同位素　2007 20 (1): 36-41　ISSN: 1000-7512　CN: 11-2566/TL

研究简报

单次化疗后肿瘤内$^{99}Tc^{m}$-Annexin Ⅴ的分布与bcl-2、bax

张欣

大连医科大学附属第一医院核医学科

收稿日期 2006-7-19 修回日期 2006-12-26 网络版发布日期: 2007-4-11

摘要　目的 评价应用^{99}Tcm-rh-AnnexinⅤ显像检测单次化疗后肿瘤细胞凋亡的可行性，并探讨其在肿瘤组织内的分布与凋亡调控蛋白bcl-2、bax表达的相关性。方法 采用直接标记法标记rh-AnnexinⅤ作为核素凋亡显像示踪剂。将小鼠肝癌细胞（Hca-F25）接种于小鼠右腋下部位；随机分为A（n=9，对照组）、B（n=10，化疗组）两组，8d后肿瘤生长至直径约1cm时，B组一次性接受环磷酰胺（cyclophosphamide）腹腔内注射，剂量为150mg/kg；20h后两组同时由鼠尾静脉注入99Tcm-rh-AnnexinⅤ；4h后行SPECT显像并处死、取材，应用井型闪烁探测器检测荷瘤小鼠肿瘤组织内示踪剂分布，以%ID/g（每克组织百分注射剂量率）表示。采用TUNEL法检测肿瘤细胞凋亡；采用采用免疫组化SP法检测标本中bcl-2、bax蛋白表达。结果 单次化疗后B组肿瘤组织的%ID/g、TUNEL检测阳性细胞数及bax蛋白表达均明显多于A组（P<0.01）；bcl-2蛋白表达A、B两组间差异无显著性（P＝0.220）；A组bcl-2/bax明显高于B组（P<0.01）。相关性研究表明，在A、B组中肿瘤组织的%ID/g与TUNEL阳性细胞数均呈明显正相关（r=0.801，r=0.769），而bcl-2蛋白表达与bax蛋白表达间无明确相关性；A组肿瘤组织内bcl-2、bax蛋白表达与肿瘤组织的%ID/g及TUNEL阳性细胞数均无明确相关性；B组肿瘤组织内，bcl-2蛋白表达与%ID/g及TUNEL阳性细胞数均无明确相关性，bax蛋白表达与%ID/g及TUNEL阳性细胞数均呈明显正相关（r＝0.849、0.652），而bcl-2／bax比值与%ID/g及TUNEL阳性细胞数均呈明显负相关（r＝－0.820、－0.694）。结论 肿瘤组织内99Tcm-rh-AnnexinⅤ的分布可以反映化疗后早期肿瘤组织细胞凋亡的状况以及凋亡调控蛋白bax表达水平的变化。

关键词　放射性核素显像　膜联蛋白Ⅴ　bcl-2蛋白　细胞凋亡　bax蛋白

分类号

Distribution of $^{99}Tc^{m}$-rh-AnnexinⅤ and Its Relationship with Expression of bcl-2、bax in Tumor After a Single Dose of Chemotherapy

Abstract Objective To determine the effectiveness of imaging with 99mTc labelled recombinant human annexinⅤ(99mTc-rh-annexinⅤ) as a reflection of the degree of apoptosis in tumor， and investigate the distribution of 99Tcm-rh-AnnexinⅤand its relationship with expression of bcl-2、bax after the single dose of chemotherapy. Methods Eight days after being inoculated with allogenic hepatoma cells(Hca-F25) into the subcutaneouly of the right axillary fossa, the mice (purebred 615) were randomly divided into tow groups (group A was control group, n=9； group B was treated group, n=10). Group B was received a single dose of chemotherapy intraperictoneally (cyclophosphamide, 150mg/kg). Group A and group Bwere injected 99mTc-rh-annexinⅤ(3.7MBq/0.5μg/per mouse) intravenously 20 hrs later. 4 hrs after 99mTc-rh-annexinⅤ injection, the animals were imaged and sacrified, the tumor samples were weighed and the radioactivity was determined with a well-type scintillation counter. The accumulation of 99mTc-rh-annexinⅤ in tumor was expressed as the %ID/g(percentage activity of injection dose per gram of tissue).Tumor cell apoptosis was examined by TUNEL methods, and the expression of bcl-2 and bax in tumor were determined with immunohistochemical methods. Results Single dose of chemotherapy significantly increased the tumor uptake of 99mTc-rh-annexinⅤ and the positive number of TUNEL, as well as the expression of bax (P<0.01). The expression of bcl-2 had no significant difference in group A and group B(P=0. 220), but the bcl-2/bax was significantly high in group A than in group B(P<

0.01). The %ID/g in tumor correlated well with the positive number of TUNEL in group A and gr oup B(r=0. 801, r=0.769), but the expression of bcl-2 had no relationship with the expression of bax. In group A, the expression of bcl-2 and bax had no relationship with the %ID/g and the posi tive number of TUNEL in tumor. In group B, the expression of bax correlated well with the %ID/ g and the positive number of TUNEL(r=0. 849, r=0.652), but the bcl-2/bax correlated negatively with %ID/g and the positive number of TUNEL(r=-0. 820, r=-0. 694). Conclution The distributi on of 99mTc-rh-annexin Ⅴ can not only truly reflected the degree of apoptosis in tumor, but also t he change of bax expression after the single dose of chemotherapy.

Key words Radionuclide imaging Apoptosis；Annexin Ⅴ bcl-2 Apoptosis bax

DOI

通讯作者 张欣 zhhw2000@126.com