High hyperdiploid acute lymphoblastic leukaemia

Barbara Gibbons

NE London Regional Cytogenetics Laboratory 2nd Floor, Queen Square House Institute of Neurology Queen Square London WC1N 3BG, UK (BG)

Clinics and pathology

Disease
Acute lymphoblastic leukaemia (ALL)

Phenotype/cell stem origin
c-ALL or early pre-B immunophenotype.

Epidemiology
This type of leukaemia is most common in children (20-30% of childhood ALL), peaking at 3-5 years although it is rare in infants and has a low incidence in adults (5% of adult ALL); excess of females.

Clinics
High hyperdiploidy is associated with a low white cell count, and FAB type L1 or L2.

Prognosis
Prognosis for children is good with long term survival of 70%-80%; adults do less well although event free survival of 59% at 3 years has been reported; the good prognosis is thought to be related to leukaemic cell sensitivity to a number of anti-leukaemic drugs and the propensity of cells to respond by apoptosis; it is unclear why a proportion of patients fail to achieve long term remission but there is evidence that higher chromosome counts of >56 chromosomes and the presence of trisomies 4 and 10 may be associated with a good prognosis whereas the presence of i(17q) is clearly associated with a poor prognosis.

Cytogenetics

Note
The hyperdiploid karyotype is thought to arise from a single step mechanism; maintenance of heterozygosity has been demonstrated suggesting that the hyperdiploidy does not arise from a near haploid precursor.

Cytogenetics morphological
Patients with hyperdiploidy of >50 chromosomes have clones of 51-68 chromosomes; although high hyperdiploid clones are rarely identical, they tend to show a pattern of chromosome gain with extra copies of chromosomes 4, 6, 10, 14, 18 and 21; the gains, apart from chromosome 21, more often result in trisomy rather than tetrasomy for the gained chromosomes.

Cytogenetics molecular
High hyperdiploidy can be detected by application of a panel of probes which will detect the characteristic pattern of gain; this technique can be applied to interphase blasts but care must be exercised in interpretation and the non-random translocations such as t(9;22), t(1;19), t(12;21) and t(4;11) should be excluded by application of appropriate probes.

Additional anomalies
Translocations and other structural chromosome abnormalities are present in approximately half of high hyperdiploid cases; duplication 1q is the most common additional change; duplication of 1q, deletion of 6q and random structural abnormalities have no known prognostic impact; however, the presence of non-random translocations such as t(9;22), t(4;11), t(1;19) and t(12;21) indicate that the translocation is most likely the primary change and that the hyperdiploidy is probably a secondary event; in such cases the leukaemia should be classified according to the translocation rather than the ploidy group in order to assign the correct prognostic implications.
References


This article should be referenced as such: