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Title: Mutation of *C-kit* in high-risk gastrointestinal stromal tumors and its correlation with prognosis: report of 32 cases

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摘要: 目的 分析高危型胃肠道间质瘤(gastrointestinal stromal tumor, GIST)的临床病理特征,探讨相同侵袭危险度GIST生物学行为的可能影响因素。方法 收集我科2008年1月至2010年12月高危型GIST患者32例进行CD117、CD34、DOG1、Ki67和P16免疫组化染色及石蜡切片DNA抽提,PCR扩增-直接测序,观察其临床病理特征,分析不同基因型、表现型及与肿瘤复发和转移的关系。结果 32例高危型GIST中梭形细胞型20例,上皮样/混合细胞型12例,随着发病部位不同组织形态略有不同。24/32例(75%)患者具有C-kit基因突变,9例为exon11区包含codon557-558位点缺失;3例为exon9突变。获得随访资料的21例患者中有17例检测到C-kit基因突变,上皮样/混合细胞型有8例,其中6例发生肿瘤复发/死亡。发生肿瘤复发/死亡者其核分裂象数和P16蛋白过表达例数明显高于肿瘤无进展者,差别有显著性。结论 高危型GIST是一组异质性肿瘤,联合基因型与表现型特点评估处于同一级别GIST的预后有实际意义,P16蛋白过表达可能是高危型GIST预后不佳的因素之一。

Abstract: Objective To analyze the clinicopathological characteristics of high-risk gastrointestinal stromal tumor (GIST) and discuss the probable prognostic factors in GIST with the same malignant risk. Methods The expression of CD117, CD34, DOG1, Ki67 and P16 were detected by immunohistochemical assay in the tissue samples from 32 patients with high-risk GISTs admitted in our hospital during January 2008 to December 2010. Mutation of *C-kit* gene was tested by

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PCR-direct sequencing. The clinicopathologic, immunohistochemical and mutation results were analyzed. The correlation was analyzed between the clinical outcomes of GISTs and the different genotypes and phenotypes of *C-kit*. **Results** There were 20 cases of pure spindled phenotype and 12 cases of epithelioid/mixed phenotype. The histomorphology of GISTs was different with various anatomic sites. *C-kit* mutation was detected in 24 cases (75%), including loss of codon (557-558) in exon 11 in 9 cases, and mutations in exon 9 in 3 cases. Among the 21 cases with available follow-up data, there were 17 cases found with *C-kit* mutation, 8 cases of epithelioid/mixed phenotype, and 6 cases died or recurred. The mitosis count and the expression of P16 were significantly greater in the cases of dead/tumor-recurrence patients than the patients with non-progression. **Conclusion** High-risk GISTs are tumor with heterogeneity. Comprehensive evaluation of phenotype and genotype is of great significance for clinical practice for GISTs at the same risk. Overexpression of P16 might be a negative prognostic factor.

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