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多发性骨髓瘤患者外周血CD4$^+$CD25$^+$CD127^{low}调节性T 细胞数量及凋亡相关蛋白水平*

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Quantity and apoptosis-related protein levels of CD 4$^+$, CD 25$^+$, and CD127^{low} regulatory T cells in peripheral blood of multiple myeloma patients

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摘要

目的：探讨外周血CD4+CD25+CD127lo w调节性T 细胞（regulatory T cells ，Tregs）在多发性骨髓瘤（multiple myeloma，MM）治疗中的作用。方法：采用流式细胞术检测30例初治、27例完全缓解（CR）MM患者以及25例健康成年人外周血CD4+T 细胞、Tregs数量，并检测Tregs表面功能分子CTLA- 4 及其凋亡相关蛋白CD95、bcl- 2、Caspase3 的表达，分析其与临床特点及疗效的关系。结果：初治组CD4+T 细胞占外周血单个核细胞的比例低于对照组（P<0.05），Ⅲ期初治患者CD4+T 细胞明显低于Ⅰ、Ⅱ期患者（P<0.05）；初治MM组Tregs占CD4+T 细胞比例显著高于CR组和正常对照组（P<0.05），初治Ⅲ期患者Tregs占CD4+T 细胞比例明显高于初治Ⅰ、Ⅱ期患者（P<0.05）。初治组、CR组和正常对照组Tregs的表面 CD95表达无统计学差异（P>0.05），初治组CTLA- 4 表达高于 CR组（P<0.05）和对照组（P<0.01），CR患者 CTLA- 4 高于对照组（P<0.05），初治组 Tregs胞浆内 bcl- 2 水平高于 CR组（P<0.05）和对照组（P<0.01），CR组高于对照组（P<0.05），初治组和CR组Tregs胞内Caspase3 的水平低于对照组（P<0.05）。 初治组Tregs占CD4+比例与骨髓瘤数量呈正相关（P<0.05），且Tregs比例与治疗前后浆细胞下降值成反比（r=0.735，P<0.05）。 结论：MM患者外周血Tregs水平升高，与瘤细胞负荷及疾病的分期呈正相关，与疗效呈负相关；Tregs水平增高与其抗凋亡能力增强有关。

关键词 ： 多发性骨髓瘤，调节性T 细胞，流式细胞术，凋亡

Abstract :

Objective:To investigate the role of CD 4+, CD 25+, and CD 127low regulatory T cells (Tregs) in multiple myeloma (MM). Methods:Levels of CD4+ T cells and Tregs, as well as expression of CTLA-4 and apoptosis-related proteins, such as CD95, bcl-2, and Caspase3 of Tregs in peripheral blood of 30 patients with newly diagnosed cases,27 patients under of complete remission (CR) from multiple myeloma patients, and 25 healthy adults were analyzed by flow cytometry Results: The percentage of CD 4 +T cells in the untreated group was significantly lower than that of the control group (P<0.05). The percentage of Tregs in CD 4+ T cells in the untreated group was significantly higher than that of the CR group and control group (P<0.05), which in ISS Ⅲ patients of the untreated group was significantly higher than that in I/II(P<0.05). No significant difference of CD95 expression in Tregs was observed among the three groups. The expression of CTLA- 4 in Tregs from the untreated group was significantly higher than that of the CR group (P<0.05) and control group (P<0.01), and so was in CR group than this in controls (P<0.05). The expression of bcl- 2 in Tregs in the untreated group was significantly higher than that of the CR group (P<0.05) and control group (P<0.01), and so was in CR group than this in controls(P<0.05). The expression of Caspase 3 in Tregs from the untreated group and CR group were all significantly lower than that of the control group (P<0.05). The percentage of Tregs in CD 4+ T cells in the untreated group was positively correlated with the proportion of bone marrow plasma cells (P<0.05). The percentage of Tregs in CD 4+ T cells from 15 MM patients who received bortezamib and dexamethasone (VD) chemotherapy was negatively correlated to the ratio of plasma cell reduction after the first VD chemotherapy (r= 0.735, P<0.01). Conclusion:The level of Tregs in the peripheral blood of MM patients was positively correlated with tumor burden and progression of disease, but was negatively correlated with curative effect. The increased level of Tregs was associated with their strengthened anti-apoptosis function.

Key words : multiple myeloma regulatory T cells flow cytometry apoptosis

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