

doi: 10.3978/j.issn.2095-6959.2016.10.023

View this article at: http://dx.doi.org/10.3978/j.issn.2095-6959.2016.10.023

乳腺癌转移、化疗抵抗与STC1的表达情况分析

张亚莉^{1,2}, 翟雪洁²

(1. 遵义医学院, 贵州 遵义 563003; 2. 大连大学附属中山医院肿瘤科, 辽宁 大连 116001)

[摘要] 目的: 考察人斯钙素1(stanniocalcin 1, STC1)表达水平与乳腺癌的转移、化疗抵抗等病理参数相关性。方法: 采用免疫组织化学法分析76例乳腺癌组织中STC1蛋白表达水平, 并比较其表达水平和癌症转移、化疗抵抗等病理参数关系。结果: 在76例乳腺癌组织中STC1阳性表达33例、阴性表达43例。两组间年龄、肿块直径、分期差异无统计学意义($P>0.05$), 但两组间乳腺癌的转移率和化疗抵抗发生率差异具有统计学意义($P<0.05$)。Pearson相关系数检验证实STC1表达水平与转移率和化疗抵抗发生率正相关($r=0.413$; $r=0.359$)。结论: 人斯钙素1的表达与乳腺癌组织的转移、化疗抵抗相关, 是预后预测的参考指标。

[关键词] 乳腺癌; 人斯钙素1; 转移; 化疗抵抗

The correlation between the expression level of STC1 and the pathological parameters of breast cancer metastasis and chemotherapy resistance

ZHANG Yali^{1,2}, ZHAI Xuejie²

(1. Zunyi Medical University, Zunyi Guizhou 563003; 2. Cancer Department, The Dalian University Affiliated Zhong Shan Hospital, Dalian Liaoning 116001, China)

Abstract **Objective:** To investigate the correlation between the expression level of human stanniocalcin 1 (STC1) and the pathological parameters of breast cancer metastasis and chemotherapy resistance. **Methods:** The expression levels of STC1 in 76 breast cancer tissues were analyzed by immunohistochemistry, and the relationship between the expression levels and pathological parameters such as metastasis and chemotherapy resistance were studied. **Results:** In 76 cases of breast cancer, 33 cases of positive expression and 43 cases of negative expression. There was no significant difference in the age, tumor diameter and stage between the two groups ($P>0.05$), but there were significant difference between the two groups in the incidence of metastasis and chemotherapy resistance ($P<0.05$). Pearson correlation coefficient test confirmed that the expression level of STC1 was positively correlated with the rate of metastasis and chemotherapy resistance ($r=0.413$; $r=0.359$). **Conclusion:** The expression of human calcium 1 is related to the metastasis and chemotherapy resistance of breast cancer. It is a reference index for prognosis prediction.

Keywords breast cancer; human stanniocalcin 1 (STC1); metastasis; chemotherapy resistance

收稿日期 (Date of reception): 2016-07-06

通信作者 (Corresponding author): 张亚莉, Email: yali4809@qq.com

乳腺癌在女性中发病率较高, 对女性的健康造成严重威胁, 虽然相比于肺癌和消化道肿瘤, 乳腺癌的预后相对较好, 但若出现肿瘤转移和化疗抵抗则同样会引起不良预后^[1-3]。寻找肿瘤转移和化疗抵抗的标志物有助于改善乳腺癌的治疗。人斯钙素1(stanniocalcin 1, STC1)是一种分泌性糖蛋白, 广泛存在于人类和其他哺乳动物组织中, 已有研究^[4-6]表明STC1的表达异常与多种肿瘤的发生甚至转移和化疗抵抗有关。但是, 在乳腺癌组织中STC1的表达水平及其意义尚未有详尽研究, 因此本研究拟探讨STC1在乳腺癌组织中的表达水平及与癌组织转移和化疗抵抗的关系, 为预测和治疗乳腺癌提供数据支持。

1 资料与方法

1.1 标本来源

随机选取76例乳腺癌组织样本均来自我院手术治疗患者经医院伦理委员会批准且患者知情同意后入组, 其中51例患者预后发生了癌细胞转移, 25例未发生转移。14例化疗抵抗, 62例无化疗抵抗。

1.2 方法

采用免疫组化法检测乳腺癌组织中STC1表达水平, 兔抗人单克隆抗体及二抗均由上海生工生物公司提供, 免疫组织化学依据试剂盒说明书进行, 标本经10%中性福尔马林固定、常规脱水、包埋后4 μm切片, 二甲苯脱蜡并梯度乙醇水化, EDTA修复抗原, DAB显色, 苏木精复染。以染色强度和阳性细胞百分率相乘得出的SI指数进行评估。染色强度判断: 无阳性染色(0分)、弱阳性染(1分)、中等阳性染(2分)、强阳性染(3分)。染色区域判断: 肿瘤细胞少于25%(1分)、25%~50%(2分)、51%~75%(3分)、>75%(4分)。各因子的表达水平由SI指数决定, SI指数≥4分为阳性, SI指数≤3分为阴性^[7]。已知阳性切片作为阳性对照(图1), PBS代替一抗作为阴性对照(图2)。

1.3 统计学处理

采用SPSS20.0软件分析, 计数资料采用卡方检验, 相关性分析采用Pearson检验, $P < 0.05$ 为差异具有统计学意义。

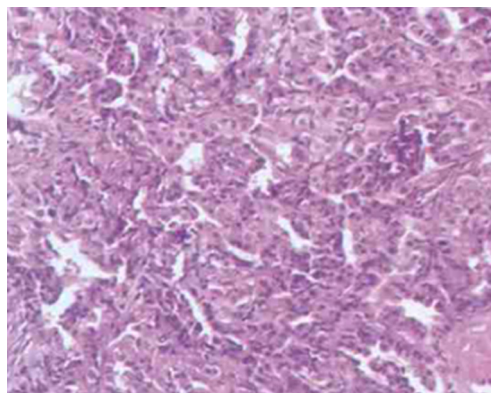


图1 STC1乳腺癌样本阳性对照(DAB显色, 苏木精复染, ×400)

Figure 1 Positive control of STC1 breast cancer sample (DAB color and Hematoxylin counterstain, ×400)

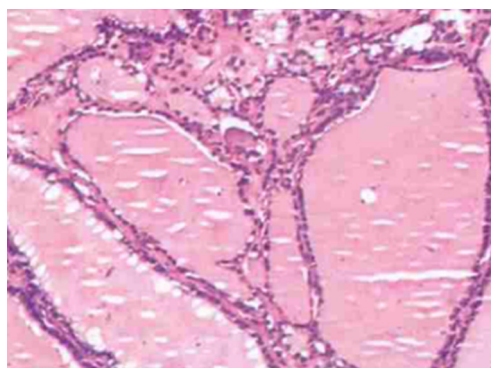


图2 STC1乳腺癌样本阴性对照(DAB显色, 苏木精复染, ×400)

Figure 2 Negative control of STC1 breast cancer sample (DAB color and Hematoxylin counterstain, ×400)

2 结果

2.1 STC1表达与乳腺癌临床病理特征关系

两组间年龄、肿块直径、分期差异无统计学意义($P > 0.05$), 但两组间乳腺癌组织的转移率和化疗抵抗发生率差异具有统计学意义($P < 0.05$), 具体结果见表1。

2.2 STC1表达与临床病理因素相关性

Pearson相关系数检验证实STC1表达水平与转移率和化疗抵抗发生率正相关($r = 0.413$; $r = 0.359$), 具体结果见表2。

表 1 STC1 表达与乳腺癌临床病理特征关系

Table 1 Relationship between the STC1 expression and clinicopathological features of breast cancer

临床病理参数	例数	STC1		χ^2	P
		阳性	阴性		
年龄 / 岁				0.48	0.49
<57	38	18	20		
≥ 57	38	15	23		
肿瘤直径 /cm				1.34	0.25
<4	38	14	24		
≥ 4	38	19	19		
转移				5.72	0.17
是	51	27	24		
否	25	6	19		
化疗抵抗				7.73	0.01
是	14	10	4		
否	62	23	49		
TNM 分期				3.70	0.54
I + II	44	15	29		
III + IV	32	18	14		
分级				2.02	0.36
G1	6	1	5		
G2	30	13	17		
G3	40	19	21		

表2 STC1表达与临床病理因素相关性

Table 2 The correlation between STC1 expression and clinicopathological factors

STC1	TNM分期(n=76)	分级(n=76)	肿瘤直径(n=76)	转移(n=76)	化疗抵抗(n=76)
Pearson相关性	0.213	0.038	0.094	0.413	0.359
显著性	>0.05	>0.05	>0.05	<0.01	<0.01

3 讨论

在乳腺癌的发生和发展过程中, 由各类肿瘤相关基因调控的肿瘤微环境起到了重要的作用。STC1蛋白在多种肿瘤组织中具有表达异常, 如在肝癌组织中STC1的表达高于癌旁组织, 但在卵巢癌中则低于癌旁组织^[8-9]。李佳涛等^[10]发现在乳腺癌组织中STC1的表达与乳腺癌的肺转移具有相关性, 可以作为乳腺癌肺转移的预测因子。张延涛^[11]同样证实STC1在结肠癌组织中的表达也具有促进癌细胞转移的作用。除转移外, 化疗抵抗也是影响乳腺癌患者疗效的重要原因。在过去的研究中, Liu等^[12]在肺癌细胞微环境的考察中发现STC1的表达与肺癌细胞的耐药性存在相关性。

Shirakawa等^[13]在食管鳞状细胞癌组织中的研究也得到了类似的结论。提示STC1在多种细胞的转移和化疗抵抗的机制中可能具有重要作用。

本研究证实, 76例乳腺癌组织中STC1阳性表达33例、阴性表达43例, 阳性表达率43.4%。阴性表达和阳性表达两组间年龄、肿块直径、分期差异无统计学意义($P>0.05$), 但两组间乳腺癌组织的转移率和化疗抵抗发生率差异具有统计学意义($P<0.05$)。提示, 乳腺癌组织中的STC1表达与乳腺癌的转移和化学抵抗有关。进一步进行相关性检验也证实, STC1表达水平与转移率和化疗抵抗发生率正相关($r=0.413$; $r=0.359$)。表明乳腺癌组织的转移率和化疗抵抗的发生与STC1的表达存在联系。

综上所述, 人斯钙素1的表达与乳腺癌组织的转移、化疗抵抗相关, 虽然具体机制仍需进一步探讨, 但可以作为预后预测的重要参考指标。

参考文献

1. Tao Z, Shi A, Lu C, et al. Breast Cancer: Epidemiology and Etiology[J]. Cell Biochem Biophys, 2015, 72(2): 333-338.
2. Kohler BA, Sherman RL, Howlander N, et al. Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State[J]. J Natl Cancer Inst, 2015, 107(6): djv048.
3. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012[J]. CA Cancer J Clin, 2015, 65(2): 87-108.
4. Chang AC, Doherty J, Huschtscha LI, et al. STC1 expression is associated with tumor growth and metastasis in breast cancer[J]. Clin Exp Metastasis, 2015, 32(1): 15-27.
5. Ryazantsev A, Rubiaco G, Risco M, et al. Circulating Stanniocalcin-1 In The Diagnosis Of Lung Cancer[M]. D30. Novel Clinical Approaches to Thoracic Malignancies. American Thoracic Society, 2016: A6659-A6659.
6. Murai R, Tanaka M, Takahashi Y, et al. Stanniocalcin-1 promotes metastasis in a human breast cancer cell line through activation of PI3K[J]. Clin Exp Metastasis, 2014, 31(7): 787-794.
7. 杨莹, 房辉, 徐刚, 等. 甲状腺乳头状癌组织中STC1的表达及其临床意义[J]. 临床与实验病理学杂志, 2015, 31(11): 1263-1266.
8. Ismail RS, Baldwin RL, Fang J, et al. Differential gene expression between normal and tumor-derived ovarian epithelial cells[J]. Cancer Res, 2000, 60(23): 6744-6749.
9. Okabe H, Satoh S, Kato T, et al. Genome-wide analysis of gene expression in human hepatocellular carcinomas using cDNA microarray: identification of genes involved in viral carcinogenesis and tumor progression[J]. Cancer Res, 2001, 61(5): 2129-2137.
10. 李佳涛, 李惠, 胡国宏. 乳腺癌中 STC1 的表达与乳腺癌肺转移相关[J]. 复旦学报: 医学版, 2015, 42(5): 618-622.
11. LI Jiatao, LI Hui, HU Guohong. STC1 expression in breast cancer is correlated with breast cancer lung metastasis[J]. Fudan University Journal of Medical Sciences, 2015, 42(5): 618-622.
12. 张延涛. 斯钙素-1在结肠癌组织中表达的初步研究[D]. 昆明: 昆明医学院, 2010.
13. ZHANG Yantao. Previous Study of the Stanniocalcin-1 Expression in Colon Cancer[D]. Kunming: Kunming Medical College, 2010.
14. Liu R, Wei S, Chen J, et al. Mesenchymal stem cells in lung cancer tumor microenvironment: their biological properties, influence on tumor growth and therapeutic implications[J]. Cancer Lett, 2014, 353(2): 145-152.
15. Shirakawa M, Fujiwara Y, Sugita Y, et al. Assessment of stanniocalcin-1 as a prognostic marker in human esophageal squamous cell carcinoma[J]. Oncol Rep, 2012, 27(4): 940-946.

本文引用: 张亚莉, 翟雪洁. 乳腺癌转移、化疗抵抗与STC1的表达情况分析[J]. 临床与病理杂志, 2016, 36(10): 1585-1588. doi: 10.3978/j.issn.2095-6959.2016.10.023

Cite this article as: ZHANG Yali, ZHAI Xuejie. The correlation between the expression level of STC1 and the pathological parameters of breast cancer metastasis and chemotherapy resistance[J]. Journal of Clinical and Pathological Research, 2016, 36(10): 1585-1588. doi: 10.3978/j.issn.2095-6959.2016.10.023