del(6q) abnormalities in lymphoid malignancies

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Identity

Note
Deletion of the long arm of chromosome 6 (del(6q)) is more frequently described in lymphoid proliferations than in other hematological malignancies; del(6q) is observed in acute lymphoblastic leukemia (ALL), in chronic lymphocytic leukemia (CLL), in prolymphocytic leukemia and in non-Hodgkin lymphomas (NHL) (15% cases, sometimes associated with t(14;18)(q32;q21)); these deletions are mainly reported to be terminal, but also interstitial.

Phenotype/cell stem origin
Lack of specificity for a particular immunophenotype.

Epidemiology
Found in 5-15% of patients after conventional cytogenetic analysis, in 30% after FISH analysis, in 5 to 25% of cases in loss of heterozygosity studies.

Prognosis
Not significantly different from patients lacking a 6q rearrangement.

Disease
Childhood T-cell acute lymphoblastic leukemia (T-ALL)

Epidemiology
del(6q) is one of the most frequent cytogenetic aberration occurring in 10-20% of cases and often associated with 14q11 or del(9p) abnormalities.

Prognosis
Outcome similar to cases with normal diploid karyotypes.

Disease
Adult acute lymphoblastic leukemia

Phenotype/cell stem origin
T-cell phenotype found in 50% of cases (ALL).

Epidemiology
del(6q) in adult-ALL occur with a lower frequency (5%) than in children and is reported predominantly in young adult (15 to 40 years aged).

Prognosis
Patients with a 6q change tented to have longer event free survival (EFS) (median: 11 months; 3
years EFS: 47%) than did patients without 6q changes (median EFS: 7 month; 3 years EFS: 20%).

Disease
B-cell small lymphocytic lymphoma

Epidemiology
del(6)(q21q23) is the most common recurrent cytogenetic abnormality in this disease.

Clinics
In cases with del(6q), a morphological appearance of peripheral blood large prolymphocytes, a mature B-cell phenotype and a typical clinical course of other well-differentiated lymphocytic neoplasms are described.

Disease
Atypical chronic lymphocytic leukemia

Prognosis
Complex karyotypes with +12, del(13)(q14), del(11q), del(6)(q21q23) and possible 4q or 10q anomalies are associated with a poor prognosis.

Disease
Multiple myeloma

Phenotype/cell stem origin
Multiple myeloma (MM) is a malignant plasma cell proliferation of mature differentiated B-cell.

Epidemiology
del (6q) in multiple myeloma represent 15% of cases of MM.

Prognosis
del(6q) are more frequent in the hypodiploid group of multiple myeloma, bearing a worse prognosis (med survival of 1.5 yr).

Cytogenetics

Cytogenetics morphological
The frequency of the deletions is difficult to estimate by conventional cytogenetic analysis because small interstitial deletions are beyond the sensitivity of the technique; furthermore, many studies have reported conflicting data on the putative region of overlap and the number of region involved; the break occurs predominantly in 6q21, but 6q15 is also often described; overall, del(6q) cases encompassed the 6q21 band.

In acute lymphoblastic leukemia (ALL), del(6q) is the sole anomaly in about 30% of cases, or associated with other structural abnormalities such as del(12p) (early pre-B ALL), del(9p) (B and T-cell immunophenotype), specific aberrations, such as t(4;11), t(1;19), t(9;22), t(12;21) or with random chromosomal changes.

Genes involved and proteins

Note
6q21 band loss suggests the presence of a recessive tumour suppressor gene whose absence might contribute to malignant transformation and development of both T and precursor B-ALLs; the lack of specificity for a particular immunophenotype may imply that the gene or genes affected by 6q abnormalities are broadly active in the multistep process of lymphoid leukemogenesis.

Putative tumour suppressor gene(s) on chromosome arm 6q remains to be identified; to demonstrate this loss of heterozygosity of informative markers (LOH) was analysed using PCR amplification of polymorphic microsatellite sequences; using polymorphic markers located from the 6q14-15 to telomere, LOH was detected in 5 to 25% of childhood ALL cases.

Regarding LOH results, two distinct regions were identified:
- first region flanked by D6S283 and D6S302 loci at 6q21-22
- second region flanked by D6S275 and D6S283 loci at 6q21.

Using LOH analysis on several cases, the authors demonstrated an identical 6q21-22 structure at diagnosis and at relapse, suggesting that 6q deletion may be an initial event in leukemogenesis and may occur less frequently during progression of the disease.

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