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肿瘤防治

原发性与继发性胶质母细胞瘤中MGMT与突变型P53蛋白表达的差异及其生物学意义

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摘要 背景与目的： 探讨O6-甲基鸟嘌呤-DNA甲基转移酶(O6-methylguanina-DNA methyltransferase, MGMT)与突变型P53蛋白在原发性与继发性胶质母细胞瘤(glioblastoma, GBM)中表达的差异性及其生物学意义。 材料与方法： 应用免疫组织化学法检测39例GBM(原发性组13例和继发性组26例)中MGMT与突变型P53蛋白的表达，比较两者在原发性与继发性GBM中的表达差异；分析MGMT与突变型 P53蛋白表达的相关性及其与预后的关系。 结果： 原发性和继发性GBM间突变型 P53蛋白的阳性表达率和表达强度差异均有统计学意义(P均<0.01)。继发性GBM中MGMT的阳性表达强度降低而突变型 P53蛋白的表达强度明显增强(P<0.01)，两者表达呈负相关(r=-0.602,P<0.01)。原发性GBM中MGMT的表达与突变型 P53蛋白的表达无关(P>0.05)。Kaplan-Meier生存分析结果显示：原发性GBM和MGMT高表达患者的生存时间缩短(Log-rank检验，P<0.05或P<0.01)。Cox多因素相关分析表明GBM的分型和MGMT的阳性表达是影响患者生存期的独立预后因素(分别为P<0.05和P<0.01)。 结论: P53基因突变是继发性GBM的发生过程中的高发事件，突变型P53蛋白的表达强度增强与MGMT表达减弱有关。而原发性GBM中MGMT的表达与突变型 P53蛋白的表达无关。提示原发性和继发性GBM在发生、发展的过程中有着不同的分子遗传学途径。GBM的分型、MGMT的阳性表达是影响GBM患者生存期的独立预后因素。

关键词 胶质母细胞瘤； p53基因； MGMT

Differences of MGMT and Mutant P53 Protein Expression between Primary and Secondary Glioblastomas and the Biological Implications

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Abstract BACKGROUND AND AIM: To study the expression differences of O6-methulguanine-DNA methyltransferase (MGMT) and mutant P53 protein between primary and secondary glioblastomas(GBM) and the biological implications. MATERIALS AND METHODS: Immunohistochemistry(IHC) methods was used to measure the expressions of MGMT and mutant P53 protein in 39 cases of GBM(13 primary and 26 secondary),and the correlation with prognosis. The relationship between these gene expressions in primary and secondary GBM were analyzed. RESULTS: The differences of positive rate and expression intensity of mutant P53 protein expression were statistically signifiant between primary and secondary GBM (P<0.01； P<0.01 ,respectively). Moreover, there was an inverse correlation between MGMT and mutant P53 protein expression intensity in secondary GBM(r=-0.602, P<0.01).but in primary GBM, there is no correlation between MGMT and mutant P53 protein expression(P>0.05).Kaplan-Meier analysis revealed that primary GBM and high expression of MGMT were significantly related to short survival(Log-rank test， P<0.05,P<0.01, respectively).Cox multivariate analysis revealed that subtype of GBM and MGMT expression were prognosticators for GBM(P<0.05, P<0.01, respectively). The survival period of GBM patients was not associated with age,gender,tumour size or mutant P53 protein expression. CONCLUSION: P53 gene mutations was frequent in tumorigenesis of secondary GBM,and the strong mutant P53 protein expression might be related to the weak MGMT expression. But in

primary GBM, there is no correlation between MGMT and mutant P53 protein expression.It implicates different genetic pathways of developing in primary and secondary GBM. The subtype of GBM and MGMT expression were prognosticators for GBM.

Keywords Glioblastoma p53 gene MGMT

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