

Leukaemia Section

Mini Review

inv(2)(p23q35)

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Clinics and pathology

Disease

Translocations involving 2p23 are found in more than half cases of anaplastic large cell lymphoma (ALCL), a high grade non Hodgkin lymphoma (NHL). They involve ALK, and are therefore called ALK+ ALCL.

The most frequent ALK+ ALCL being the the t(2;5)(p23;q35) with NPM1 -ALK fusion protein, which localises both in the cytoplasm and in the nucleus.

The inv(2)(p23q35) is very rare., and, like other t(2;Var) involving various partners and ALK, the fusion protein has a cytoplasmic localization; they are therefore called "cytoplasm only" ALK+ ALCL.

Phenotype/cell stem origin

CD30+; ALK+.

Epidemiology

At least 7 known cases, aged 12 yrs to 52 yrs (med 23 yrs); no sex unbalance so far, in contrast with the general feature found in ALK+ ALCL.

Clinics

ALK+ ALCL without the t(2;5) (so called cytoplasmic only ALK cases) show clinical features similar to those of classical ALK+ ALCL: young age, male predominance, presentation with advanced disease, systemic symptoms, frequent involvement of extranodal sites, and a good prognosis. Nothing in particular is known concerning inv(2) cases, as cases are not fully documented.

Prognosis

Not well documented.

Cytogenetics

Cytogenetics morphological

Difficult to identify, as breakpoints lie in telomeric regions; an apparent i(2q) -when present- in ALCL should ring the bell; in some other cases, with numerous anomalies, there is no apparent breakpoint on chromosomes 2.

Cytogenetics molecular

FISH analyses are thereof essential.

Additional anomalies

ider(2)(q10)inv(2) has been found in some cases, carrying 2 additional copies of the ATIC-ALK hybrid gene, as detected with FISH; frequent complex karyotypes.

Genes involved and proteins

ALK

Location

2p23

Protein

1620 amino acids; 177 kDa; glycoprotein (200 kDa mature protein) ; membrane associated tyrosine kinase receptor.

ATIC

Location

2q35

Protein

591 amino acids, 64 kDa; bifunctional purine biosynthesis:9th and 10th step of the de novo purine synthesis.

Result of the chromosomal anomaly

Hybrid gene

Description

5' ATIC- 3' ALK.

Fusion protein

Description

791 amino acids, 87 kDa. 229 N-term amino acid from ATIC containing the IMPCH domain and the dimerization domain fused to the 562 C-term amino acids from ALK (i.e. the entire cytoplasmic portion of ALK with the tyrosine kinase domain).

Expression / Localisation

Cytoplasmic localisation (in contrast with the t(2;5)(p23;q35) with NPM1-ALK, which localizes both in the cytoplasm and in the nucleus).

Oncogenesis

ATIC seems to provoke the dimerization of ATIC-ALK, which should lead to constitutive autophosphorylation and activation of the ALK tyrosine kinase, as for NPM1-ALK (see t(2;5)(p23;q35)).

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