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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