Interphase fluorescence in situ hybridization identifies chromosomal abnormalities in plasma cells from patients with monoclonal gammopathy of undetermined significance


Karyotypic studies in patients with monoclonal gammopathy of undetermined significance (MGUS) have been hampered by a low percentage of bone marrow plasma cells (BMPC), which are predominantly nonproliferating. By combining cytomorphology and interphase fluorescence in situ hybridization (FISH) we investigated whether or not chromosomal abnormalities occur in BMPC from patients with MGUS. Studying chromosomes 3, 7, 11, and 18, which we found to be frequently aneuploid by FISH in multiple myeloma (MM), we observed three hybridization signals for one of these chromosomes 3 were most common, occurring in 38.9% of patients, followed by gains of chromosomes 11 (25%), 7 (16.7%), and 18 (5.6%) Among BMPC, the frequency of aneuploid cells was 18.9% +/- 13.9% (mean +/- SD) for chromosome 3, 22.3% +/- 9.2% for chromosome 11, 23.2% +/- 22.0% for chromosome 7, and 6.1% +/- 2.3% for chromosome 18. In five patients, chromosomal abnormalities were shown to be restricted to BMPC expressing cytoplasmic immunoglobulins corresponding to the serum paraprotein. No gain of hybridization signals was observed in normal and reactive plasma cells. In one patient with MGUS, metaphase cytogenetics revealed one abnormal metaphase with 47, XY, +4, and trisomy 4 was also demonstrated in a subpopulation of BMPC by interphase FISH. FISH results from patients with MGUS and newly diagnosed MM at stage IA (n = 14) indicated that aberrations involving > or = 2 chromosomes occurred significantly more often in early stage MM (P < .01). With respect to clinical and laboratory features, MGUS patients with and without chromosomal abnormalities were indistinguishable. Our results indicate that MGUS already has the chromosomal characteristics of a plasma cell malignancy.

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