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Leukaemia Section
Mini Review

1q rearrangements in multiple myeloma

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Clinics and pathology

Disease

Multiple myeloma (MM) is a malignant plasma cell proliferation (chronic lymphoproliferative disorder).

Phenotype / cell stem origin

Phenotype of mature differentiated B-cell, but also with CD56 expression, which origin is not found in normal plasma cell; CD38+, CD40+, CD138+.

Etiology

Differents factors like cytotoxic drugs, ionizing radiation or oncogenic viruses are suspected to induce decondensation of pericentric heterochromatin, which, in turn, favours the formation of triradials, giving rise to 1q extra copies; such could be the case during evolution of multiple myeloma.

Epidemiology

Multiple myeloma's annual incidence: $30/10^6$; mean age: 62 yrs; rearrangements of chromosome 1q are one of the most frequent structural abnormalitie in MM (16-26% of abnormal cases), but always as a secondary change.

Clinics

Bone pain; susceptibility to infections; renal failure; neurologic dysfunctions.

Pathology

MM staging:
- stage I: low tumour cell mass; normal Hb; low serum calcium; no bone lesion; low monoclonal Ig rate;
- stage II: fitting neither stage I nor stage II;
- stage III: high tumour cell mass; low Hb and/or high serum calcium and/or advanced lytic bone lesions and/or high monoclonal Ig rate.

Evolution

Multiple myeloma can evolve towards plasma cell leukemia.

Prognosis

Prognosis (highly variable) is according to the staging and other parameters, of which are now the karyotypic findings (see below).

Cytogenetics

Cytogenetics, morphological

Duplication of all or part of 1q chromosome and whole arm translocation of 1q can result from unbalanced derivative translocation chromosomes, isochromosomes, or jumping translocations; these structural rearrangements are reported as secondary aberrations and associated with tumour progression and advanced disease.

1q has been found translocated with telomeres from differents chromosomes partners: 8pter, 9pter, 12qter, 13pter, 15pter, 17qter, 19pter, 19qter, 21pter, 22pter; whole-arm centromere to centromere translocations occurred most frequently between 16p and 1q; the observation that extra copies of 1q occur in patients with decondensation of centromeric heterochromatin suggests that hypomethylation of this region may play a role in the somatic pairing, fragility and formation of triradial configurations involving the long arm of chromosome 1.

Genes involved and Proteins

Note: the observation of extra copies of 1q suggests a (low-level) gene amplification of genes related to MM biology: the interleukin 6 (IL-6) signaling pathway may possibly be affected by the amplification of the 1q21 region, which is the site of IL-6RA; other genes of interest in this region include C-reactive protein (CRP) and amyloid P component (APCS), both localized to 1q21-23, and pre-B cell leukemia transcription factor 1 (PBX1) in 1q23.

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