Presence of cytogenetic abnormalities in Spitz naevi: a diagnostic challenge for fluorescence in-situ hybridization analysis

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Aims: Spitz naevi are difficult to diagnose, because of significant overlap with melanomas. It has been recently demonstrated that the LSI RREB1(6p25)/LSI MYB(6q23)/LSI CCND1(11q13)/CEP6 fluorescence in-situ hybridization (FISH) assay is a reliable tool with which to distinguish benign naevi and melanomas. Little is known about its diagnostic usefulness in Spitz naevi.

Methods and results: We investigated 51 patients with Spitz naevi and long-term median follow-up (8.18 years) with the multicolour FISH probe. Control groups included 11 benign naevi and 14 melanomas. Spitz naevi from 32 (63%) patients did not show cytogenetic abnormalities (FISH−). In contrast, Spitz naevi from 19 (37%) patients showed changes in the investigated loci (FISH+). Spitz naevi with the FISH+ profile showed chromosome X polysomy in 14/18 (78%) patients. All Spitz naevi with the FISH− profile were disomic. All melanomas displayed a FISH+ profile, and 4/11 (36%) showed chromosome X polysomy. No differences in clinicopathological features were detected between Spitz naevi with and without genetic abnormalities.

Conclusions: The presence of gene copy number changes in Spitz naevi as detected by FISH is higher than expected, and Spitz naevi at the genetic level represent a heterogeneous group. The findings of similar cytogenetic alterations in Spitz naevi and melanomas suggest that there should be cautious interpretation of FISH analysis in this setting.

Keywords: fluorescence in-situ hybridization, polysomy, Spitz naevus

Abbreviations: CEP6, centromere of chromosome 6; CGH, comparative genomic hybridization; FISH, fluorescence in-situ hybridization

Introduction

Spitz naevi are benign melanocytic lesions that share many histological features with melanomas. These similarities raise uncertainty regarding their biological potential, and make differential diagnosis a common problem in dermatopathology. Previous studies have demonstrated that Spitz naevi and melanomas display different, non-overlapping genetic patterns of aberration. The most frequently found alterations in primary melanomas (i.e. losses in 9p, 10q and 6q, and gains in 7p, 8q, 6p and 1q) are absent in Spitz naevi, which are generally characterized by a normal chromosomal complement, with the exception of a subgroup distinguished by extra copies of chromosome 11p. On the basis of this evidence, a new fluorescence in-situ hybridization (FISH) assay targeting 6p25 (RREB1), 6q23 (MYB), 11q13 (CCND1) and centromere of chromosome 6 (CEP6) has been developed. Despite some differences in interpretation criteria (i.e. different cut-off values to define FISH-positive cases), many authors have recently demonstrated that the FISH strategy is a reliable tool for the following: (i) assisting in differentiating benign from malignant