世界华人消化杂志®
wcjd@wjgnet.com

世界华人消化杂志 2006年6月28日; 14(18): 1836-1838
ISSN 1009-3079 CN 14-1260/R

临床经验 CLINICAL PRACTICE

丙型肝炎肝硬化CD56⁺T细胞和NK细胞数量及抗肿瘤活性

范荣山, 于德军, 孙德荣

■背景资料
通过流行病学调查研究，慢性丙型肝炎发展为肝硬化和肝癌的比例较高，其确切机制目前还不清楚. 肝脏局部的免疫环境在肝癌的发生 发展中的作用越来越受到人们的重视. 肝脏中分布着大量天然和获得性的T细胞 NK细胞和CD56+T细胞(NKT), NKT同时表达T细胞受体和NK细胞受体，是抗肿瘤早期起作用的效应细胞，其重要性受到广泛的关注.

■相关报道
Kawarabayashi *et al*研究了手术得到的标本，分析了肝癌和非肝癌患者肝脏中NK和NKT细胞数量及抗肿瘤活性; Ogasawara *et al*认为IFN-γ是NK及NKT发挥抗肿瘤作用的重要的细胞因子.

范荣山，孙德荣，大庆市第二医院内科 黑龙江省大庆市 163461
于德军，大庆市第二医院检验科 黑龙江省大庆市 163461
通讯作者: 范荣山，163461，黑龙江省大庆市红岗区解放一街，大庆市第二医院内科. rsfan519@163.com
电话: 0459-5202419
收稿日期: 2005-07-11 接受日期: 2005-08-11

Numbers and activities of CD56⁺ T cells and natural killer cells in cirrhotic livers with hepatitis C

Rong-Shan Fan, De-Jun Yu, De-Rong Sun

Rong-Shan Fan, De-Rong Sun, Department of Internal Medicine, the Second Hospital of Daqing City, Daqing 163461, Heilongjiang Province, China
De-Jun Yu, Department of Laboratory, the Second Hospital of Daqing City, Daqing 163461, Heilongjiang Province, China
Correspondence to: Rong-Shan Fan, Department of Internal Medicine, the Second Hospital of Daqing City, Daqing 163461, Heilongjiang Province, China. rsfan519@163.com
Received: 2005-07-11 Accepted: 2005-08-11

Abstract

AIM: To study the numbers and anti-tumor activities of CD56⁺ T cells and natural killer (NK) cells in cirrhotic liver with hepatitis C (HC).

METHODS: Hepatic mononuclear cells (MNC) were isolated from liver specimens obtained from the patients (n = 16) with HC-induced cirrhosis by liver biopsy. In addition, the numbers of CD56⁺ T cells and natural killer cells were determined by flow cytometry. Liver MNC and peripheral blood mononuclear cells (PBMC) were co-cultured with the interleukin-2 (IL-2), respectively, and the production of interferon-γ (IFN-γ) and the antitumor activity were measured.

RESULTS: The percentages of CD56⁺ T cells among hepatic MNC in health individuals, HC and HC-induced cirrhosis patients were 20.4% ± 6.2%, 11.2% ± 3.1% and 5.0% ± 1.6%, respectively; the proportions of NK cells among liver MNC in the three groups were 31.1% ± 9.7%, 31.6% ± 8.3% and 18.3% ± 5.4%, respectively; the productions of IFN-γ in the three groups were 7.4 ± 2.4, 3.2 ± 1.8 and 1.9 ± 0.5 μg/L, respectively; the anti-tumor activities hepatic MNC in the three groups were 61.1% ± 17.1%, 59.2% ± 14.6%, and 26.7% ± 8.5%, respectively. For the above four groups of parameters, the changes in HC-induced cirrhosis patients was the most significant (P < 0.05).

CONCLUSION: The numbers and anti-tumor activities of CD56⁺T cells and NK cells are decreased in cirrhotic livers with HC.

Key Words: Hepatitis C; Liver cirrhosis; CD56⁺ T cell; Natural killer cell; Cell number; Activity

Fan RS, Yu DJ, Sun DR. Numbers and activities of CD56⁺ T cells and natural killer cells in cirrhotic livers with hepatitis C. Shijie Huaren Xiaohua Zazhi 2006;14(18):1836-1838

摘要

目的: 研究CD56⁺T细胞和NK细胞在丙型肝炎肝硬化时的数量及抗肿瘤细胞活性变化.

方法: 丙型肝炎肝硬化患者18例，快速肝穿获得肝组织，分离肝脏单个核细胞(MNC)，流式细胞仪分析CD56⁺T细胞及NK细胞数量，肝脏MNC和外周血单个核细胞(PBMC)分别与IL-2混合培养，检测IFN-γ含量及抗肿瘤细胞活性.

结果: 健康志愿者 慢性丙型肝炎患者 丙型肝炎肝硬化患者肝脏MNC中CD56⁺T细胞数量百分比分别是20.4% ± 6.2%，11.2% ± 3.1%和5.0% ± 1.6%; NK细胞比例分别是31.1% ± 9.7%，31.6% ± 8.3%和18.3% ± 5.4%; 肝脏MNC的IFN-γ产量分别是7.4 ± 2.4，3.2 ± 1.8和1.9 ± 0.5 μg/L; 抗肿瘤细胞的细胞毒性分别是61.1% ± 17.1%，59.2% ± 14.6%，26.7% ± 8.5%. 以上四组数据均以肝炎肝硬化患者变化最为显著(P<0.05).

结论: 丙型肝炎肝硬化时肝脏CD56⁺T细胞和NK细胞数量及抗肿瘤细胞活性分别下降.

关键词: 丙型肝炎; 肝硬化; CD56⁺T细胞; NK细胞;

细胞数量; 细胞活性

范荣山, 于德军, 孙德荣. 丙型肝炎肝硬化CD56+T细胞和NK细胞数量及抗肿瘤活性. 世界华人消化杂志 2006;14(18):1836-1838
http://www.wjgnet.com/1009-3079/14/1836.asp

0 引言

, 10-29 a, 35.1%-51% , 10.6%-23.4% , 15.3%[1]. $CD56^+$T NK [2-3], $CD56^+$T NK .

1 材料和方法

1.1 材料 1 12 ; 2 16 ; 3 18 . : 2000-09 . HAV HBV HDV HEV , , . , ; . , (0.5 g/L) DNAse (0.1 mg/L) 37 20 min, 200 , RPMI 1640 , 3 , 100 kU/L 330 g/L Percoll , 2 000 r/min 15 min, . , 50 mL/L FBS-RPMI 2 , MNC, PBMC.

1.2 方法 MNC PBMC FITC NKR-P1 , PE CD56 , - αβTCR , , 0.1 L (0.01 mg/L) CD3 4 96 , 3 . MNC PBMC 100 mL/L RPMI 1640 0.2 mL, CD3 96 , 50 mL/L CO_2, 37 . MNC IL-2 (20 mg/L), 48 h , -80 ELISA , MNC 5 d , . ELISA kit MNC IFN-γ , , . NK YAC-1 , 100 mL/L FBS RPMI 1640 , 3.7 MBq $Na_2(^{51}Cr)O_4$ 60 min, 37 , MNC PBMC , E/T = 10 1, 4 h , , Gamma , <15%.

统计学处理 t , 3 .

2 结果

2.1 肝脏MNC中$CD56^+$T和NK细胞 (1) MNC $CD56^+$T : 1 20.4%±6.2%, 2 11.2%±3.1%, 3 5.0%±1.6%(P<0.05). (2) MNC NK : 1 31.1%±9.7%, 2 31.6%±8.3%, 3 18.3%±5.4%(P<0.05). , , $CD56^-$T . PBMC .

2.2 肝脏MNC在IL-2刺激下产生IFN-γ MNC IL-2 IFN-γ : 1 7.4±2.4 μg/L, 2 3.2±1.8 μg/L, 3 1.9±0.5 μg/L (P<0.05). PBMC IL-2 IFN-γ .

2.3 肝脏MNC在IL-2刺激下抗肿瘤细胞毒性 IL-2 MNC YAC-1 : 1 61.1%±17.1%, 2 59.2%±14.6%, 3 26.7%±8.5%(P<0.05). PBMC IL-2 , .

3 讨论

, MNC IFN-γ , , MNC PBMC IFN-γ . MNC $CD56^+$T NK , MNC IFN-γ , MNC . , CCl_4 NKT , MNC HCC [4]. MNC , NKT [5]. IL-7 mRNA, IL-7 NKT [6]. , [7], NKT NK , [8-10]. IFN-γ [11-12], IFN-γ

■创新盘点
本文研究了丙型肝炎 肝硬化患者肝活检组织中的NK和NKT数量和活性, 从不同的角度证明NK和NKT在丙型肝炎肝硬化时数量减少及活性下降减弱了肝脏局部抗肿瘤免疫功能.

■应用要点
改善肝脏局部的抗肿瘤免疫功能, 可能成为预防肝炎肝硬化发生肝癌的有效措施.

[13-14]. $CD56^+$T $CD56^-$T NK
HCV IFN-γ, IL-2 IL-12, $CD56^-$T
[15], IFN-γ
MNC $CD56^+$T NK .
$CD56^+$T NK
IL-2 IL-12 , IFN-γ,
, [16-17].
PBMC $CD56^+$T NK IL-2 IL-12 ,
[18].
$CD56^+$T NK IFN-γ,
,
, $CD56^+$T NK
,
.

4 参考文献

1 王豪. 丙型肝炎的流行病学与预防. 中华肝脏病杂志 2003; 11: 366-367
2 邱大鹏, 邱双健, 吴志全, 樊嘉, 叶胜龙, 余耀, 周俭, 蔡晓燕. NKT细胞在肝癌组织中的分布状况与肝癌局部免疫的研究. 中国临床医学 2004; 11: 567-569
3 Kawachi Y, Watanabe H, Moroda T, Haga M, Iiai T, Hatakeyama K, Abo T. Self-reactive T cell clones in a restricted population of interleukin-2 receptor beta+ cells expressing intermediate levels of the T cell receptor in the liver and other immune organs. *Eur J Immunol* 1995; 25: 2272-2278
4 Kawachi Y, Arai K, Moroda T, Kawamura T, Umezu H, Naito M, Ohtsuka K, Hasegawa K, Takahashi-Iwanaga H, Iwanaga T. Supportive cellular elements for hepatic T cell differentiation: T cells expressing intermediate levels of the T cell receptor are cytotoxic against syngeneic hepatoma, and are lost after hepatocyte damage. *Eur J Immunol* 1995; 25: 3452-3459
5 Lombard C, McKallip RJ, Hylemon PB, Nagarkatti PS, Nagarkatti M. Fas Ligand-dependent and -independent mechanisms of toxicity induced by T cell lymphomas in lymphoid organs and in the liver. *Clin Immunol* 2003; 109: 144-153
6 Miyaji C, Watanabe H, Osman Y, Kuwano Y, Abo T. A comparison of proliferative response to IL-7 and expression of IL-7 receptors in intermediate TCR cells of the liver, spleen, and thymus. *Cell Immunol* 1996; 169: 159-165
7 Tavian M, Peault B. Embryonic development of the human hematopoietic system. *Int J Dev Biol* 2005; 49: 243-250
8 Watanabe H, Miyaji C, Seki S, Abo T. c-kit+ stem cells and thymocyte precursors in the livers of adult mice. *J Exp Med* 1996; 184: 687-693
9 Massa S, Balciunaite G, Ceredig R, Rolink AG. Critical role for c-kit (CD117) in T cell lineage commitment and early thymocyte development *in vitro*. *Eur J Immunol* 2006; 36: 526-532
10 Shimizu T, Bannai M, Kawamura H, Yamamoto S, Oya H, Maruyama S, Minagawa M, Kawamura T, Watanabe H, Hatakeyama K, Abo T. Organ specificity of c-kit+ lymphoid precursors in the liver, thymus, and bone marrow. *Eur J Haematol* 2000; 64: 416-425
11 Banerjee D, Liou HC, Sen R. c-Rel-dependent priming of naive T cells by inflammatory cytokines. *Immunity* 2005; 23: 445-458
12 Heink S, Ludwig D, Kloetzel PM, Kruger E. IFN-gamma-induced immune adaptation of the proteasome system is an accelerated and transient response. *Proc Natl Acad Sci USA* 2005; 102: 9241-9246
13 Schijns VE, Wierda CM, van Hoeij M, Horzinek MC. Exacerbated viral hepatitis in IFN-gamma receptor-deficient mice is not suppressed by IL-12. *J Immunol* 1996; 157: 815-821
14 Khan S, Zimmermann A, Basler M, Groettrup M, Hengel H. A cytomegalovirus inhibitor of gamma interferon signaling controls immunoproteasome induction. *J Virol* 2004; 78: 1831-1842
15 Kawarabayashi N, Seki S, Hatsuse K, Ohkawa T, Koike Y, Aihara T, Habu Y, Nakagawa R, Ami K, Hiraide H, Mochizuki H. Decrease of CD56(+)T cells and natural killer cells in cirrhotic livers with hepatitis C may be involved in their susceptibility to hepatocellular carcinoma. *Hepatology* 2000; 32: 962-969
16 Kenna T, Golden-Mason L, Porcelli SA, Koezuka Y, Hegarty JE, O'Farrelly C, Doherty DG. NKT cells from normal and tumor-bearing human livers are phenotypically and functionally distinct from murine NKT cells. *J Immunol* 2003; 171: 1775-1779
17 Ogasawara K, Takeda K, Hashimoto W, Satoh M, Okuyama R, Yanai N, Obinata M, Kumagai K, Takada H, Hiraide H, Seki S. Involvement of NK1+ T cells and their IFN-gamma production in the generalized Shwartzman reaction. *J Immunol* 1998; 160: 3522-3527
18 Satoh M, Seki S, Hashimoto W, Ogasawara K, Kobayashi T, Kumagai K, Matsuno S, Takeda K. Cytotoxic gammadelta or alphabeta T cells with a natural killer cell marker, CD56, induced from human peripheral blood lymphocytes by a combination of IL-12 and IL-2. *J Immunol* 1996; 157: 3886-3892

电编 张敏 编辑 潘伯荣