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论著

多发性骨髓瘤患者血清GDF15的检测及其临床意义

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摘要:

目的: 研究多发性骨髓瘤(multiple myeloma, MM)患者血清生长分化因子15(growth differentiation factor 15, GDF15)的表达情况及其与相应临床指标的关系, 初步探讨GDF15在MM发生发展及预后评估方面的潜在作用。方法:

MM患者24例, 同期20例体检正常者作为对照组。采用酶联免疫吸附试验(enzyme-linked immunosorbent assay, ELISA)检

测MM组和对照组血清GDF15水平, 收集患者临床资料。结果: MM组血清GDF15水平明显高于对照组[(1.37±0.64) ng/mL vs (0.14±0.06) ng/mL, P<0.01]。国际分期系统(international staging system, ISS) III期患者血清GDF15水平明显高于ISS(I+II)期

[(1.57±0.48) ng/mL vs (0.77±0.34) ng/mL, P<0.05]。MM患者血清GDF15水平与血清单克隆免疫球蛋白(monoclonal proteins,

M蛋白)水平、β2微球蛋白和肌酐水平呈正相关(P<0.05), 与外周血红蛋白含量以及血小板计数均呈负相关(P<0.05), 与患者年龄、血清白蛋白、乳酸脱氢酶(lactic dehydrogenase, LDH)、C反应蛋白(C-reactive protein, CRP)、血

钙水平、外周血白细胞计数无明显相关(P>0.05)。4例MM患者经3个疗程化疗后M蛋白水平明显下降者, 其相应的血清

GDF15水平下降程度也明显; 而M蛋白水平下降程度不明显者, 其相应的血清GDF15水平升高。结论: GDF15在初治

MM患者血清中明显增高, 与ISS分期有关, 并与血清M蛋白水平、β2微球蛋白水平和肌酐水平呈正相关, 与外周血

血红蛋白含量、血小板计数呈负相关, 提示其在反映MM患者体内的肿瘤负荷方面具有一定意义。GDF15水平变化和M

蛋白变化可能具有一定的联系, 提示其可能用于评估治疗反应。

关键词: 多发性骨髓瘤 血清 生长分化因子15 单克隆免疫球蛋白

Expression of serum GDF15 and its clinical significance in multiple myeloma patients

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Abstract:

Objective: To determine the serum level of the growth differentiation factor 15 (GDF15) in multiple myeloma (MM) patients and analyze its level with other clinical parameters, and to investigate its significance in the formation, development and prognosis assessment of MM.

Methods: We used enzyme-linked immunosorbent assay (ELISA) to measure the serum level of GDF15 in an MM group (24 pre-treatment patients) and in 20 healthy controls. All patients' clinical data were collected. Results: The serum GDF15 level was significantly higher in the MM group [(1.37±0.64) ng/mL]

than in the normal control group [(0.14±0.06) ng/mL, P<0.01]. The mean serum GDF15 level in the MM patients in ISS stage III was (1.57±0.48) ng/mL, significantly higher than that of ISS stage (I+II) [(0.77±0.34) ng/mL, P<0.05]. There was no significant positive correlation between the serum GDF15 level and serum monoclonal proteins (M protein) level, β2-microglobulin and creatinine (P<0.05), but significant inverse correlation was found between the GDF15 level with hemoglobin concentration and platelet count respectively (P<0.05). Serum GDF15 level was not associated with patients' age, albumin, lactic dehydrogenase (LDH), C-reactive protein (CRP), calcemia or leukocyte count (P>0.05). After 3 cycles of chemotherapy, patients with a >50% reduction of M protein had a significant reduction of GDF15, while for the patients whose M

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protein did not decrease obviously, their corresponding serum GDF15 level increased. Conclusion: The serum GDF15 level may reflect the tumor burden in the MM patients, which increases obviously, is related with ISS, positively correlated with serum M protein level,  $\beta$ 2-microglobulin level, serum creatinine and negatively with hemoglobin concentration and platelet count. The change of serum GDF15 level has some relation with the extent of M protein reduction, suggesting it may be used as a marker for therapy response.

Keywords: multiple myeloma serum growth differentiation factor 15 monoclonal protein

收稿日期 2013-08-05 修回日期 网络版发布日期

DOI: 10.11817/j.issn.1672-7347.2014.03.008

基金项目:

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#### 参考文献:

1. Blade J, Rosinol L, Cibeira MT. Prognostic factors for multiple myeloma in the era of novel agents [J]. Ann Oncol, 2008, 19(Suppl 7): i117-i120.
2. 胡慧瑾, 陆化, 费小明, 等. 多发性骨髓瘤患者骨髓间充质干细胞趋化相关因子基因表达异常 [J]. 中国实验血液学杂志, 2011, 19(1): 59-63.  
HU Huijin, LU Hua, FEI Xiaoming, et al. Chemotaxis-related factors are expressed abnormally in bone marrow mesenchymal stem cells of multiple myeloma patients [J]. Journal of Experimental Hematology, 2011, 19(1): 59-63.
3. Arnulf B, Lecourt S, Souldier J, et al. Phenotypic and functional characterization of bone marrow mesenchymal stem cells derived from patients with multiple myeloma [J]. Leukemia, 2007, 21(1): 158-163.
4. Reagan MR, Ghobrial IM. Multiple myeloma mesenchymal stem cells: characterization, origin, and tumor-promoting effects [J]. Clin Cancer Res, 2012, 18(2): 342-349.
5. Corre J, Mahtouk K, Attal M, et al. Bone marrow mesenchymal stem cells are abnormal in multiple myeloma [J]. Leukemia, 2007, 21(5): 1079-1088.
6. Bootcov MR, Bauskin AR, Valenzuela SM, et al. MIC-1, a novel macrophage inhibitory cytokine, is a divergent member of the TGF $\beta$  superfamily [J]. Proc Natl Acad Sci USA, 1997, 94(21): 11514-11519.
7. Eling TE, Baek SJ, Shim M, et al. NSAID activated gene (NAG-1), a modulator of tumorigenesis [J]. J Biochem Mol Biol, 2006, 39(6): 649-655.
8. Proutski I, Stevenson L, Allen WL, et al. Prostate-derived factor--a novel inhibitor of drug-induced cell death in colon cancer cells [J]. Mol Cancer Ther, 2009, 8(9): 2566-2574.
9. Ye L, Lewis-Russell JM, Kyanaston HG, et al. Bone morphogenetic proteins and their receptor signaling in prostate cancer [J]. Histol Histopathol, 2007, 22(10): 1129-1147.
10. Wang X, Baek SJ, Eling TE. The diverse roles of nonsteroidal antiinflammatory drug activated gene (NAG-1/GDF15) in cancer [J].

- Biochem Pharmacol, 2013, 85(5): 597-606.
11. Trovik J, Salvesen HB, Cuppens T, et al. Growth differentiation factor-15 as biomarker in uterine sarcomas [J]. Int J Gynecol Cancer, 2014, 24(2): 252-259.
12. Liu T, Bauskin AR, Zaunders J, et al. Macrophage inhibitory cytokine 1 reduces cell adhesion and induces apoptosis in prostate cancer cells [J]. Cancer Res, 2003, 63(16): 5034-5040.
13. Zhang L, Yang X, Pan HY, et al. Expression of growth differentiation factor 15 is positively correlated with histopathological malignant grade and in vitro cell proliferation in oral squamous cell carcinoma [J]. Oral Oncol, 2007, 7(45): 627-632.
14. Aw YK, Zeng Y, Vindivich D, et al. Morphological effects on expression of growth differentiation factor 15 (GDF15), a marker of metastasis [J]. J Cell Physiol, 2014, 229(3): 362-373.
15. Griner SE, Joshi JP, Nahta R. Growth differentiation factor 15 stimulates rapamycin-sensitive ovarian cancer cell growth and invasion [J]. Biochem Pharmacol, 2013, 85(1): 46-58.
16. Chen SJ, Karan D, Johansson SL, et al. Prostate-derived factor as a paracrine and autocrine factor for the proliferation of androgen receptor-positive human prostate cancer cells [J]. Prostate, 2007, 5(67): 557-571.
17. Huang CY, Beer TM, Higano CS, et al. Molecular alterations in prostate carcinomas that associate with in vivo exposure to chemotherapy: identification of a cytoprotective mechanism involving growth differentiation factor 15 [J]. Clin Cancer Res, 2007, 13(19): 5825-5833.
18. Brown DA, Stephan C, Ward RL, et al. Measurement of serum levels of macrophage inhibitory cytokine 1 combined with prostate-specific antigen improves prostate cancer diagnosis [J]. Clin Cancer Res, 2006, 12(1): 89-96.
19. Kaur S, Chakraborty S, Baine MJ, et al. Potentials of plasma NGAL and MIC-1 as biomarker(s) in the diagnosis of lethal pancreatic cancer [J]. PLoS One, 2013, 8(2): e55171.
20. Ozkan H, Demirbas S, Ibis M, et al. Diagnostic validity of serum macrophage inhibitor cytokine and tissue polypeptide-specific antigen in pancreatobiliary diseases [J]. Pancreatology, 2011, 11(3): 295-300.
21. Selander KS, Brown DA, Sequeiros GB, et al. Serum macrophage inhibitory cytokine-1 concentrations correlate with the presence of prostate cancer bone metastases [J]. Cancer Epidemiol Biomarkers Prev, 2007, 16(3): 532-537.
22. Staff AC, Trovik J, Eriksson AG, et al. Elevated plasma growth differentiation factor-15 correlates with lymph node metastases and poor survival in endometrial cancer [J]. Clin Cancer Res, 2011, 17(14): 4825-4833.
23. Basil CF, Zhao Y, Zavaglia K. Common cancer biomarkers [J]. Cancer Res, 2006, 66(6): 2953-2961.
24. Corre J, Labat E, Espagnolle N, et al. Bioactivity and prognostic significance of growth differentiation factor GDF15 secreted by bone marrow mesenchymal stem cells in multiple myeloma [J]. Cancer Res, 2012, 72(6): 1395-1406.
25. 张之南, 沈悌. 血液病诊断及疗效标准

[M]. 3版. 北京: 科学出版

社, 2007: 232-234.

ZHANG Zhinan, SHEN Ti. Diagnostic and Curative Criteria of Hematopathy

[M]. 3th ed. Beijing: Science Press, 2007: 232-234.

26. Greipp PR, San MJ, Durie BG, et al. International staging system for multiple myeloma

[J]. J Clin Oncol, 2005, 23(15): 3412-3420.

27. Brown DA, Lindmark F, Stattin P, et al. Macrophage inhibitory cytokine

1: a new prognostic marker in prostate cancer

[J]. Clin Cancer Res,

2009, 15(21): 6658-6664.

28. 林放, 赵树铭. 骨髓基质细胞对血小板生成的影响

[J]. 国际检验

学杂志, 2012, 33(8): 959-961.

LIN Fang, ZHAO Shuming. Effects of bone marrow stromal cells on platelet production

[J]. International Journal of Laboratory Medicine,

2012, 33(8): 959-961.

29. Shah J, Blade J, Sonneveld P, et al. Rapid early monoclonal protein reduction after therapy with bortezomib or bortezomib and pegylated liposomal doxorubicin in relapsed/refractory myeloma is associated with a longer time to progression

[J]. Cancer, 2011, 117(16): 3758-3762.

#### 本刊中的类似文章

1. 王继贵; .血清IV型胶原水平的测定及该胶原在各型肝病患者体内的变化[J]. 中南大学学报(医学版), 2001, 26(6): 546-

2. 许辉; 孙明; 周宏研; 陶立坚; .高血压病患者血清转化生长因子- $\beta$ 1及其与血压的关系[J]. 中南大学学报(医学版), 2002, 27(4): 381-

3. 聂亚雄; 黎杏群; 梁清华; .脑溢安含药血清对谷氨酸致培养大鼠皮层神经元损伤的保护作用[J]. 中南大学学报(医学版), 2002, 27(5): 429-

4. 谢建民; 齐振华.急性白血病血清中血管内皮生长因子的表达及临床意义[J]. 中南大学学报(医学版), 2003, 28(2): 183-

5. 石奕武; 胡维新; 汤立军; 田菁燕; 易伟峰; 谭达人; .多发性骨髓瘤的基因表达谱分析[J]. 中南大学学报(医学版), 2003, 28(3): 201-

6. 王梦昌 刘陕西 刘蓬勃 .

## 雄黄对多发性骨髓瘤细胞株RPMI 8226细胞基因表达谱的作用

[J]. 中南大学学报(医学版), 2006, 31(01): 24-27

雄黃對多發性骨髓瘤細胞株RPMI 8226細胞基因表达譜的作用[J]. 中南大學學報(醫學版). 2006, 31(02): 222-226

8. 黄卓1, 雷闻湖1, 柳岸1, 唐吉斌1, 陈伶2, 高艳娥2. 雄黄对MMP-9水平的影响[J]. 中南大学学报(医学版), 2006, 31(03): 367-372

9. 朱文晖1, 张晓红2, 肖渊茗1. 超声心动图评价心力衰竭大鼠模型心功能改变[J]. 中南大学学报(医学版), 2009, 34(05): 453-456

10. 包珊, 杨舒盈, 王历. 无排卵性功能失调性子宫出血患者血清标志物

的筛选、鉴定及其在月经血中的表达[J]. 中南大学学报(医学版), 2009, 34(07): 616-623

11. 郭霞1, 阿布力孜·阿布杜拉1, 武贵臻1, 刘开江2. 维吾尔族妇女宫颈癌患者血清蛋白质组的二维液相色谱分

析[J]. 中南大学学报(医学版), 2009, 34(07): 624-629

12. 蒋铁斌, 李昕, 周俊, 周洋, 袁洪, 向辉, 阳国平, 阎宏伟, 邢晓为, 刘竞. PDCD5在多发性骨髓瘤中的表达及其

与BCL-2相关性[J]. 中南大学学报(医学版), 2008, 33(09): 814-820

13. Feng-huang Zhan, Bart Barlogie, John Shaughnessy Jr. 基因表达谱鉴定高危多发性骨髓瘤[J]. 中南大学学报(医学版), 2007, 32(02): 191-203

14. 高艳娥1, 惠慧1, 张菊2, 樊江波1, 阎小君2. 高危HPV16 E4基因的表达纯化及临床应用[J]. 中南大学学报(医学版), 2008, 33(08): 676-681

15. 周价1, 黄昕1, 何华先2, 张潇1, 刘爱忠1, 杨土保1, 李硕颀1, 汤学民1, 谭红专1.洪灾区钩端螺旋体宿主动物及健康人群

感染情况的流行病学研究[J]. 中南大学学报(医学版), 2009, 34(02): 99-103

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