

慢性肾盂肾炎患者机体免疫功能的研究

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内容提要 本文报道用单克隆抗体和间接免疫荧光技术,对30例慢性肾盂肾炎患者和36例健康志愿者外周血T细胞亚群的检测。发现慢性肾盂肾炎患者存在着细胞介导免疫功能紊乱。用至灵胶囊或转移因子并结合各种抗生素治疗3月后,患者细胞介导免疫功能和临床症状明显改善。认为外周血 CD_4/CD_8 比例降低是肾功能正常的慢性肾盂肾炎患者免疫学改变的一个标志,可能与疾病复发有关;用至灵胶囊或转移因子并结合各种抗生素治疗较单用抗生素或清热解毒药效果更理想。

关键词 慢性肾盂肾炎 细胞介导免疫 至灵胶囊 转移因子

慢性肾盂肾炎(CPN)属临床常见病。国外统计,女性尿路感染(UTI)发病率为2~10%,无症状性真性菌尿约4%。国内资料表明,女性UTI发病率为2.05%^[1],CPN仍为慢性尿毒症的第二病因。目前肾盂肾炎与免疫之间的关系已引起临床广泛重视,为此,我们用单克隆抗体(McAb)和间接免疫荧光技术,对CPN患者和正常人外周血T细胞亚群进行检测,进而观察至灵胶囊(ZLC)和转移因子(TF)对机体免疫功能的影响。

资料与方法

一、病例选择

1987年1月~1989年4月UTI专科门诊中选择女性CPN患者30例,年龄24~53岁(平均 38.57 ± 6.70),BUN、血Cr均在正常范围。全部病例均参照UTI的诊断、治疗标准〔中华肾脏病杂志 1985; 1(4):13〕。中医辨证分型^[2,3]:(1)脾肾气虚、余邪未清型18例,主要以轻度浮肿、纳差、腰酸、乏力、尿频、少腹坠胀等为主证,舌质胖、苔薄白或腻,脉细弱;(2)肾阴不足(或气阴两虚)、湿热留恋型10例,主要表现为低热或手足心热、腰痛、淋漓不已或时作时休为主证,兼气虚者有神疲乏力、易感冒、劳累或受凉即发,舌红,苔薄黄或腻,脉细数;(3)肝郁气滞型2例,以腹胀、嗝气、胸闷、两肋不适、纳差、小腹

急胀不适、小便不畅为主证。

正常人对照组36例,均为本院健康女职工,年龄23~56岁(平均为 31.94 ± 9.10)。

二、方法

对照组一次静脉取血(肝素抗凝),测 CD_3 、 CD_4 、 CD_8 及 CD_4/CD_8 比值。

CPN患者首次静脉取血,测 CD_3 、 CD_4 、 CD_8 及 CD_4/CD_8 后,在抗菌治疗同时,另给Z-LC/TF。用药选择:(1)根据患者意愿;(2)ZLC有一定胃肠道反应,患者原有胃肠道疾病或不适者,不宜用ZLC而选TF。ZLC3片,每日3次口服;TF(脾血)4ml,每周1次皮下注射,3个月为1个疗程。疗程结束及停药(Z-LC或TF)3个月后比较观察上述指标的变化。

所有患者外周血白细胞计数均在正常范围;均在UTI非感染期取血;取血前停用各种对CMI有影响的中西药物:生晒参、刺五加、黄芪、核酪、免疫核糖核酸等;患者中除外对 CD_3 、 CD_4 、 CD_8 测定有影响的其它疾病,如SLE、肝炎、病毒性心肌炎等;除外有尿路结石、畸形等不利因素存在者。

CD_3 、 CD_4 、 CD_8 检测方法:取肝素化静脉血5ml,用Ficol淋巴细胞分离液分离出淋巴细胞,以2%牛血清PBS洗涤3次,然后对淋巴细胞进行计数,要求细胞密度为 1×10^6 细胞/ml,加入McAb(CD_3 、 CD_4 、 CD_8),同条件洗涤3次后加入荧光抗体,再洗3次,在

荧光显微镜下计数阳性细胞百分率。

结 果

一、外周血 T 细胞亚群比较

从表 1 可见 CPN 组与对照组比较, CD_3 、 CD_4 及 CD_4/CD_8 比值显著降低, CD_8 显著增高 ($P < 0.001$); 脾肾气虚组和肾阴不足组与对照组比较, 两组 CD_3 、 CD_4 及 CD_4/CD_8 比值显著降低, CD_8 显著增高 (P 值见附表), 但两组间无显著差异; ZLC 组治疗前后比较, 治疗后 CD_3 、 CD_4 显著增高 ($P < 0.05$; $P < 0.01$), CD_8 及 CD_4/CD_8 比值无显著差异 ($P > 0.05$); TF 组治疗前后比较, 治疗后 CD_3 、 CD_4 及 CD_4/CD_8 比值显著增高 ($P < 0.05$; $P < 0.01$; $P < 0.001$), CD_8 无显著差异 ($P > 0.05$); 治疗后 24 例 (ZLC 组 + TF 组) 与对照组比较, CD_3 、 CD_4 无显著差异 ($P > 0.05$), CD_8 及 CD_4/CD_8 比值分别是显著增高和降低 ($P < 0.001$; $P < 0.01$); 停药前后比较, 停药 3 个月后 CD_4 显著下降 ($P < 0.05$), CD_3 、 CD_8 及 CD_4/CD_8 比值无显著差别 ($P > 0.05$)。

患者治疗后, 腰酸、乏力、尿频症状有所

附表 CPN 患者与正常人外周血
细胞亚群的比较 ($\bar{x} \pm S$)

组 别	n	CD_3	CD_4	CD_8	CD_4/CD_8
对 照	36	58.50 ± 5.34	48.15 ± 4.63	33.10 ± 4.20	1.47 ± 0.19
CPN	30	53.16 $\pm 6.32^{***}$	43.15 $\pm 5.89^{***}$	38.75 $\pm 7.19^{***}$	1.14 $\pm 0.24^{***}$
脾肾气虚	18	53.41 $\pm 5.66^{**}$	42.74 $\pm 6.24^{***}$	33.10 $\pm 4.20^{**}$	1.15 $\pm 0.20^{***}$
肾阴不足	10	50.96 $\pm 5.37^{***}$	44.64 $\pm 4.73^*$	40.01 $\pm 9.08^{***}$	1.16 $\pm 0.32^{**}$
治 前					
ZLC	13	50.28 ± 6.27	44.44 ± 2.87	39.48 ± 6.34	1.17 ± 0.25
TF	11	54.22 ± 4.11	41.6 ± 8.22	37.88 ± 6.23	1.11 ± 0.23
治 后					
ZLC	13	54.86 $\pm 4.38^*$	49.10 $\pm 4.83^{**}$	38.32 ± 3.24	1.27 ± 0.17
TF	11	58.34 $\pm 4.75^*$	47.82 $\pm 5.55^{**}$	36.58 ± 4.01	1.36 $\pm 0.24^{***}$
治 疗 后	24	56.45 ± 4.79	48.51 ± 5.09	37.52 $\pm 3.64^{***}$	1.31 $\pm 0.23^{**}$
停 药 后	9	54.42 ± 6.28	44.77 $\pm 6.05^*$	39.21 ± 5.13	1.16 ± 0.26

注: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; n=例数

二、治疗前后临床症状比较

改善, 分别为 60.87% (14/23)、71.43% (15/21)、33.33% (3/9), 治疗期间 16.67% (4/24) 的患者急性发作。但两组间比较, 各项值均无显著差异 ($P > 0.05$), ZLC 组 13 例, 治疗后腰酸、乏力、尿频症状改善及无急性发作者 (例) 分别为 7/12、9/12、3/6 及 10/13; TF 组 11 例分别为 7/11、6/9、0/3 及 10/11。

讨 论

为探讨 CPN 复发机理和提高疗效, 结果发现, CPN 患者循环中总 T 细胞百分数 (CD_3) 显著下降, 分别为 CD_4 (具有辅助和诱导功能, T_H/T_i) 和 CD_8 (具有抑制和细胞毒功能, T_s/T_c) 百分率的下降和增高, 从而导致 CD_4/CD_8 比值下降 (P 均 < 0.001), 结果与 Favaro 等一致^[2], 证明了 CPN 患者存在着 CMI 功能的紊乱。本结果有助于解释临床上部分无不利因素存在的 CPN 患者同样易反复急性发作, 提示免疫学因素在这部分患者的发病中起一定作用, 可能与疾病复发有关, 认为外周血 CD_4/CD_8 比值降低是肾功能正常的 CPN 患者免疫学改变的一个标志。

在抗菌治疗同时, 患者用 ZLC/TF 3 个月, 外周血 CD_3 、 CD_4 明显增高 ($P < 0.05$; $P < 0.01$), CD_8 无明显改善 ($P > 0.05$), 与此同时临床症状明显好转。停 ZLC 或 TF 3 月后, CD_4 显著下降 ($P < 0.05$), 说明两药作用时间较短, 需要较长期用药。

总之, 从实验结果及临床疗效来看, ZLC 或 TF 并结合各种抗生素治疗, 较单用抗生素或清热解毒药效果理想, 这对无不利因素存在、易反复发作的 CPN 患者, 或确有 CMI 功能紊乱者, 是一种值得推荐的方法。

参 考 文 献

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59. They were $39.7 \pm 7.4\%$, $31.2 \pm 5.8\%$, $8.5 \pm 2.7\%$ and 41.84 ± 2.66 respectively in the deficiency of Kidney-Yang(阳). The results of normal group were $65.5 \pm 6.8\%$, $53.6 \pm 6.7\%$, $11.9 \pm 3.4\%$ and 54.78 ± 3.34 in their given order. The differences in three groups each other were marked significantly. The authors have found the difference between the patients of chronic glomerulonephritis and the normal individuals was significant statistically. (Original article on page 399)

Cell-Mediated Immunity in Chronic Pyelonephritis

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The authors used monoclonal antibody (CD_3 , CD_4 , CD_8) and indirect immunofluorescence technic to study peripheral blood lymphocyte surface markers in patients with chronic pyelonephritis (CPN) and in normal controls. In CPN patients, a significant decrease in CD_3 , a lower percentage of CD_4 and significant higher percentage of CD_8 leading to a decrease in the CD_4/CD_8 ratio were noted. No differences could be observed between Spleen-Kidney Yang(阳) deficiency and Kidney Yin(阴) deficiency. The overall picture shown by the CPN patients was compatible to a cell-mediated immune response defection. The CPN patients were then treated with Zi-Ling capsule (至灵胶囊, ZLC)/transfer factor (TF) and various antibiotics for three months, during which period the authors found a significant increase in CD_3 , CD_4 , but no significant change in CD_8 . Symptoms such as lumbago, fatigue, frequency of urination were improved. A significant decrease in CD_4 after cessation of treatment with ZLC and TF was observed. These observations suggested that both ZLC and TF could also improve the immune function, however, they mainly affect CD_4 but not CD_8 cells, and the effect lasted for only a short period. In conclusion, ZLC/TF and antibiotics administered together would serve as a useful therapeutic measure to be recommended for patients with CPN.

(Original article on page 402)

Effect of Baoshen Wan(保肾丸) on Serum LPO Level of Nephritis

Treating by Differentiation-Syndromes

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This paper deals with the treatment of 22 cases of chronic nephritis with Baoshen Wan (protecting kidney pills) according to the differentiation of syndromes; the result showed that 3 cases had got perfect remission, 6 cases fundamental remission, and 10 cases partial remission; thus its effective rate reached to 86.4%. Before treatment, the mean value of serum LPO of the 22 patients was 4.44 ± 0.099 ($\bar{x} \pm S\bar{x}$, $\mu\text{mol/L}$), which compare with the normal value (3.69 ± 0.075), $P < 0.05$. After treatment, the serum LPO level was lowered to 3.95 ± 0.11 , $P < 0.05$. It suggested that Baoshen Wan could dispell the free radical and lower the serum LPO level in the patients with chronic nephritis.

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Effect of Blood-Activating and Stasis-Removing Drugs on

Hypercoagulable Data in Nephrotic Syndrome

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Platelet aggregation test (PAgT), plasma factor VIII related antigen (VIII R:Ag) and kaolin partial thromboplastin time (KPTT) in 32 nephrotic children were determined. Results: (1) PAgT induced by ADP and adrenaline which included 1 minute and 5 minute aggregation rate in the patients ($30.78 \pm 7.44\%$, $72.56 \pm 18.09\%$, $22.16 \pm 9.24\%$, $67.53 \pm 22.32\%$) was significantly increased ($P < 0.02 \sim 0.001$) as compared with the normal control group ($30.65 \pm 8.38\%$, $57.98 \pm 13.60\%$, $18.14 \pm 7.33\%$, $55.92 \pm 16.10\%$) except 1 minute aggregation rate induced by ADP ($P > 0.05$). (2) VIII R:Ag and KPTT in patients ($226.97 \pm 50.47\%$, 32.04 ± 5.88 sec) were obviously different ($P < 0.001$, $P < 0.02$) from the normal control group ($107.11 \pm 24.55\%$, 35.42 ± 5.00 sec). The results suggested that PAgT, VIII R:Ag and KPTT could be used as laboratory data reflecting the hypercoagulable state in nephrotic children. According to their age, sex and the clinical types of nephrotic syndrome, 24 nephrotic children with abnormality of PAgT, VIII R:Ag and KPTT were random divided into group 1 given prednisone only and group 2 given prednisone, blood-activating and stasis-removing drugs. Results: the difference of