The significance of sex chromosome loss as the only karyotype anomaly in hematological disorders has not been clearly established yet. The hypotheses and questions regarding this abnormal karyotype began in 1960s. From that time several studies have supported the theory that ‘Y’ loss is a nonphenotypic event associated with aging process in males.1-4 But, on the contrary some other studies have also shown that age is not clearly related and the X and Y chromosomes that are lost reappeared after therapy and during clinical remission. The question arises of whether there is a primary neoplastic event which precipitated the ‘Y’ loss or loss of X.7 There is one article in this issue (Bakshi et al) which states that the loss of sex chromosome is not related to age but related to the acute stage of the disease. The authors have shown that out of 270 patients of acute myeloid leukemia (AML) 22 patients had loss of sex chromosomes at the time of diagnosis. Six out of 22 patients have loss of ‘X’ chromosome and the rest sixteen had loss of ‘Y’ Chromosome. Fifty percent of these 22 patients were below the age of 14 years. Therefore, it supports the hypothesis that the loss of sex chromosome is due to evolution of malignant clone. But in which way it has influenced the malignant process is difficult to say. Loss of Y chromosome is frequently observed in myeloproliferative diseases, myelodysplastic syndromes (MDS) and ANLL and can also be seen in lymphoproliferative disorders like lymphomas. The pattern of X loss is more striking in bonemarrow aspirate karyotypes than PHA stimulated lymphocyte studies. Subjects with no evidence of disease rarely exhibit more than 75% of cells with 45X, -Y. Thus if fewer than 75% of metaphase cells are -Y, the disease association is uncertain. However, if 75-100% of metaphase cells are -Y, the karyotype probably is disease – associated even in older men. Chromosome rearrangements involving the Y chromosomes are rare in cancer and leukemias. Loss of Y chromosomes in contrast is a common secondary change in cancer cells and in a few leukemias.

In association with t(9:22) in CML and with t(8:21) in FAB M2 ANLL, loss of Y chromosome is generally considered a secondary event of non added clinical significance. Speculatively loss of the Y could provide a proliferative advantage, simply because it tends to replicate late in ‘S’ phase. Its loss might therefore shorten the cell cycle slightly.

Loss of X chromosome is very rare. Carolyn et al reported loss of X chromosome in the bonemarrow as the sole abnormality in a 53 year old woman in one ANLL case. After therapy there was complete reappearance of the X chromosome. Therefore, the possibility exists that an event of submicroscopic nature may underlie all the conditions like MDS, myeloproliferative diseases, leukemias, lymphomas in which case the chromosomal changes would be of secondary, though critical. The chromosomal instability in the genome may be responsible for this secondary event which can be investigated using comparative genomic hybridisation (CGH).

References


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**Announcement**

The editorial board of the Indian Journal of Human Genetics is pleased to inform its reader that the journal is now indexed with Excerpta Medica/EMBASE, Netherlands and INIST, France.