Leukaemia Section
Mini Review

+18 or trisomy 18 in lymphoproliferative disorders

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Clinics and pathology

Note
Trisomy 18 seen with other abnormalities is fairly nonspecific, having been reported in most lymphoproliferative disorders. Trisomy 18 as a sole abnormality is also nonspecific, having been reported in MDS, AML, ALL (14 cases), lymphoma (3 of 6 reported cases were follicular lymphoma), Hodgkin’s disease (two cases) and CLL (10 cases).

Disease
Acute lymphocytic leukemia (ALL)

Note
Trisomy 18 is common in hyperdiploid ALL with more than 50 chromosomes (15-27% of cases). The great majority of karyotypes with trisomy 18 also exhibit trisomy 4, 6, 10, and 14, either trisomy 21 or tetrasomy 21, and an extra X chromosome. More than half either have trisomy 17 or an isochromosome 17q. It is unusual to see trisomy 18 in a hyperdiploid ALL with fewer than 50 chromo-somes. It is likewise unusual to find trisomy 18 associated with one of the common structural changes in ALL, such as the t(1;19). However, at least two hyperdiploid ALL cases have been reported with trisomy 18 and tetrasomy 21 in which a t(12;21) was detected by FISH analysis; further research is indicated.

Epidemiology
Of 14 reported ALL cases with trisomy 18 as the sole cytogenetic abnormality, nine were reported from India. Is there an environmental component to this unusual distribution of cases?

Prognosis
The prognosis appears to be neutral to favorable in a karyotype with >51 chromosomes that includes trisomy 18. There is some evidence of an unfavorable prognosis if the karyotype is isolate trisomy 18.

Disease
Multiple myeloma.

Note
Trisomy 18 is observed in roughly 10% or multiple myeloma (MM) karyotypes. In MM with trisomy 18, the karyotype is usually hyperdiploid (49-60 chromosomes) with multiple trisomies, tetrasomies, and structural abnormalities. The most common structural anomalies that appear with trisomy 18 are chromosome 1 rearrangements (30%) and 14q32 rearrangements (25%) about half of which are t(11;14). The most common trisomies (25-35%) are: +3, +5, +6, +9, +11, and +15, with less frequent (10-20%) trisomy 1, 10, 14, and 17, and monosomy 8.

Prognosis
No correlation between trisomy 18 and prognosis.

Disease
Hodgkin’s disease

Note
Trisomy 18 in Hodgkin’s disease has been reported in a few quite complex near-triploid karyotypes (59-83 chromosomes, and in hyperdiploid karyotypes with simple trisomies and only an occasional chromosome rearrangement. Among these latter cases are two with isolated trisomy 18, and others with up to 52 chromosomes and common recurrence of trisomies 2, 7, 12, and 21.

Cytology
The Hodgkin’s disease cases with trisomy 18 have included both the mixed cellularity and the nodular sclerosis types.
Disease
Chronic lymphocytic leukemia

Note
Trisomy 18 is very uncommon in CLL. When observed, it usually presents as the sole abnormality, or with a karyotype of 49, +12, +18, +19. The karyotype is occasionally more complex.

Epidemiology
Of CLL cases reported with trisomy 18, about 15% exhibited apparently independent cytogenetically abnormal cell populations, with isolated trisomy 18 as one of two, three, or more clones. The clinical significance of these clones is not understood.

Disease
Non-Hodgkin’s lymphoma

Note
Trisomy 18 is observed in 15-33% of lymphomas, including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and marginal zone B-cell lymphoma (MZBCL). Trisomy 18 may be less frequent in other NHL sub-types.

Trisomy 18 is strongly associated with a t(14;18) or at least a 14q32 abnormality, and may represent a variant of the +der(18)(t(14;18), which duplicates the segment 18pter-18q21. Trisomy 18 is rarely observed as the primary cytogenetic change in NHL.

In DLBCL, the karyotype with trisomy 18 is usually hyper-diploid with 47-52 chromosomes and with multiple chromosome rearrangements. Trisomy 3 accompanies trisomy 18 in about 30% of cases, and trisomies 7, 12, and 21 in about 10% each. About 10% have a t(14;18) or +der(18)(t(14;18), about 5% have a t(8;14), and another 10% have another 14q32 rearrangement. About 20% have a 6q rearrangement or an i(6)(p10) that results in loss of 6q, and about 20% have an extra X chromosome, many of which are structurally abnormal.

In FL, the general cytogenetic pattern of cases with trisomy 18 is similar to that of DLBCL. The principle difference is that about 75% of cases exhibit a t(14;18) or an add(14)(q32), and associa-tion of trisomy 18 and a t(8;14) is very uncommon.

Trisomy 18 is a recurrent finding in MZBCL, seen in 39% of cases in one study. About a third of marginal zone lymphomas with trisomy 3 also exhibit trisomy 18.

About 10% of peripheral T-cell lymphomas exhibit trisomy 18, and then usually as part of a fairly complex karyotype.

Phenotype/cell stem origin
Overexpression of BCL2 has been reported in trisomy 18 without t(14;18). CGH studies suggest duplication 18q (which would include trisomy 18) tend to occur early in the cytogenetic evolution. In FL, 18q gains were most common in young males and occurred with similar frequency in FL with and without t(14;18).

Prognosis
Trisomy 18 as a secondary abnormality in NHL has no significant influence on tumor grade or overall survival.

References


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