557~563.吉西他滨化疗联合树突状细胞瘤内注射对小鼠巨大淋巴瘤的治疗作用[J].胡守友,朱学军,范振芳,孔祥图,陈玉超,陈健一,季建敏,孙雪梅.中国肿瘤生物治疗杂志,2009,16(6)

吉西他滨化疗联合树突状细胞瘤内注射对小鼠巨大淋巴瘤的治疗作用

点此下载全文

胡守友 朱学军 范振芳 孔祥图 陈玉超 陈健一 季建敏 孙雪梅

江苏省中医院 肿瘤科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029;江苏省中医院 肿瘤科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029;江苏省中医院 血液科，江苏 南京 210029

基金项目：江苏省医学重点人才基金资助项目（No. RC2007002)

DOI：10.3872/j.issn.1007-385X.2009.6.002

摘要：

目的：观察吉西他滨对荷B细胞淋巴瘤小鼠脾脏中髓源抑制性细胞（myeloid derived suppressor cell, MDSC）的影响，以及吉西他滨化疗联合树突状细胞（dendritic cells, DCs）治疗巨大淋巴瘤的疗效。方法：小鼠皮下接种A20淋巴瘤细胞，30 d后形成巨大肿瘤，流式细胞仪分析吉西他滨化疗前后荷瘤小鼠脾脏中Gr 1 +CD11b + MDSC的比例，免疫磁珠纯化的脾脏MDSC体外加入吉西他滨共培养后，Annexin V/PI标记法检测细胞凋亡；观察荷瘤小鼠接受吉西他滨化疗联合DCs瘤内注射后肿瘤生长情况及小鼠存活期。结果：荷A20淋巴瘤小鼠脾脏中MDSC的比例显著上调，是正常小鼠脾脏中的10倍以上。体外吉西他滨时间依赖性诱导MDSC凋亡与坏死；荷瘤小鼠体内注射吉西他滨后，脾脏中绝大部分的MDSC被清除。单独吉西他滨注射或DCs瘤内注射对肿瘤生长产生一定的抑制作用，小鼠平均存活天数分别为（48.8±3.6）d和（47.2±7.4）d，而对照组小鼠平均存活天数为（38.8±2.2）d；吉西他滨化疗联合DCs瘤内注射后瘤体持续显著缩小，60%小鼠存活时间均超过90 d。结论：吉西他滨可有效清除荷瘤小鼠脾脏MDSC，吉西他滨化疗与DCs瘤内注射免疫治疗具有协同效应，可以提高对巨大淋巴瘤的疗效，本实验为应用生物化疗综合治疗模式治疗复发、难治性淋巴瘤提供了实验依据。

关键词：淋巴瘤 吉西他滨 髓源抑制性细胞 树突状细胞 生物化疗

Gemcitabine chemotherapy combined with intratumoral injection of dendritic cells in treatment of mouse large lymphoma

Download Fulltext

HU Shou-you ZHU Xue-jun FAN Zhen-fang KONG Xiang-tu CHEN Yu-chao CHEN Jian-yi JI Jian-min SUN Xue-mei

Department of Oncology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Hematology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Hematology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Oncology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Hematology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Hematology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China;Department of Hematology, Traditional Chinese Medicine Hospital of Jiangsu Province, Nanjing 210029, Jiangsu, China

Fund Project:Supported by the Key Project of Outstanding Medical Talents of Jiangsu Province (No. RC2007002)

Abstract:

Objective:To investigate the effect of gemcitabine on myeloid derived suppressor cells (MDSC) in the spleen of B lymphoma cell bearing mice, and the therapeutic effect of gemcitabine combined with intratumoral injection of dendritic cells (DCs) in treatment of large B lymphoma. Methods: BALB/c mice were inoculated subcutaneously with B lymphoma A20 cells; large tumors were formed 30 d after inoculation. Gr 1 +CD11b + MDSC proportion in the spleen was analyzed by flow cytometry before and after gemcitabine treatment. Splenic MDSC sorted by immunomagnetic beads was further treated with gemcitabine, and then the apoptosis of MDSC was examined by Annexin V/PI staining. Tumor growth and survival time of A20 tumor bearing mice were observed after treatment with gemcitabine and intratumoral injection of DCs. Results: Splenic Gr 1 +CD11b +MDSC ratio in A20 cell bearing mice was 10 times higher than that in the normal mice. Gemcitabine induced apoptosis and necrosis of purified MDSC in vitro in a time dependent manner. The percentage of MDSC in the spleen of A20 tumor bearing mice was decreased after injection of a single dose of gemcitabine. Gemcitabine or intratumoral injection of DCs alone inhibited growth of tumor to a certain degree, with the mean survival periods of mice in the gemcitabine, DCs, and untreated groups being (48.8±3.6) d, (47.2±7.4) d, and (38.8±2.2) d, respectively. Gemcitabine chemotherapy combined with intratumoral DC injection resulted in continuous shrink of the tumors, and 60% of the mice survived for more than 90 d. Conclusion: Gemcitabine can effectively eliminate splenic MDSC in tumor bearing mice. Gemcitabine chemotherapy and DCs immunotherapy can work synergistically in the treatment of huge lymphoma. These results provide an experimental basis for the comprehensive chemotherapy and immunotherapy of relapsed or refractory lymphoma.

Keywords:lymphoma gemcitabine myeloid derived suppressor cell dendritic cell chemotherapy immunotherapy

查看全文 查看/发表评论 下载PDF阅读器