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临床经验 CLINICAL PRACTICE

乙型肝炎患者血清IL-27的检测及其意义

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Assay of serum IL-27 and its significance in HBV-infected patients

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Abstract

AIM: To investigate the change and clinical significance of serum chemokine IL-27 in HBV-infected patients.

METHODS: The serum concentration of IL-27 was detected by enzyme linked immunosorbent assay (ELISA); HBV DNA was detected by fluorescent quantitive polymerase chain reaction (FQ-PCR); liver function was assayed by automatic biochemistry analyzer.

RESULTS: Serum concentrations of IL-27 in control group (n = 41), acute hepatitis B group (n = 33), mild chronic hepatitis B (CHB) group (n = 32), moderate CHB group (n = 30) and severe CHB group (n = 32) were 14.123 ± 15.627 ng/L, 56.880 ± 15.813 ng/L, 23.872 ± 22.801 ng/L, 29.849 ± 24.300 ng/L, 35.703 ± 18.575 ng/L, respectively. The concentration of IL-27 was significantly higher in all HB groups than in control group (P < 0.05 or 0.01). The concentration of IL27 was significantly higher in severe CHB group than in mild CHB group (P < 0.05). However, the disparity of IL-27 concentration between mild CHB and moderate CHB group was statistically significant.

CONCLUSION: It is possible that IL-27 promotes immune clearance in acute hepatitis, however, in chronic hepatitis B it may have some cytopathic effect (CPE).

Key Words: Chemokine; Interleukin-27; Hepatitis B; Enzyme-linked immunosorbent assay

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摘要

目的: 探讨乙肝患者血清IL-27的变化规律及其临床意义.

方法: 采用酶联免疫吸附法(ELISA)检测血清IL-27的浓度; 荧光定量聚合酶链反应法(FQ-PCR)检测HBV DNA; 全自动生化仪检测肝功能.

结果: 对照组(n = 41)、急性乙肝组(n = 33)、慢性乙肝(轻度)组(n = 32)、慢性乙肝(中度)组(n = 30)、慢性乙肝(重度)组(n = 32)血清IL-27浓度分别为14.123±15.627 ng/L、56.880±15.813 ng/L、23.872±22.801 ng/L、29.849±24.300 ng/L、35.703±18.575 ng/L. 急性乙肝组血清IL-27浓度显著高于慢性乙肝组及对照组(均P<0.01); 慢性乙肝(轻、中、重度)组血清IL-27浓度显著高于对照组(P<0.05或<0.01); 慢性乙肝(重度)组血清IL-27浓度明显高于慢性乙肝(轻度)组(P<0.05); 慢性乙肝(轻度)组血清IL-27浓度与慢性乙肝(中度)组比较, 差异无统计学意义; 慢性乙肝(中度)组血清IL-27浓度与慢性乙肝(重度)组比较, 差异无统计学意义.

结论: 在急性乙型肝炎中IL-27可能促进了病毒清除; 在慢性乙型肝炎感染中可能有一定的致细胞病变效应.

■背景资料
IL-27是经典的IL-6/IL-12家族的螺旋状的细胞因子, 是机体促炎反应的环境下由抗原提呈细胞产生的一种细胞因子. 研究表明, IL-27能促进辅助性T细胞的分化, 增强杀伤性T淋巴细胞的活性, 并可通过多种机制促进Th1型免疫的发生, 诱导B细胞转化, 并主要作用于固有免疫系统和适应性免疫系统的各种细胞而发挥广泛的免疫调节作用.

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■应用要点
消除免疫耐受, 提高人体免疫功能, 尤其是特异性细胞免疫功能, 清除细胞内、外的HBV cccDNA, 是清除HBV的关键.

关键词: 细胞因子; 白介素27; 乙型肝炎; 酶联免疫吸附法

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0 引言

IL-27是经典的IL-6/IL-12家族的螺旋状的细胞因子[1], 是机体促炎反应的环境下由抗原提呈细胞产生的一种细胞因子. 研究表明, IL-27能促进辅助性T细胞的分化[2], 增强杀伤性T淋巴细胞的活性, 并可通过多种机制促进Th1型免疫的发生, 诱导B细胞转化, 并主要作用于固有免疫系统和适应性免疫系统的各种细胞而发挥广泛的免疫调节作用[3]. 而IL-27与乙型肝炎的发病是否有关目前尚未见报道.

1 材料和方法

1.1 材料 病例组: 127例乙肝患者, 来源于2004-11/2008-08我院住院患者, 其中, 急性乙肝患者33例、慢性乙肝(轻度)患者32例、慢性乙肝(中度)30例、慢性乙肝(重度)32例, 男92例, 女35例, 年龄(39.5±12.2)岁. 诊断标准符合依据2000年全国传染病与寄生虫病学术会议修订的《病毒性肝炎防治方案》诊断标准: HBsAg(+), 有临床症状, 肝功能异常, 病程在6 mo之内诊断为急性乙型肝炎, 超过6 mo诊断为慢性乙型肝炎[3]. 所有病例均未接受免疫调节和抗病毒治疗, 均为汉族. 排除HAV、HCV、HDV、HEV感染; 排除酒精性肝炎、脂肪肝、自身免疫性肝炎等其他肝炎; 排除肿瘤、自身免疫性疾病、感染性疾病和心血管疾病. 41例正常对照来源于同一时期我院健康体检人群, 其中男29例, 女12例, 年龄(36±15)岁, 排除HBV感染, 均为汉族, 其他排除标准同病例组. 所有受试者均知情同意.

1.2 方法

1.2.1 标本收集: 所有受试者均清晨抽取空腹外周血2 mL, 肝素抗凝, 30 min内常规离心, 分离血清, 血清标本冻存于-80℃超低温冰箱待测.

1.2.2 IL-27的检测: 用酶联免疫吸附法(ELISA)检测血清IL-27, 试剂盒购于美国rapidbio(RB)公司, 严格按说明书操作.

统计学处理 采用SPSS13.0统计软件分析, 数据以mean±SD表示, 多个样本均数两两比较采用LDS法方差分析.

表 1 乙型肝炎患者组与正常对照组血清IL-27浓度 (ng/L)

分组	*n*	IL-27(ng/L)
正常对照组	41	14.123 ± 15.627[bcfh]
急性乙肝组	33	56.880 ± 15.813
慢乙肝(轻度)组	32	23.872 ± 22.801
慢乙肝(中度)组	30	29.849 ± 24.300
慢乙肝(重度)组	32	35.703 ± 18.575

[b]*P*<0.01 *vs* 急性乙肝组; [c]*P*<0.05 *vs* 慢乙肝(轻度)组; [f]*P*= 0. 01 *vs* 慢乙肝(中度)组; [h]*P*<0.01 *vs* 慢乙肝(重度)组.

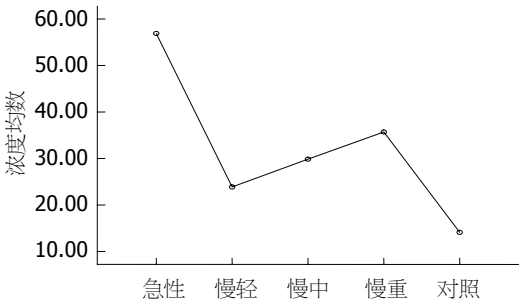

图 1 乙型肝炎患者组与正常对照组血清IL-27浓度均数图.

2 结果

急性乙肝组、慢性乙肝(轻度)组、慢性乙肝(中度)组、慢性乙肝(重度)组及正常对照组各组血清IL-27浓度经过方差齐性检验,结果为(F = 23.866, P<0.001)具有方差齐性.

急性乙肝组、慢性乙肝(轻度)组、慢性乙肝(中度)组、慢性乙肝(重度)组血清IL-27浓度均显著高于正常对照组血清IL-27浓度(P值分别为<0.01、<0.05、<0.01、<0.01); 急性乙肝组血清IL-27浓度显著高于慢性乙肝(轻、中、重)组血清IL-27浓度(均P<0.01); 慢性乙肝(轻度)组血清IL-27浓度显著低于慢乙肝(重度)组血清IL-27浓度(P = 0.016); 慢性乙肝(中度)组与慢性乙肝(轻、重)度组血清IL-27浓度比较, 差异无统计学意义(表1). 急性乙肝组、慢性乙肝(轻、中、重)组与正常对照组血清IL-27浓度均数比较见图1.

3 讨论

目前研究认为Th1/Th2细胞比例失衡可能是HBV感染慢性化的机制之一[4-5]. 急性自限性乙肝患者表现为强烈的、多克隆和非特异性的CTL和Th1细胞反应, 相反在慢性乙肝患者中则以Th2细胞反应占优势, 难以检测到特异性的Th1细胞应答, 从而倾向于发生持续性的HBV感染[6]. 消除免疫耐受, 提高人体免疫功能, 尤其是特异性细胞免疫功能, 清除细胞内、外的HBV

cccDNA, 是清除HBV的关键.

体外实验研究表明, IL-27可通过多种机制促进Th1型免疫的发生[7-8], IL-27诱导Th1类细胞因子及干扰素的信号表达, IL-27可诱导NK细胞产生IFN-γ, 而在缺少IL-27受体的细胞内IFN的表达降低[9-12]. 另外IL-27可增强初始$CD4^+$ T细胞MHC Ⅰ的表达, 可促进初始$CD4^+$ T细胞的增殖, 但目前尚不清楚目前还不清楚IL-27通过哪条信号转导途径诱导初始$CD4^+$ T细胞的增殖[13-15].

本实验研究发现, 乙型肝炎(急性乙肝组、慢性轻、中、重)各组血清IL-27水平均明显高于正常对照组, 且急性乙肝组明显高于慢性(轻、中、重)组, 慢性(重度)组显著高于慢性(轻度)组, 但慢性(中度)组与慢性(重度)组比较, 差异无统计学意义, 有待于扩大样本量深入研究. 这提示在急性乙型肝炎的发病过程中, IL-27可能促进机体Th1型免疫的发生, 促进了细胞免疫反应, 从而对清除乙肝病毒起到了积极作用; 在慢性乙型肝炎发病中, IL-27有可能在促进病毒清除的过程中同时增强了肝脏的炎症反应, 从而加重了肝细胞的损伤. 具体IL-27如何发挥上述生物学作用, 以及何种机制调节人体内IL-27的浓度, 尚待进一步研究IL-27及其受体在HBV感染中的生物学功能.

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■同行评价

本文对乙肝的研究有一定的积极意义, 试验设计比较合理, 但简单.