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老年社区获得性肺炎患者 TNF- α 和 sTREM-1 的表达及临床意义*

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摘要 目的:探讨老年社区获得性肺炎患者 TNF- α 和 sTREM-1 表达水平及其临床意义。**方法:**从我院选择 48 例社区获得性肺炎患者为 CAP 组(重症组和普通组),另选取对照组 48 例。收集两组患者的血浆及 BALF,分别收集重症组患者住院后 1 天、4 天的血浆和 BALF,对比各组 sTREM-1 和 TNF- α 的表达水平。**结果:**对照组 TNF- α 和 sTREM-1 的表达水平均低于 CAP 组 ($P < 0.05$);重症患者的 TNF- α 和 sTREM-1 表达水平高于普通组和健康对照组($P < 0.05$)。重症患者 TNF- α 表达水平与对照组无显著差异($P > 0.05$),而 sTREM-1 表达高于对照组,差异有统计学意义($P < 0.05$)。**结论:**TNF- α 和 sTREM-1 表达水平与 CAP 的发病过程密切相关,其表达水平与 CAP 的严重程度呈正相关。

关键词:社区获得性肺炎; CAP; TNF- α ; sTREM-1

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Expression of TNF- α and sTREM-1 in Patients with Community-acquired Pneumonia and its Clinical Significance*

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ABSTRACT Objective: To explore the clinical significance of the expression of TNF- α and STREM-1 in elderly patients with community-acquired pneumonia (CAP). **Methods:** 48 CAP patients from Department of Respiratory Medicine in our hospital were enrolled based on the selection criteria and divided into severe group and ordinary group. The plasma and bronchoalveolar lavage fluid (BALF) of CAP group, control group, severe CAP patients' first day and fourth day after treatment in hospital were collected. The expression levels of sTREM-1 and TNF- α of each group were compared. **Results:** TNF- α and STREM-1 levels of control group were lower than those of CAP group with statistically significant differences ($P < 0.05$). TNF- α and STREM-1 levels of severe CAP patients were higher than ordinary CAP patients and healthy controls ($P < 0.05$). No obvious differences existed between TNF- α level of severe CAP patients and lung cancer controls ($P > 0.05$). Significant differences existed between sTREM-1 level of severe CAP patients and lung cancer controls ($P < 0.05$). **Conclusion:** The expression levels of TNF- α and sTREM-1 were associated with pathogenesis and progression and severity of CAP.

Key words: Community-acquired pneumonia; CAP; TNF- α ; sTREM-1

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前言

随着空气污染的加重,呼吸系统的疾病的发病率也日趋严重,病死率也是有增无减。根据权威调查显示^[1],2010 年的全国的人口死亡病因中呼吸系统疾病占第三,其中,我国社区肺部感染发病率高达 10%-15%。社区获得性肺炎(communitary-acquired pneumonia, CAP)是指在医院外罹患的感染性肺实质肺炎,包括具有明确潜伏期的病原体感染而在入院后潜伏期内发

病的肺炎^[2,3]。

随着我国人口老龄化加剧,老年人口基数加大,另外老年人免疫力低下合并多种疾病,老年老年社区获得性肺炎也日益严重,其全球病死率高达占 10%左右^[4]。但由于老年社区获得性肺炎患者往往缺少典型的临床表现,临床上对老年 CAP 的研究比较少,也缺少明确诊断的指标^[5,6]。可溶性髓系细胞触发受体 1 (soluble triggering receptor expressed on myeloid cell-1, sTREM-1)在免疫过程发挥重要作用,也是促炎因子^[7,8],另外

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促肿瘤坏死因子(tumor necrosis factor, TNF- α)大量释放不但与免疫反应相关还与感染密切相关^[9]。本文通过对老年 CAP 患者疾病发展过程 TNF- α 和 sTREM-1 的表达水平变化的观察,探究 TNF- α 和 sTREM-1 的表达水平的临床价值。

1 资料和方法

1.1 一般资料

从 2012 年度我院呼吸内科住院部的患者中选 48 例 CAP 患者,男 28 例,女 20 例,重症 16 例,普通 32 例,平均年龄(71.3 $\pm$ 5.6)岁,均按照临床诊断标准诊断为 CAP,所有入选患者均未接受抗生素治疗。选取与患者同一小区内同期体检无肺部感染的老年人 48 人为对照组,其中 18 例为肺癌患者分为对照组 1,均经射线诊断为肺部包块,病理检查结果显示为肺癌,但患者不伴有感染;30 例健康老年人分为对照组 2。对照组平均年龄(72.2 $\pm$ 6.1)岁,男 26 例,女 22 例。纳入标准:研究组患者均经入院常规检查符合中华医学会呼吸病学分会 2006 年的 CAP 诊断标准:出现每分钟呼吸频率 $\geq$ 30 次、PaO₂< 60 mmHg、少尿:尿量小于 20 mL/h、并发脓毒症休克、并发急性肾功能衰竭、透析治疗、多侧肺叶受累病灶大于 50%其中一种或者一种以上的情况判定为重症患者。

1.2 方法

所有患者空腹采血并将血浆经生化仪分析,纤维支气管镜检收集受试者第一、四天的肺泡灌洗液(BALF);收集 TNF- α 和 sTREM-1 使用酶联免疫法测定,严格按照试剂盒的说明书操作,分别比较各对照组和研究组的 TNF- α 和 sTREM-1 的表达水平。

1.3 统计学方法

统计软件使用 SPSS17.0,计量资料使用均数 $\pm$ 标准差($\bar{x} \pm s$),多组资料比较使用方差,两两比较使用 T 检验,检验水准取为 0.05。

2 结果

2.1 各组血浆中的 TNF- α 和 sTREM-1 的比较情况

健康对照组 TNF- α 水平低于重症组及肺癌对照组,差异有统计学意义($P < 0.05$);重症组高于普通组及肺癌对照组,但差异无统计学意义($P > 0.05$);sTREM-1 水平与 TNF- α 相似,健康对照组低于重症组、普通组、肺癌对照组,差异有统计学意义($P < 0.05$);重症组与普通组,普通组与肺癌组无显著差异($P > 0.05$)。见表 1。

表 1 各组血浆的 TNF- α 和 sTREM-1 的对比情况

Table 1 Comparison of plasma TNF- α and sTREM-1 levels of each group

Group	N	TNF- α (ng/L)	sTREM-1 (ng/L)
Severe CAP group	16	97.52 $\pm$ 14.28	75.67 $\pm$ 28.78
Ordinary CAP group	32	83.70 $\pm$ 5.48	65.81 $\pm$ 16.12
Control group 1	30	92.50 $\pm$ 7.10	57.21 $\pm$ 4.78
Control group 2	18	72.79 $\pm$ 4.37	44.81 $\pm$ 4.22

Note: T test was used for inter-group comparison.

2.2 各组 BALF 中的 TNF- α 和 sTREM-1 的比较情况

BALF 中,对照组和普通组 TNF- α 水平均低于重症组,差异有统计学意义($P < 0.05$),重症组高于普通组及肺癌组,但差异无统计学意义($P > 0.05$);BALF 中 sTREM-1 水平与 TNF- α 相似,健康对照组低于重症组和普通组,差异有统计学意义($P < 0.05$);但健康对照组 sTREM-1 水平与肺癌组差异无统计学意义($P > 0.05$)。见表 2。

表 2 各组 BALF 中的 TNF- α 和 sTREM-1 的对比情况

Table 2 Comparison of BALF TNF- α and sTREM-1 levels of each group

Group	N	TNF- α (ng/L)	sTREM-1 (ng/L)
Severe CAP group	16	57.12 $\pm$ 8.19	245.67 $\pm$ 48.34
Ordinary CAP group	32	43.43 $\pm$ 5.48	205.26 $\pm$ 46.58
Control group 1	30	52.35 $\pm$ 5.26	175.42 $\pm$ 14.34
Control group 2	18	37.56 $\pm$ 4.61	164.59 $\pm$ 24.04

Note: Samples from severe CAP group were collected for the first time, and T test was used for inter-group comparison.

3 讨论

通常入侵机体病原体的数量、毒素释放的量,机体免疫应答的强弱是决定肺炎病情的严重的主要因素^[10]。老年人免疫力低,CAP 易导致老年人死亡,加上老年患者新陈代谢较弱,患者一般少痰,不会表现出呼吸道疾病(CAP)的典型症状,临床易出现漏诊及误诊^[11]。因此,开发一种特异性强、敏感度高的检测标志物是目前研究的重点。

肿瘤坏死因子 TNF- α 和髓系细胞触发受体 TREM-1 都被确认参与炎症反应的过程,是参与脓毒症的重要介质^[12]。TNF- α 是一种小蛋白分子,其分泌可能通过多种途径,TNF- α 的释放后启动炎症的级联反应,但 TNF- α 的水平过高时炎症反应过度反倒会损伤组织,使整个炎症反应过程失调^[13]。sTREM-1 分子结构包括三个部分:胞外域、跨膜域、胞浆区。中性粒细胞和巨噬细胞等细胞表达 sTREM-1 的量最多,在炎症级联反应中发挥着放大作用^[14]。据相关研究证实,TNF- α 和 sTREM-1 与 CAP 发展过程有关,老年 CAP 患者严重感染时,受体及细胞因子的表达活跃程度显著提高^[15]。也有研究发现,TNF- α 和 TREM-1 与脓毒症的诊断和预后评估有密切联系^[16]。还有研究证实,sTREM-1 水平的高低反应了感染的程度,严重感染时会显著升高,临床可用于评估感染性疾病的发展和预后^[17]。大量文献表明,酶联免疫法能快速检测出 sTREM-1 的表达水平,肺部感染患者较健康未感染者的血浆及肺部灌洗液中 TNF- α 和 sTREM-1 都显示较高水平^[18-20]。

本研究中,CAP 组的 TNF- α 和 sTREM-1 表达水平显著高于对照组的 TNF- α 和 sTREM-1 表达水平($P < 0.05$),重症 CAP 组患者的 TNF- α 和 sTREM-1 的水平显著高于普通 CAP 组($P < 0.05$),提示 TNF- α 和 sTREM-1 与老年 CAP 病情严重程度正相关,说明 TNF- α 和 sTREM-1 是评估老年 CAP 的指标。

综上所述,TNF- α 和 sTREM-1 水平能提示 CAP 不同阶段的病情及其严重程度,有助于合理使用抗生素的对症治疗,提高治疗效果和改善老年 CAP 的预后。

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