



白细胞介素-4、C-反应蛋白与特应性皮炎及度普利尤单抗 治疗效果的关系*

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【摘要】目的 分析白细胞介素(interleukin, IL)-4、C-反应蛋白(C-reactive protein, CRP)与特应性皮炎发病、病情严重程度及度普利尤单抗治疗疗效的关系。**方法** 回顾性选取2022年2月-2023年11月就诊的106例特应性皮炎患者作为研究组,另选同期健康志愿者50例作为对照组,检测研究组不同分期(急性期、亚急性期、慢性期)、不同病情严重程度(轻、中、重)与对照组的IL-4、CRP水平,使用受试者工作特征(receiver operating characteristic, ROC)曲线分析IL-4、CRP对特应性皮炎的诊断价值。使用Spearman分析特应性皮炎患者病情严重程度与IL-4、CRP水平的关系。所有特应性皮炎患者均接受规范16周的度普利尤单抗治疗,分为治疗有效组与治疗无效组,比较患者治疗前及治疗4周、8周、12周、16周的IL-4、CRP水平变化,分析治疗后各时间点的IL-4、CRP与疗效的相关性。**结果** IL-4、CRP水平均为慢性期<亚急性期<急性期($P<0.05$),轻度组<中度组<重度组($P<0.05$);治疗前研究组IL-4、CRP水平分别为(14.88 ± 3.91) pg/mL、(6.07 ± 3.02) mg/L,高于对照组的(8.27 ± 1.09) pg/mL、(1.06 ± 0.31) mg/L,差异有统计学意义($P<0.05$)。IL-4、CRP及二者联合诊断特应性皮炎的曲线下面积分别为0.831[95%置信区间(confidence interval, CI): 0.763 ~ 0.886]、0.776(95%CI: 0.702 ~ 0.839)、0.882(95%CI: 0.821 ~ 0.928)($P<0.05$);Spearman分析显示,特应性皮炎患者IL-4、CRP水平与病情严重程度均呈正相关($r=0.643$ 、 0.659 , $P<0.05$);随着治疗时间的增加,IL-4、CRP水平逐渐降低,有效组与治疗无效组间差异有统计学意义($P<0.05$);治疗有效组患者治疗前后各时点的IL-4、CRP水平均低于治疗无效组同期($P<0.05$);Spearman分析显示,特应性皮炎患者IL-4、CRP水平与治疗12周($r=0.267$ 、 0.280 , $P<0.05$)、治疗16周的疗效均呈正相关($r=0.214$ 、 0.377 , $P<0.05$)。**结论** IL-4、CRP与特应性皮炎的发生、发展存在相关性,度普利尤单抗治疗后患者IL-4、CRP水平显著下降,且IL-4、CRP在特应性皮炎诊断中具有一定价值。

【关键词】 白细胞介素-4 C-反应蛋白 特应性皮炎 度普利尤单抗治疗 临床疗效

The Relationship Between Interleukin-4, C-reactive Protein, Atopic Dermatitis, and the Therapeutic Effect of Dupilumab

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【Abstract】 Objective To analyze the relationship between interleukin-4 (IL-4), C-reactive protein (CRP), and the incidence, severity, and therapeutic efficacy of Dupilumab in atopic dermatitis. **Methods** A total of 106 patients with atopic dermatitis treated from February 2022 to November 2023 were retrospectively selected as the study group, and 50 healthy volunteers from the same period were selected as the control group. The levels of IL-4 and CRP were measured at different stages (acute, subacute, chronic) and severities (mild, moderate, severe) in both the study and control groups. Receiver operating characteristic (ROC) curves were used to analyze the diagnostic value of IL-4 and CRP in atopic dermatitis. Spearman analysis was used to assess the relationship between the severity of atopic dermatitis and the levels of IL-4 and CRP in patients. All patients with atopic dermatitis received standardized 16-week treatment with pembrolizumab and were divided into effective and ineffective treatment groups. Changes in IL-4 and CRP levels before treatment and at 4, 8, 12, and 16 weeks of treatment were compared, and the correlation between IL-4, CRP, and treatment efficacy at each time point after treatment was analyzed. **Results** The levels of IL-4 and CRP were lowest in the chronic phase, higher in the subacute phase, and highest in the acute phase ($P < 0.05$), with the mild group showing lower levels than the moderate group, and the moderate group lower than the severe group ($P < 0.05$). Before treatment, the levels of IL-4 and CRP in the study group were (14.88 ± 3.91) pg/mL and (6.07 ± 3.02) mg/L, respectively, both

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significantly higher than those in the control group, which were (8.27 ± 1.09) pg/mL and (1.06 ± 0.31) mg/L ($P < 0.05$). The areas under the curve for IL-4, CRP, and their combined diagnosis of atopic dermatitis were 0.831 (95% CI: 0.763-0.886), 0.776 (95% CI: 0.702-0.839), and 0.882 (95% CI: 0.821-0.928), respectively ($P < 0.05$). Spearman analysis showed that IL-4 and CRP levels in patients with atopic dermatitis were positively correlated with disease severity ($r = 0.643, 0.659, P < 0.05$). As treatment time increased, IL-4 and CRP levels gradually decreased, with a statistically significant difference between the effective and ineffective groups ($P < 0.05$). At all time points before and after treatment, IL-4 and CRP levels in the effective treatment group were lower than those in the ineffective treatment group ($P < 0.05$). Spearman analysis also showed that IL-4 and CRP levels in patients with atopic dermatitis were positively correlated with treatment efficacy at 12 weeks ($r = 0.267, 0.280, P < 0.05$) and 16 weeks ($r = 0.214, 0.377, P < 0.05$). **Conclusion** IL-4 and CRP are correlated to the occurrence and development of atopic dermatitis. After treatment with Dupilumab, the levels of IL-4 and CRP in patients significantly decreased. IL-4 and CRP have diagnostic value for atopic dermatitis.

[Key words] Interleukin-4 C-reactive protein Atopic dermatitis Dupilumab treatment Clinical curative effect

特应性皮炎是全球范围内最常见的非致命性皮肤病,患者通常合并鼻炎、哮喘、过敏体质等其他特应性疾病,故也被认为是一种系统性疾病^[1]。特应性皮炎具有慢性、易复发、炎症性皮肤病等倾向,临床认为这与基因异常导致的免疫失衡密切相关,除此外皮肤屏障功能、食物过敏、皮肤菌群紊乱等因素也参与其中^[2]。流行病学报告显示,全球范围内成人特应性皮炎发病率约为10%,儿童特应性皮炎发病率约为20%,我国儿童特应性皮炎发病率约为13%^[3]。大多数特应性皮炎患者在婴儿期发病,随着年龄增长病情大部分可逐渐好转,但仍有相当一部分患者在成年期甚至老年期发病,这类患者往往表现出更强的持续性、反复性,患者就诊时往往还伴有严重睡眠障碍、神经障碍^[4]。特应性皮炎并非单纯性皮肤病,而是以皮肤瘙痒、免疫失衡为表现的全身性疾病,严重影响患者生活质量^[5]。度普利尤单抗治疗是现阶段中、重度特应性皮炎新型治疗方法,通过双靶点的作用机制可以显著降低参与辅助型T细胞2(T helper 2 cell, Th2)炎症反应的基因表达,其可覆盖年龄6个月以上全段^[6]。白细胞介素(interleukin, IL)-4属于IL家族成员,IL成员在免疫应答过程与白细胞间发挥重要作用,IL-4作为Th2细胞因子参与免疫细胞分化、激活^[7]。C-反应蛋白(C-reactive protein, CRP)是一种球蛋白,对感染、非感染引起的炎症反应均具有较高的敏感度,属于非特异的炎症标志物^[8]。鉴于此背景,本研究选取2022年2月-2023年11月于邢台市中心医院就诊的106例特应性皮炎患者进行研究,分析了IL-4、CRP在特应性皮炎中的临床意义以及度普利尤单抗治疗前后的变化。

1 资料与方法

1.1 一般资料

本研究经邢台市第三医院伦理委员会审批(批准号:

2022-KY-18)。回顾性选取2022年2月-2023年11月于邢台市中心医院就诊的106例特应性皮炎患者作为研究组。纳入标准:①参考《中国特应性皮炎诊疗指南(2020版)》^[9]临床诊断为特应性皮炎;②患者年龄 ≥ 18 岁,入组前4周未接受相关系统性治疗且符合度普利尤单抗治疗标准;③患者对本研究知情同意;④在我院接受规范16周度普利尤单抗治疗。排除标准:①合并感染、恶性肿瘤、严重心脑血管疾病、内分泌疾病、精神障碍患者;②治疗期间病情急性加重给予其他药物联用;③合并其他皮肤病。另选同期进行健康体检的健康志愿者50例作为对照组。纳入标准:年龄 ≥ 18 岁、无特应性皮炎家族史、无慢性感染性疾病、无自身免疫性疾病、无恶性肿瘤及心脑血管疾病史、近6个月内未使用免疫调节药物。在入组时,对所有对照组人员进行详细问卷调查及体格检查,排除皮肤疾病、过敏史及其他可能影响炎症指标的疾病,确保与研究组在年龄、性别、基础健康状态等关键混杂因素方面具有同质性。

1.2 方法

1.2.1 指标检测方法

收集研究组患者治疗前及治疗4周、8周、12周、16周的以及健康志愿者体检当日空腹静脉血,离心半径8 cm, 3 000 r/min离心10 min,取上层清液,使用ELISA法检测IL-4、CRP水平,试剂盒购自上海科爱博生物。

1.2.2 不同分期分组方法

依据患者皮肤损害特点及病程,由2名高年资皮肤科医师共同判定分期。急性期:皮疹以红斑、丘疹为主,伴有明显渗出、水肿,瘙痒剧烈;亚急性期:红肿减轻,以鳞屑、结痂为主要表现,瘙痒程度稍缓;慢性期:皮肤粗糙肥厚,有苔藓样变,瘙痒呈阵发性。

1.2.3 病情严重程度分组方法

使用特应性皮炎评分指数(Scoring Atopic Dermatitis

Index, SCORAD)^[10]评估研究组患者病情严重程度,该量表从皮肤损伤、皮肤瘙痒、夜间睡眠等维度评估患者病情严重程度,总分103分,其中0~24分纳入轻度组,25~50分纳入中度组,51~103分纳入重度组。

1.2.4 度普利尤单抗治疗方法

所有特应性皮炎患者给予Sanofi Winthrop Industrie公司生产的度普利尤单抗注射液〔批号: 2022004,规格300 mg(2 mL/支)〕皮下注射,初始剂量600 mg,之后每2周后给予300 mg皮下注射1次,共进行16周。

1.2.5 临床疗效评估方法

根据患者治疗16周后病情改善情况,将疗效分为有效: SCORAD评分下降幅度为50%~100%;无效: 未达上述有效标准^[9]。

1.3 统计学方法

本研究选用SPSS23.0统计软件进行数据的分析,经检验符合正态分布的计量资料采用 $\bar{x} \pm s$ 来表示,两组间比较使用两独立样本 t 检验,两组内比较使用配对样本 t 检验,多组间比较采用秩和检验或 F 检验;计数资料使用例

(%)表示,使用卡方检验。使用受试者工作特征(receiver operating characteristic, ROC)曲线分析IL-4、CRP对特应性皮炎的诊断价值。将IL-4与CRP同时纳入二元logistic回归模型构建联合指标,基于回归系数计算联合预测概率,再使用ROC曲线分析两个指标联合检测对特应性皮炎的诊断价值。使用Spearman分析特应性皮炎患者病情严重程度与IL-4、CRP水平的关系及治疗后各时间点IL-4、CRP水平与疗效的关系。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 研究组与对照组的一般资料比较

研究组年龄21~65岁,平均(41.23±9.54)岁;男64例,女42例;体质量指数20.15~25.68 kg/m²,平均(23.14±2.35) kg/m²;吸烟史38例、饮酒史31例。对照组年龄28~60岁,平均(40.27±7.92)岁;男31例,女19例;体质量指数20.08~25.36 kg/m²,平均(22.56±2.16) kg/m²;吸烟史22例、饮酒史18例。两组一般资料比较具有同质性,差异无统计学意义($P>0.05$),见表1。

表 1 研究组与对照组的一般资料比较

Table 1 Comparison of general data between study group and control group

Group	<i>n</i>	Sex/case (%)		Age/yr.	Body mass index/(kg/m ²)	Smoking history/case (%)		Drinking history/case (%)	
		Female	Male			Yes	No	Yes	No
Study	106	64 (60.38)	42 (39.62)	41.23 ± 9.54	23.14 ± 2.35	38 (35.85)	68 (64.15)	31 (29.25)	75 (70.75)
Control	50	31 (62.00)	19 (38.00)	40.27 ± 7.92	22.56 ± 2.16	22 (44.00)	28 (56.00)	18 (36.00)	32 (64.00)
t/χ^2		0.038		0.618	1.475	0.954		0.720	
P		0.846		0.538	0.142	0.329		0.396	

2.2 研究组不同分期的IL-4、CRP水平比较

依据患者皮肤损害特点及病程分组,最终慢性期纳入53例,亚急性期纳入36例,急性期纳入17例。慢性期患者IL-4、CRP水平均低于亚急性期,亚急性期患者IL-4、CRP水平均低于急性期,且3组间比较,差异有统计学意义($P<0.05$),见表2。

表 2 研究组不同分期的IL-4、CRP水平比较

Table 2 Comparison of IL-4 and CRP levels during different staging in study group

Stage	<i>n</i>	IL-4/(pg/mL)	CRP/(mg/L)
Chronic	53	12.84 ± 2.16	4.72 ± 1.36
Subacute	36	15.28 ± 3.59 ^a	6.15 ± 2.68 ^a
Acute	17	20.39 ± 4.73 ^{a,b}	10.11 ± 2.64 ^{a,b}
H		34.952	57.243
P		< 0.001	< 0.001

IL-4: interleukin-4; CRP: C-reactive protein. ^a $P<0.05$, vs. chronic stage;
^b $P<0.05$, vs. subacute stage.

2.3 研究组与对照组的IL-4、CRP水平比较

治疗前研究组IL-4、CRP水平高于对照组,差异有统计学意义($P<0.05$),见表3。

表 3 研究组与对照组的IL-4、CRP水平比较

Table 3 Comparison of IL-4 and CRP levels between study group and control group

Group	<i>n</i>	IL-4/(pg/mL)	CRP/(mg/L)
Study	106	14.88 ± 3.91	6.07 ± 3.02
Control	50	8.27 ± 1.09	1.06 ± 0.31
t		11.723	11.682
P		< 0.001	< 0.001

IL-4: interleukin-4; CRP: C-reactive protein.

2.4 IL-4、CRP对特应性皮炎的诊断效能分析

ROC曲线分析结果显示,IL-4、CRP联合诊断特应性皮炎的曲线下面积高于IL-4、CRP单独检测($P<0.05$)。见表4、图1。

表 4 IL-4、CRP对特应性皮炎的诊断效能分析
Table 4 Diagnostic efficiency of IL-4 and CRP in atopic dermatitis

Index	AUC	P	95% CI
IL-4	0.831	< 0.001	0.763-0.886
CRP	0.776	< 0.001	0.702-0.839
Combination	0.882	< 0.001	0.821-0.928

IL-4: interleukin-4; CRP: C-reactive protein; AUC: area under the curve.

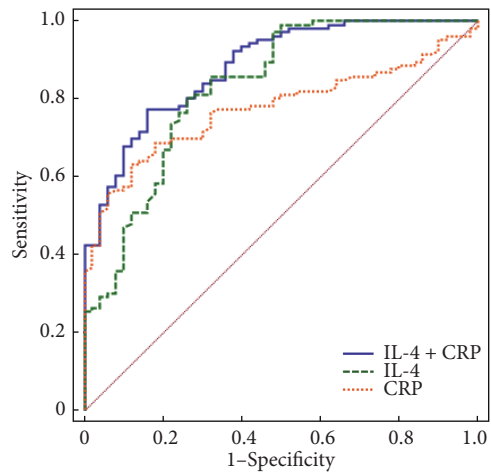


图 1 IL-4、CRP诊断特应性皮炎的ROC曲线
Fig 1 ROC curves of IL-4 and CRP in diagnosis of atopic dermatitis
IL-4: interleukin-4; CRP: C-reactive protein.

2.5 不同病情严重程度患者的IL-4、CRP水平比较

使用SCORAD评估,按照病情的严重程度分组,最终轻度组纳入58例,中度组纳入33例,重度组纳入15例。轻度组患者IL-4、CRP水平均低于中度组,中度组患者IL-4、CRP水平均低于重度组,且3组间比较差异有统计学意义($P < 0.05$),见表5。

表 5 不同病情严重程度患者的IL-4、CRP水平比较
Table 5 Comparison of IL-4 and CRP levels in patients with different disease severity

Group	n	IL-4/(pg/mL)	CRP/(mg/L)
Mild	58	12.97 ± 2.01	4.42 ± 1.47
Moderate	33	15.56 ± 3.26 ^a	7.06 ± 2.54 ^a
Severe	15	20.75 ± 4.40 ^{a,b}	10.26 ± 3.40 ^{a,b}
H		39.473	51.578
P		< 0.001	< 0.001

IL-4: interleukin-4; CRP: C-reactive protein. ^a $P < 0.05$, vs. mild group; ^b $P < 0.05$, vs. moderate group.

2.6 特应性皮炎患者病情严重程度与IL-4、CRP水平的相关性分析

使用Spearman分析特应性皮炎患者IL-4、CRP水平与病情严重程度的相关性,赋值方式:病情严重程度以SCORAD得分赋实际值,IL-4、CRP赋实际值。Spearman分析显示,特应性皮炎患者IL-4、CRP水平与病情严重程

度均呈正相关($r = 0.643$ 、 0.659 , $P < 0.05$),见附表1。相关性散点图见附图1、附图2。所有附表和附图见网络资源附件。

2.7 特应性皮炎患者度普利尤单抗治疗前及治疗后不同时间点IL-4、CRP水平比较

随着治疗时间的增加,IL-4、CRP水平逐渐降低,各组间差异有统计学意义($P < 0.05$),见附表2。

2.8 不同疗效特应性皮炎患者IL-4、CRP水平比较

106例特应性皮炎患者经过度普利尤单抗治疗临床疗效评估,治疗有效91例,治疗无效15例。随治疗时间延长,两组患者IL-4、CRP水平均呈持续下降趋势,且治疗有效组治疗后各时间节点(4周、8周、12周、16周)的IL-4、CRP水平均低于同期治疗无效组,组间差异具有统计学意义($P < 0.05$),见表6。

表 6 治疗有效组与治疗无效组的IL-4、CRP水平比较
Table 6 Comparison of IL-4 and CRP levels between effective treatment group and ineffective treatment group

Measure	Effective treatment group (n = 91)	Ineffective treatment group (n = 15)	t	P
IL-4/(pg/mL)				
Before treatment	14.42 ± 3.54	17.69 ± 4.75	3.149	0.002
After 4 of treatment	12.72 ± 3.16 ^a	15.56 ± 3.57 ^a	3.167	0.002
After 8 of treatment	10.11 ± 2.84 ^{a,b}	13.27 ± 3.12 ^{a,b}	3.938	< 0.001
After 12 of treatment	7.87 ± 1.24 ^{a,b,c}	10.53 ± 1.83 ^{a,b,c}	7.152	< 0.001
After 16 of treatment	6.02 ± 2.00 ^{a,b,c,d}	7.83 ± 1.80 ^{a,b,c,d}	3.290	0.001
Difference 1	1.70 ± 0.56	2.13 ± 0.64	2.700	0.008
Difference 2	4.31 ± 0.74	4.42 ± 0.66	0.541	0.589
Difference 3	6.55 ± 1.06	7.16 ± 1.12	2.049	0.043
Difference 4	8.40 ± 1.68	9.86 ± 2.11	3.004	0.003
CRP/(mg/L)				
Before treatment	5.75 ± 2.75	8.01 ± 3.73	2.795	0.006
After 4 of treatment	4.92 ± 1.68 ^a	7.06 ± 2.45 ^a	4.259	< 0.001
After 8 of treatment	3.96 ± 1.38 ^{a,b}	6.28 ± 2.11 ^{a,b}	5.553	< 0.001
After 12 of treatment	2.57 ± 0.79 ^{a,b,c}	4.63 ± 0.86 ^{a,b,c}	9.243	< 0.001
After 16 of treatment	2.04 ± 0.52 ^{a,b,c,d}	3.33 ± 1.10 ^{a,b,c,d}	7.348	< 0.001
Difference 1	0.83 ± 0.11	0.95 ± 0.14	3.761	< 0.001
Difference 2	1.79 ± 0.45	1.73 ± 0.42	0.483	0.630
Difference 3	3.18 ± 0.87	3.38 ± 0.85	0.827	0.410
Difference 4	3.71 ± 0.91	4.68 ± 1.06	3.736	< 0.001

IL-4: interleukin-4; CRP: C-reactive protein. ^a $P < 0.05$, vs. before the treatment; ^b $P < 0.05$, vs. after 4 weeks of treatment; ^c $P < 0.05$, vs. after 8 weeks of treatment; ^d $P < 0.05$, vs. after 12 weeks of treatment; Difference 1: difference between results before treatment and those after 4 weeks of treatment; Difference 2: difference between results before treatment and those after 8 weeks of treatment; Difference 3: difference between results before treatment and those after 12 weeks of treatment; Difference 4: difference between results before treatment and those after 16 weeks of treatment.

2.9 特应性皮炎患者治疗后各时间点IL-4、CRP水平与疗效的相关性分析

使用Spearman分析特应性皮炎患者治疗后各时间点IL-4、CRP水平与疗效的相关性分析,赋值方式:疗效以SCORAD得分赋实际值,IL-4、CRP赋实际值。Spearman分析显示,特应性皮炎患者IL-4、CRP水平与治疗12周的疗效均呈正相关($r=0.267, 0.280, P<0.05$);与治疗16周的疗效均呈正相关($r=0.214, 0.377, P<0.05$),见附表3。

3 讨论

现阶段治疗特应性皮炎以抗过敏药物为主,通过抑制免疫系统的异常激活,调节一系列过度升高的炎症因子,但传统药物只对抗组胺,疗效难以达到理想效果^[11]。度普利尤单抗是针对常规治疗疗效不佳患者的新型治疗手段,2017年在美国获批使用,2020年在我国获批使用,目前用药支持证据尚不丰富^[12]。与传统治疗方法相比,度普利尤单抗治疗具有精准性、高效性,可快速、持续改善瘙痒,进而提高患者生活、工作质量^[13]。度普利尤单抗作为首个靶向调节特应性皮炎关键免疫发病机制的人源化单克隆抗体,可以选择性阻断IL-4等信号传导,发挥调节免疫系统平衡的作用,抑制2型炎症反应,抑制促炎细胞因子的释放^[14]。意大利学者研究指出度普利尤单抗显示出对青少年特应性皮炎体征和症状的显著改善且安全性良好,对中、重度青少年特应性皮炎有效性和安全性良好^[15]。王佳怡等^[16]学者研究指出度普利尤单抗可有效改善中重度特应性皮炎患者皮肤瘙痒、皮损,提高患者生活质量。基于此,本研究分析了IL-4、CRP在特应性皮炎中的临床意义以及度普利尤单抗治疗前后的变化。

特应性皮炎患者急性期IL-4、CRP水平高于亚急性期与慢性期,表明炎症因子水平与疾病活动度密切相关。急性期皮损以渗出、水肿为特征,大量Th2细胞浸润并释放IL-4、IL-13,同时表皮屏障破坏导致微生物定植增加,进一步激活Toll样受体通路,促使CRP等炎症介质释放。慢性期患者因长期搔抓导致皮肤苔藓样变,Th1/Th17细胞比例上升,Th2型炎症相对减弱,可能解释了IL-4水平的下降^[17]。本研究将特应性皮炎患者IL-4、CRP水平与健康志愿者进行了比较,发现特应性皮炎患者IL-4、CRP水平异常偏高,这与既往研究结果相符^[18]。Th2细胞的过量产生导致人体免疫向Th2倾斜,IL-4等细胞因子产生增加,又进一步导致外周血和组织中的IgE抗体和嗜酸性粒细胞被影响,发生炎症反应,使CRP等炎症指标表达上升,炎症破坏表皮屏障,表皮破坏如损伤、感

染又会进一步导致持续炎症,刺激角质细胞使IL-4、CRP进一步升高,持续激活Th2介导的免疫反应,持续的IL-4刺激导致表皮中中间丝相关蛋白表达的减少,急性炎症阻碍了角质化细胞分化中涉及的其他蛋白质的合成,影响受损的屏障重建,则加剧病情^[19-20]。本研究构建ROC曲线分析发现IL-4、CRP及二者联合诊断特应性皮炎均具有一定诊断价值。但考虑IL-4、CRP受多种因素影响,可将其作为辅助诊断指标。进一步将患者按照不同病情严重程度分组,发现不同病情严重程度3组患者间IL-4、CRP水平比较有统计学差异,且Spearman分析显示,特应性皮炎患者IL-4、CRP水平与病情严重程度均呈正相关,随着病情加重,患者IL-4、CRP水平持续上升。特应性皮炎患者屏障功能障碍诱导2型免疫偏离,这是由屏障破坏的表皮产生的IL-4等细胞因子导致,病情严重患者2型显性免疫偏离更严重,IL-4等细胞因子在屏障破坏的表皮衍生的角质细胞中过度表达^[21]。除此外,特应性皮炎患者还表现出广泛的全身性炎症,CRP是全身炎症的非特异性炎症标记物,通过检测CRP可反映患者全身炎症程度,这也与其免疫信号相关^[22]。度普利尤单抗治疗16周内,患者IL-4、CRP水平呈进行性下降,表明度普利尤单抗治疗特应性皮炎有显著效果,可调节患者机体免疫,改善全身炎症反应,与武颖等^[23]学者研究结果类似。这一现象可能与度普利尤单抗快速抑制Th2炎症的作用机制相符,药物通过阻断IL-4/IL-13信号,减少Th2细胞因子分泌,同时下调趋化因子表达,抑制免疫细胞向皮损部位募集^[24]。治疗12周时IL-4、CRP与疗效的相关性最强,可能与药物达到稳态血药浓度、炎症负荷显著减轻相关。治疗有效组患者各时间点IL-4、CRP水平均低于无效组,提示基线炎症水平可能影响度普利尤单抗疗效。无效组患者可能存在Th2/Th17混合炎症表型,或合并IL-17、IL-22等细胞因子升高,导致对IL-4/IL-13通路阻断反应不足。此外,无效组患者可能存在药物代谢差异或依从性问题,需通过治疗药物监测进一步验证。

综上所述,特应性皮炎患者IL-4、CRP水平,异常高表达,且随着病情的加重持续上升,IL-4、CRP与特应性皮炎的发生、发展密切相关,有望成为未来特应性皮炎临床治疗靶点。同时,度普利尤单抗治疗特应性皮炎患者可使IL-4、CRP水平下降,调节患者机体免疫,改善全身炎症反应,IL-4、CRP在特应性皮炎诊断中具有一定价值。本研究的不足在于纳入样本量不足且未对患者进行随访,后续研究将扩大样本量,对患者进行分类,探究不同类型患者IL-4、CRP水平差异及特应性皮炎患者度普利尤单抗治疗后的复发情况。

* * *

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