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Short Communication

i(3)(q10) in non-Hodgkin's lymphoma (NHL)

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Abstract

Partial or complete chromosome 3 gains resulting from the presence of trisomy 3, unbalanced translocation or isochromosome formation has been observed in different types of non-Hodgkin's lymphomas (NHL). Among them, the isochromosome of the long arm of chromosome 3 is a relatively rare chromosome aberration, associated mainly with B-cell NHL. However, its occurrence is not restricted to lymphomas, as the detection of +i(3)(q10) is considered a specific marker of polyclonal B-cell lymphocytosis with binucleated lymphocytes (PPBL) associated with an increase frequency of chromosome 3 instability as well as it may also be found in myeloid malignancies.

Keywords
chromosome 3; B-cell lymphomas; T-cell lymphomas

Clinics and pathology

Disease

B-cell non-Hodgkin's lymphoma and less frequently T-cell lymphomas.

Phenotype/cell stem origin

Patients had various forms of lymphomas:
Mature B-cell lymphomas in 20: 4 follicular lymphoma (FL) (Yunis et al .,1987; Ueda et al., 1997; Horsman et al., 2001; Bosga-Bouwer et al., 2003), 4 diffuse large B-cell lymphoma (DLBCL) (Poppe et al., 2005; Yoshioka et al., 2005; Chapiro et al., 2008; Arayan et al., 2013), 3 mantle cell lymphoma ID: 2062> (MCL) (Martinez-Climent et al., 2001; Au et al., 2002; Nagel et al .,2010), 3 chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) (Specchia et al., 2002; Wong et al., 2002; Struski et al., 2007), 1 splenic marginal zone B-cell lymphoma (Gazzo et al., 2007), 1 nodal marginal zone B-cell lymphoma (Chapiro et al., 2008), 1 Waldenström macroglobulinemia (Wong et al., 1995) and 3 mature B-cell neoplasms (Sandberg et al., 1984; Bloomfield et al., 1983; Hashimoto et al., 1995).
Mature T-cell lymphomas in 3: 2 angioimmunoblastic T-cell lymphoma (Lepretre et al., 2000; Temple et al., 2004) and 1 peripheral T-cell lymphoma, unspecified (Nelson et al., 2008).

Epidemiology

23 patients (male prevalence; 15 males, 8 females aged 52 to 83 years; median 64 years).

Prognosis

Gain of 3q in complex karyotypes reflects genomic instability and patients may show a more aggressive course of the disease and poor response to chemotherapy.

Cytogenetics

FISH using a probe specific for 3q such as the probe for BCL6 is recommended for the confirmation of 3q trisomy in complex karyotypes. Moreover, as the method is more sensitive than conventional cytogenetics, it allows for the study of non-dividing cells in lymphomas.

Cytogenetics morphological

Presents as 1 normal chromosome 3 and a i(3)(q10) chromosome replacing a normal chromosome 3, leading to trisomy 3q and monosomy 3p in 13 patients and presents as 2 normal chromosomes 3 and an extra +i(3)(q10) resulting in disomy 3p and 3q tetrasomy in 10.

Additional anomalies

Found as a part of simple karyotypes associated with +18 in 2 CLL and in a Waldenstrom macroglobulinemia patient and part of complex or highly complex rearrangements in the remaining patients. Characteristic chromosomal abnormalities associated with particular subtypes such as 14q rearrangements were found in 9 patients with B-cell NHL, among them the t(14;19)(q32;q13) was detected in 2, t(3;14)(q27;q32) in 2, t(14;18)(q32;q21) in 1, t(9;14)(p13;q32) in 1 and t(11;14)(q13;q32) in 3 patients with mantle cell lymphoma.

Result of the chromosomal anomaly

Fusion protein

Oncogenesis

Isochromosome i(3)(q10) represents a rare but recurrent abnormality in NHL, particularly in B-cell lineage lymphomas. The formation of i(3)(q10) results in a duplication of its long arm, leading to genomic imbalances in a copy number-dependent manner. Commonly overrepresented segments in complete or partial trisomies of 3q include the q21-23 region and the q25-29 region, however the gene(s) involved in pathogenesis are not known. Candidate genes on 3q may include BCL6 located on 3q27.3, MECOM on 3q26.2, SIAH2 on 3q25.1, PIK3CA on 3q26.32, PAK2 on 3q29 and the ATR gene located on 3q23. Deregulation of these genes could contribute to a possible proliferative advantage of the cells. i(3)(q10) is frequently part of a complex karyotype, therefore may be considered a secondary event. The appearance of i(3)(q10) might be related to chromosomal and genomic instability (Troussard et al., 2008) that may play a role in the emergence of a clonal and/or malignant subpopulation in NHL as a part of a multi-step process.

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