Surviving Gene Polymorphism and Serum Survivin Levels in Patients with Brain Tumors

Didem Kafadar; Ilhan Yaylim BS, PhD; Ali Metin Kafadar As.Prof. MD.; Canan Cacina; Arzu Ergen; Mehmet Yasar Kaynar MD; Turgay Isbir

Istanbul University Institute of Experimental Medicine Molecular Medicine Department

Istanbul University Cerrahpasa Medical Faculty Neurosurgery Department

Introduction

Survivin, has a key role in in the regulation of apoptosis and cell division, is one of the apoptosis inhibitor family(IAP) proteins. A single nucleotide polymorphism -31C/G was identified in the promoter region of the survivin gene seemed to be associated with over-expression of survivin protein and changed transcription in various cancer cell lines. Our aim was to investigate whether survivin gene polymorphism can be accepted as a marker of tumor risk and progression in patients with benign and malign brain tumors and if the polymorphism affects survivin serum levels.

Methods

Survivin promoter -31C/G polymorphism was genotyped by a polymerase chain recation-restriction fragment length polymorphism (PCR-RFLP) assay analysis in 82 patients with intracranial primary tumors and 65 healthy controls.

Results

There were no differences in the distribution of survivin promotor -31C>G genotypes and alleles between patients with primary brain tumours and controls. Serum survivin levels in patients with malign tumors were significantly higher than those in patients with benign tumors ($p<0.001$) and survivin levels in patients with malign glial tumors who have survivin promotor -31GG genotype were significantly higher than those in controls ($p=0.05$) and benign tumors ($p=0.04$).Patients with malign nonglial tumors carrying C allele were significantly higher than the control group.C allele frequency of the -31C/G gene polymorphism in patients with meningeal tumors diagnosed younger than 45 years was significantly higher than patients over 45. In GBM patients under 45, GG genotype was significantly higher than patients over 45.

Conclusions

We suggest that survivin Promotor -31C>G polymorphism may be as a marker of tumour risk and progression in primary brain tumors. C allele frequency is found significantly higher in various cancers in certain studies.According to our results C allele may be associated with malign nonglial tumors and young onset of meningeal origin tumors.Being under 45 at diagnosis is reported to be associated with prognosis which is consistent with our results. G allele may be associated with young onset of malign glial tumors. The patients should be followed for more precise results about prognosis and genotype relationship and the study must be verified in larger patient groups.

Learning Objectives

1)Describe the importance of survivin polymorphism.
2 Discuss serum levels and polymorphism of survivin in benign and malign brain tumors.
3)Discuss whether survivin may be a tumor therapy target.

References

1. Xu Y, Fang F, Ludewig G,ve ark. A mutation found in the promoter region of the human survivin gene is correlated to overexpression of survivin in cancer cells. DNA Cell Biol 2004;23:527-37.
2.Gazouli M, Tzanakis N, Rallis G, Theodoropoulos G, Papaconstantinou I, Kostakis A, Anagnou NP, Nikiteas N. Survivin -31G/C promoter polymorphism and sporadic colorectal cancer. Int J Colorectal Dis. 2009;24(2):145-50.
3.Cheng ZJ, Hu LH, Huang SJ. Correlation of -31G/C polymorphisms of survivin promoter to tumorigenesis of gastric carcinoma. Ai Zheng. 2008;27(3):258-63.
4. Jang JS, Kim KM, Kang KH, Choi JE, Lee WK, Kim CH, Kang YM, Kam S, KimIS, Jun JE, Jung TH, Park JY. Polymorphisms in the survivin gene and the risk of lung cancer. Lung Cancer. 2008;60(1):31-9.
5.Salmon I, Dewitte O, Pasteels JL ve ark.: Prognostic scoring in adult astrocytic tumors using patient age, histopathological grade, and DNA histogram type. J Neurosurg 1994;80: 877–883.