Complete or partial trisomy 3 in gastro-intestinal MALT lymphomas co-occurs with aberrations at 18q21 and correlates with advanced disease stage: A study on 25 cases

Jens Krugmann, Alexandar Tzankov, Stephan Dimhofer, Falko Fend, Dominik Wolf, Reiner Siebert, Pensiri Probst, Martin Erdel

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TO THE EDITOR

Taji et al[3] have reported in their study on 13 patients with gastric mucosa-associated lymphoid tissue (MALT) lymphomas an aggressive tumor course in trisomy 3 positive cases. The authors analyzed only stage I patients with classical low-grade marginal zone lymphoma of the MALT type and detected the trisomy 3 using an alpha-satellite DNA probe directed to the centromere. Their data support the observation that trisomy 3 is the most frequent cytogenetic aberration in MALT lymphomas[2,3]. In our previous published series[4] of 29 surgically resected gastrointestinal (GI) (11;18) negative MALT lymphomas, we have described an adverse prognostic impact of trisomy 18q21 detected by a MALT1-specific fluorescence in situ hybridization (FISH) probe, especially in the lymphomas with high grade component. We have additionally studied 25 of the previously reported GI lymphomas including 7 low grade marginal zone lymphomas and 18 GI diffuse large B-cell lymphomas (DLBCL, including 3 cases with low grade lymphoma component) diagnosed in stage I (n = 8) and in stage >II (n = 17) for complete and partial trisomies 3 using FISH probes for the centromere of chromosome 3 (Vysis, Downer's Groove, IL, USA) as well as for the BCL6 gene at 3q27 (flanking BAC clones RP11-528E8 and 690C8)[5]. The latter double-color assay was selected because it targets the critically gained band of chromosome 3 in MALT lymphomas and can detect breakpoints affecting the BCL6 locus, which are recurrent in extranodal DLBCL. For each hybridization, we evaluated 100 cell nuclei. The cut-off level, defined as mean false positive rate (determined in normal gastric mucosa and samples from Helicobacter pylori gastritis) plus three standard deviations, was 5.4% for the centromere 3 probe (trisomy). For the BCL6 probe mix no split or gain of signals was observed in the control samples, but according to the literature, the cut-off level for the detection of trisomy 3q27 or BCL6 breaks was set to 3%[6].

In agreement with the previously published studies, we detected trisomy 3q27 as the most frequent aberration in GI MALT lymphomas, occurring in 9/25 (36%) of the cases. In three of these nine cases, trisomy 3 was indicated by the presence of supernumerary signals for both the centromeric region and the BCL6 gene locus, whereas in the remaining six cases, a gain of 3q27/BCL6 was detected without a change in the number of centromere signals (partial trisomy 3q27). The only positive stage I lymphoma showed a partial trisomy 3q27. In three cases of the DLBCL subset, one with trisomy 3 and two with partial trisomy 3q27, a separation of the BCL6 signal pair was additionally detected indicating both a BCL6 translocation (two cases potentially with BCL6/IGH rearrangement) and overrepresentation of proximal/distal 3q27.

Trisomies 3q27 were present in 1/8 (13%) stage I and 8/17 (47%) stage >II diseases indicating a significant (P<0.01; χ² test) association of trisomy 3q27 with...
lymphoma dissemination. There was a strong correlation between the occurrence of trisomies 18q21/MALT1 and 3q27/BCL6 in the present series of GI MALT lymphomas with 5/6 (83%) 18q21 positive tumors carrying both aberration and only 1/6 (17%) case showing trisomy 18q21 without trisomy 3q27 (P<0.05). We have previously reported that trisomy 18q21/MALT1 to be associated with an unfavorable prognosis in the same series of surgically resected GI MALT lymphomas, which was particularly pronounced in the DLBCL subset[4]. With regard to trisomy 3q27, we observed a trend towards an inferior survival too, P = 0.0727.

Our data highlight that partial trisomies of chromosomes 3 and 18 have to be taken into account when evaluating the course of GI MALT lymphomas. Roughly two-thirds of the gains on the respective chromosomes might not include the centromeric region. Moreover, the co-occurrence of trisomies 3q27 and 18q21 in our group of surgically resected GI MALT lymphomas points to a possible interaction of both loci, especially in patients with an advanced stage disease.

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