·基础研究·

亲细胞非均质分子脂质局部注射治疗乳癌的实验研究

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【摘要】　目的　阐明 CHML 经皮瘤内注射治疗乳癌的效果并探讨其机理，明确 CHML 有无骨髓抑制及肝肾功能损伤等副作用。方法　5 周龄裸鼠共 30 只，分别于右腋后皮下直接种植人 MCF－7 乳癌组织块（0.2 cm×0.2 cm×0.2 cm），制成乳癌动物模型。2 周后，肿瘤直径长至 0.2～0.8 cm，随机分成 2 组，分别给予 CHML 及生理盐水局部浸润注射。治疗组 CHML 剂量按瘤体大小为 50 mg /cm^3，隔 2 d 局部注射 1 次，共 3 次。对照组给予相应容量的生理盐水。治疗前及治疗后分别测 ALT、AST、ALP、BUN 及白细胞数，以明确有无肝肾功能损伤和骨髓抑制。第 1 次注射后 48 h，两组分别处死 5 只裸鼠，对肿瘤进行原位末端标记（TUNEL），以明确有无凋亡。完成局部注射后 2 周，处死所有裸鼠，解剖并行病理检查，明确两组肿瘤愈合及淋巴结转移情况。结果　（1）局部注射后 48 h 治疗组 5 只裸鼠的肿瘤均出现不同程度的凋亡（+～++++），而对照组仅有个别细胞凋亡（－）。（2）实验结束时，治疗组肿瘤全部脱落，且无残存癌细胞；而对照组肿瘤明显增大，瘤体直径平均（0.94±0.34）cm，两组有显著统计学差异（$P<0.001$）。（3）治疗前后 ALT、AST、ALP、BUN 及白细胞均无明显变化，两组比较无统计学差异。结论　CHML 瘤内局部注射可有效杀灭乳腺癌细胞，并可诱导凋亡，且无抑制骨髓和损伤肝肾功能的副作用。

【关键词】　不饱和脂肪酸；CHML；乳癌；治疗学；凋亡

Experimental study on percutaneous intratumoral injection of cytotropic heterogeneous molecular lipids（CHML）for treatment of human breast cancer xenograft in nude mice

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【**Abstract**】　**Objective**　To illustrate the antitumoral effect and mechanism of cytotropic heterogeneous molecular lipids（CHML）injected intratumorally into human breast cancer xenograft in nude mice and to discuss the side effects of CHML such as bone marrow suppression, hepatic and renal functions impairment. **Methods**　In order to establish animal model of breast cancer, thirty five－week－old nude mice were planted subcutaneously with MCF－7 fragments（0.2 cm×0.2 cm×0.2 cm）of human breast cancer tissue at each of their right axillar back region. Two weeks later, the nude mice were divided into two groups randomly when their tumor size had reached to 0.2－0.8 cm in diameter. Group A and B underwent local injection with CHML or saline respectively. In group A CHML was injected diffusely into the tumor with a dose of 50 mg（0.5 ml）tumor area cm3, once every two days, 3 times in total, and so was saline in group B. In order to observe the toxicity of CHML, white blood cell（WBC）count and the activity of the serum alkaline phosphatase（ALP）, alanine aminotransferase（ALT）, aspartate aminotransferase（AST）and blood urea nitrogen（BUN）were determined before and after the treatment. Five nude mice in each group were killed 48 hours after the first local injection, the tumor cell apoptosis was observed with TdT－mediated dUTP nick end labeling（TUNEL）. Two weeks after the treatment, all the nude mice were killed, and the information of tumor healing and lymph node metastasis were observed with autopsy and histology. **Results**　1. There were different degrees of apoptosis（+～++++）among the 5 tumors treated with CHML, and very few apoptosis cells（－）were found in the control group. 2. All the tumors in the group A were shed and disappeared when the experiment was finished, and no residual

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tumor cells were found histological. Tumors of group B grew up continuously and became evidently large, their average size was (0.94 ± 0.34) cm in diameter. There was statistically significant difference between the two groups ($P < 0.001$. 3. There were no evident changes of ALT, AST, ALP, BUN and WBC before and after treatment and there was no significant difference between the two groups ($P > 0.05$). **Conclusions** All the human breast cancer xenografts in nude mice were killed effectively without any obvious toxicity or side effects on bone marrow, liver and kidney during the experimental period. Apoptosis of tumor cells induced by CHML might be one of the positive factors in the treatment of breast cancer.

【**Key words**】 Unsaturated fatty acid；cytotropic heterogeneous molecular lipids (CHML)；Breast cancer；Therapy；Apoptosis

·病例报告·

九次前列腺穿刺活检随访前列腺上皮内肿瘤一例

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患者男，75岁。体检发现前列腺结节12年余，排尿困难，尿流细，排尿时间延长，无尿频、尿痛、血尿等症状。直肠指诊：前列腺Ⅱ度增生，右侧叶可触及一大小1.8 cm×1.0 cm的结节，质硬，表面不平，无触痛。化验：12年内多次查血清前列腺特异性抗原（PSA）均升高，在5.9～15.0 ng/ml范围内波动，血清酸性磷酸酶及碱性磷酸酶正常。

直肠超声所见：前列腺形态饱满，大小为5.1 cm×3.0 cm×4.0 cm，内腺前后径为2.5 cm。左右对称，包膜完整，内外腺分界清晰，右侧外腺可见一低回声结节，大小1.9 cm×1.2 cm，边界不清楚，彩色多普勒检查病灶内部和周边均可见血流信号，脉冲多普勒显示上述血流呈低速动脉样血流频谱（图1，2）。超声诊断：（1）前列腺右侧外腺实性占位性病变；（2）前列腺增生。

1993年4月至2003年8月，患者先后9次行前列腺结节穿刺活检，其中6次为经直肠超声引导穿刺活检（图3）。病理诊断均报告为前列腺上皮内肿瘤（prostatic intraepithelial neoplasia，PIN）Ⅰ～Ⅱ级。

2003年11月，患者行前列腺切除术，术中所见：前列腺Ⅱ度增生，质硬，表面不平呈结节状。术后病理诊断：前列腺增生症，部分腺体呈PINⅠ～Ⅱ级改变（图4）。

讨　论

PIN也称导管－腺泡非典型增生，是前列腺癌的癌前病变，已引起临床广泛重视。PIN的组织学特征为边界清楚的局灶性病变，增厚的上皮深染与周围正常的腺体可形成明显的界限，非癌PIN的病灶一般小于4 mm，而前列腺癌中的PIN多大于4 mm，尤其是位于肿瘤附近的PIN。PIN多为多发病灶。临床无特异性症状。经直肠超声检查PIN多为低回声结节，形态不规则，有时难与前列腺癌相鉴别[1]。超声引导前列腺穿刺活检的逐步开展提高了PIN的诊断符合率，有助于前列腺癌高危人群的随访[1-3]。该患者直肠指诊前列腺有硬节，12年内多次查PSA均高于正常水平，且声像图表现与前列腺癌十分相似，临床高度怀疑前列腺癌。以超声引导前列腺穿刺活检进行长期随诊，不同时间内重复穿刺病理诊断均为PINⅠ～Ⅱ级，与术后病理结果一致。超声引导前列腺穿刺活检诊断PIN准确性高，可作为长期随访PIN的有效方法。

（本文图1～4见光盘）

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