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Leukaemia Section

Mini Review

del(17p) in myeloïd malignancies

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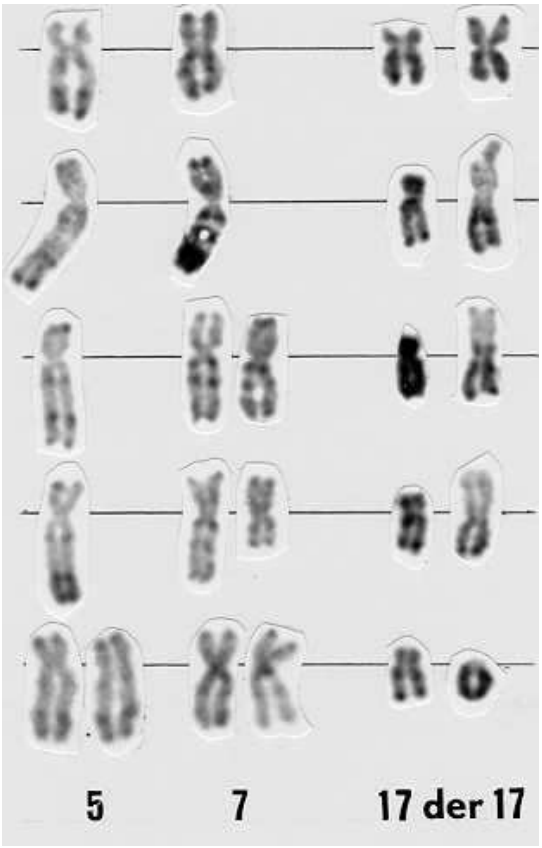
Identity

Alias: 17p syndrome in myeloïd malignancies

Note: Recently, we and others reported in ANLL and MDS a strong correlation between 17p deletion (a clonal cytogenetic anomaly consisting of a deletion of the short arm of chromosome 17), and a particular form of morphological dysgranulopoiesis, we also found in such cases a strong correlation between 17p deletion and p53 mutation; these correlations suggest that ANLL and MDS with 17p deletion constitute a new morphological-cytogenetic-molecular entity, the " 17p syndrome "



17p syndrome R- banding: various rearrangements of chromosomes 5 and/or 7, and 17 - Courtesy Jean-Luc Lai.

Clinics and pathology

Disease

Acute non lymphocytic leuemia/myelodysplastic syndromes (ANLL/MDS), chronic myelogenous leukemia (CML) in blast crisis.

Phenotype/cell stem origin

Mainly refractory anemia with excess of blasts RAEB/RAEB-t in MDS, often M2 or M6 in ANLL / multi-lineage involvement.

Etiology

About 30% of ANLL and MDS with 17p deletion are therapy related; t-ANLL and t-MDS occur after a lymphoïd neoplasm or a solid tumor treated by chemotherapy with an alkylating agent or after essential thrombocytemia or polycythemia vera treated by hydroxyurea alone or associated with other drugs.

Epidemiology

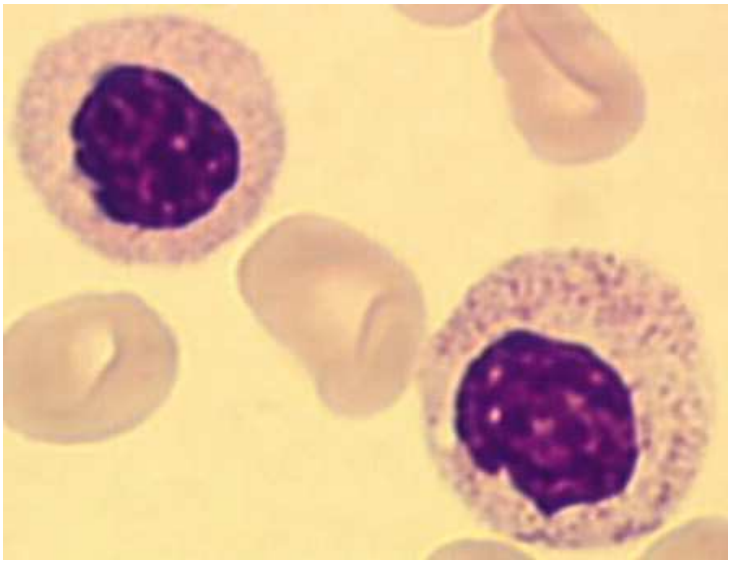
3 to 4% of ANLL and MDS.
Mean age > 60 years.
Sex ratio : about 1M/1F.

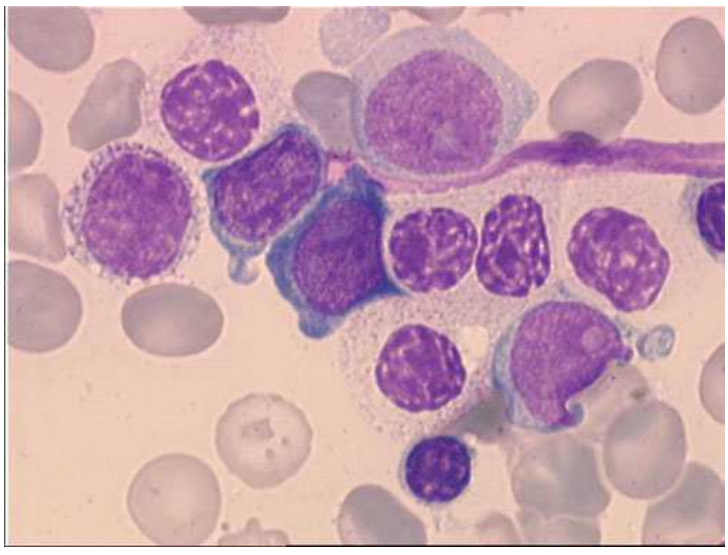
Clinics

Not specific (consequences of cytopenias infection, bleeding, anemia)

Cytology

Most cases of ANLL and MDS with 17p deletion have a particular form of morphological dysgranulopoiesis, combining both nuclear and cytoplasmic abnormalities in at least 5% of neutrophils; affected cells have reduced size and are mostly mature; nucleus is bi- or non-lobulated and chromatin is well- or heavily-clumped; cytoplasm contains variable number of small clear vacuoles and sometimes a reduced number of granules; these morphological abnormalities involve neutrophilic,





17p syndrome - Courtesy Georges Flandrin.

but also eosinophilic and basophilic lineages; such abnormalities can be observed both in the bone marrow and in the peripheral blood; however, in the latter instance, it may be difficult to demonstrate pseudo-Pelger Huët anomaly, due to frequent neutropenia; these nuclear changes mimick those found in the so-called constitutional Pelger-Huët hypolobulation of polymorphonuclear leukocytes.
Dysgranulopoiesis features are frequently associated with variable degree of dyserythropoiesis and dysmegakaryocytopoiesis.

Pathology

Not reported.

Treatment

Classical anthracycline-Ara C chemotherapy gives poor results; the only possibility of cure appears to be by allogeneic stem cell transplantation, but very few allografted cases have been reported.

Evolution

Worsening of cytopenias, progression to ANLL.

Prognosis

Very poor, median survival: 4 months.

Cytogenetics

Cytogenetics morphological

17p deletions result mainly from unbalanced translocation between 17p and another chromosome and less frequently from monosomy 17, isochromosome 17q and partial 17p deletion; chromosome 5 is the partner chromosome the most frequently involved in the unbalanced translocation, other involved chromosomes are mainly chromosomes 7, 12, 18, 21 and 22.

Cytogenetics molecular

The breakpoint on chromosome 17 and the extent of the deletion of 17p are variable, but the breakpoint is always proximal to the p53 gene; the variable extent of 17p deletion suggests the presence of tumor suppressor gene(s) on 17p, inactivated by the deletion. The p53 gene is a good candidate.

Additional anomalies

Chromosome 17p rearrangement or monosomy 17 are frequently associated to at least 2 other chromosomal rearrangements and are therefore part of complex abnormalities; the most frequent additional abnormalities include chromosomes 5 and/or 7, but also chromosomes 12, 16 and 11; complex karyotypes are associated in some cases with unidentified ring or marker chromosomes; however, some cases of iso(17q) are isolated or associated with a few additional chromosome anomalies.

Genes involved and proteins

P53

Location
17p13.1

Result of the chromosomal anomaly

Hybrid gene

Description
Inactivation of the P53 gene by deletion of one allele and mutation of the non deleted allele.

Detection
p53 deletion: conventional cytogenetics, FISH with p53 specific probes.
p53 mutation: SSCP or immunocytochemistry.

To be noted

Note
In few 17p deletion cases, whole chromosomal painting and fluorescence in situ hybridization (FISH) analysis with p53 specific probe demonstrate that unidentified ring or marker chromosomes observed in conventional cytogenetic can contain 17p material including the second p53 allele; in these few cases, the particular form of morphological dysgranulopoiesis abnormalities observed in 17p- syndrome are not observed.

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