and thrombocytopenia.

Prognosis

Extremely poor; median survival: 3 mths.

Cytogenetics

Cytogenetics, morphological

del(5q) is an interstitial deletion with variable proximal and distal breakpoints, and all the 13 bands between 5q11 and 5q35 have been implicated as breakpoints in MDS and ANLL; the more frequently reported breakpoints are 5q12-14 (proximal) and 5q31-33 (distal); a common segment within 5q31 is deleted in all cases; del(5)(q13.3q33.1) is the most common rearrangement, and is observed in all cases of 5q- syndrome which represent a distinct clinical subgroup (see above).

Additional anomalies

Monosomy 7, trisomy 8, monosomy 17p or other chromosomal defects are frequently associated with del(5q) in ANLL, leading to complex karyotypes; in such cases, it is not possible to know whether del(5q) is the primary event; unbalanced translocations involving 5q14-5q34 deletion are occasionaly reported and frequently associated with complex karyotype; identification of chromosome partners implicated in these translocations is often arduous and requires both standard R- and G-banding, and FISH techniques (chromosome painting).

Genes involved and Proteins

Note: del(5q) results in genetic event(s) which lead to loss of heterozygosity from chromosome 5, suggesting that tumor suppressor genes, important for the development of MDS and/or ANLL may be located in the deleted region; the smallest deleted region is an approximately 5 Mb region located in 5q31 band; molecular genetic and FISH techniques using panels of ordered DNA markers have been used and allowed to map this critical region: the three candidate genes on which most interest has focused are EGR1 (early growth response 1 protein), IRF1 (interferon regulatory factor 1), and CSF1R (CSF1 receptor).

To be noted

The finding of a del(5q) during course of a myeloproliferative disorder (MPD) suggests a therapy-related process, and, therefore, a complete change in the prognosis.

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