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生殖器疣与癌中 Ha-ras 及 C-myc 癌基因表达的研究

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提 要 应用免疫组化技术对50例生殖器疣、10例阴茎表皮内瘤Ⅲ级(PINⅢ)、12例宫颈表皮内瘤Ⅲ级(CINⅢ)、20例阴茎癌及30例宫颈癌Ha-ras及C-myc癌基因表达进行了研究。结果:PINⅢ/CINⅢ和浸润癌较生殖器疣均伴有ras和myc癌基因增强表达;不同的是抗P_{21}蛋白抗体的表达强度在PINⅢ/CINⅢ和生殖器疣之间无重叠。提示(1)ras和myc癌基因与生殖器癌发生相关,且它们具有协同作用;(2)该方法可用于PINⅢ/CINⅢ筛选。

关键词 疣;生殖器疾病,女性;生殖器疾病,男性;癌;癌基因
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癌基因研究是肿瘤研究的重要课题之一,癌基因活化已在很多肿瘤及癌前病变中观察到,有文献报道Ha-ras及C-myc在生殖器恶性病变中的表达与预后相关[1]。我们对生殖器疣、阴茎表皮内瘤Ⅲ级(penile intraepithelial neoplasia,PINⅢ)、宫颈表皮内瘤Ⅲ级(cervical intraepithelial neoplasia,CINⅢ)、阴茎癌及宫颈癌中Ha-ras及C-myc表达进行了研究,以探讨癌基因表达检测在临床上的应用价值。

1 材料与方法

1.1 实验对象

生殖器疣50例,男20、女30,PINⅢ10例,CINⅢ12例,阴茎癌及宫颈癌分别为20例和30例;10例包皮及10例宫颈组织为正常对照。

1.2 试剂

P_{21}:抗c-Ha-ras蛋白产物及P_{62}:抗C-myc蛋白产物单抗,由军事医学科学院提供。

ABC试剂盒:Vector Lab产品。

1.3 方法

1.3.1 ABC免疫组化染色:所有病例均为石蜡切片,厚3~5 μm,经常规脱蜡、脱水、水化后依次进行:(1)3% H_2O_2甲醇及1% BSA分别封闭30 min;(2)加一抗,一抗工作浓度以调节至正常对照不显色为基准,24~26℃孵育1 h;(3)加二抗,24~26℃,45 min;(4)加ABC(1∶50),临用前30 min配制,24~26℃孵育1h,(5)AEC显色,5~10min;以上各步骤均间以0.01 mol/L PBS缓冲液洗3×5 min,最后水洗、明胶甘油封片。

1.3.2 结果观察:阳性病例为细胞浆(P_{21})或细胞核(P_{62})呈棕红色着染,着染强度以阳性细胞百分率表示,阳性细胞百分率为100个被计数肿瘤细胞中呈现阳性反应的细胞数。

1.3.3 统计学处理:U检验与t检验。

2 结果

结果总结见附表及图1、图2、图3。

附表 P_{21}及P_{62}免疫组化染色

Table Immunochemical staining by P_{21} and P_{62}

Cytology	Total No.	Positive No. by P_{21}	Positive No. by P_{62}
Normal control	20△	0	0
Genital wart	50	6 (12.0%)	4 (8%)
PINⅢ	10	5 (50.0%)	4 (40%)
CINⅢ	12	7 (58.3%)	6 (50%)
Penile cancer	20	12 (60.0%)	13 (65%)
Cervical Carcinoma	30	20 (66.7%)	21 (70%)

△: Test concentration of first antibody correctea to not coloration in control group

由上表可见P_{21}及P_{62}在PINⅢ/CINⅢ及阴茎癌/宫颈癌中的阳性表达率非常显著高于生殖器疣($P<0.001$)。

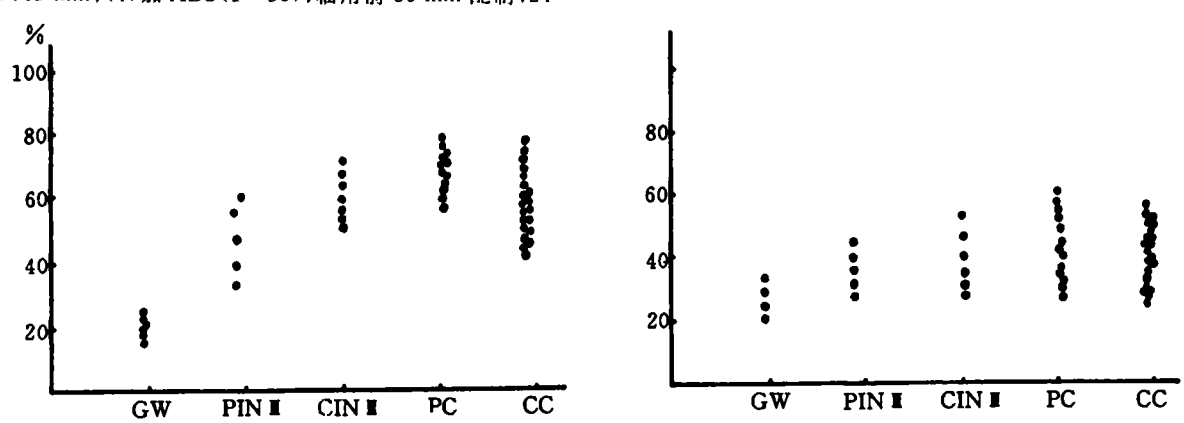
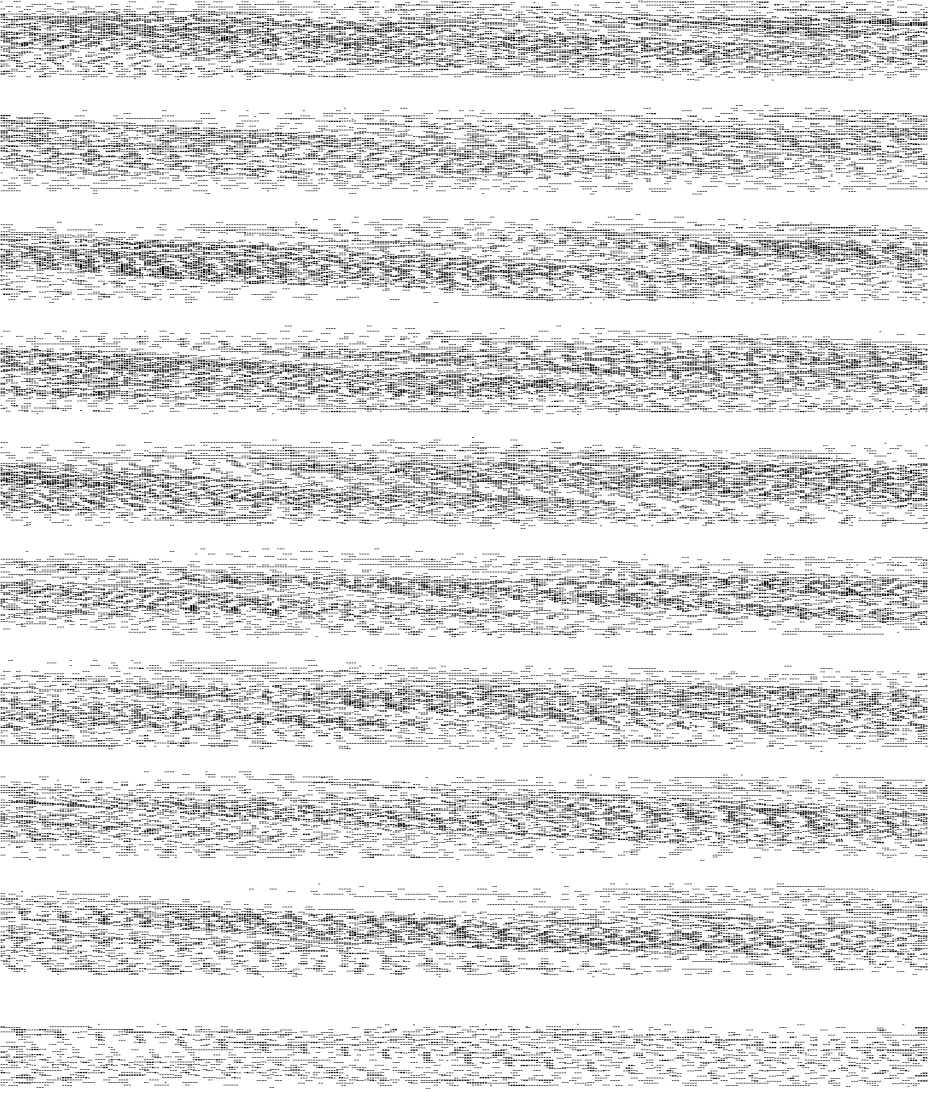


图1 生殖器疣与癌中P_{21}(上)及P_{62}(下)表达 Fig 1 P_{21}(upper) and P_{62}(lower) expression in genital wart and cancer
where: Gw: genital wart; PC: penile cancer; CC: Cervical carcinoma

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Expression of oncogenes Ha-ras and C-myc in wart and cancer of the genital organs

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Abstract The expression of the oncogenes Ha-ras and C-myc was investigated in 50 cases of wart of the genital organs, 10 cases of penile intraepithelial neoplasm in 3rd grade (PIN Ⅲ), 12 cases of cervical intraepithelial neoplasm in 3rd grade (CIN Ⅲ), 20 cases of penile cancer and 30 cases of cervival cancer with immunohistochemical method. It was found that more enhanced expression of Ha-ras and C-myc was observed in PIN Ⅲ, CIN Ⅲ and invasive cancer than in wart of the genital organs, and the expression intensity of anti-P_{21} antibodies of Ha-ras showed no overlapping between PIN Ⅲ-CIN Ⅲ and the wart of the genital organs. These findings suggest that Ha-ras and C-myc are involved in the development of the cancer of genital organs and the method to observe the expression of oncogenes can be used for the screening of CIN Ⅲ and PIN Ⅲ.

Key words warts; genital, female; genital diseases, male; carcinoma; oncogenes

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见心肌超微结构的损害。动物死亡原因与肺严重出血水肿、心脏损伤、心脏传导系统功能障碍所致的呼吸循环衰竭有关。

(7)撞击速度较低时，肺门区损伤程度重于肺泡区。撞击速度较高时，肺泡区损伤程度重于肺门区。左、右侧肺损伤伤情比值随撞击速度与压缩标准乘积的增大而逐渐减小。心肺损伤程度与撞击速度与压缩标准和乘积密切相关，肋骨损伤程度主要与压缩标准有关。

(8)与准静态撞击方式相比，动态撞击方式下动物各部位及整体伤情明显减轻，左右侧肺和左右侧肋骨损伤伤情比值增大。动物身体运动无挡板限制、应力波在由胸壁传出进入空气界质时反射小可能是引起上述损伤特征的原因。

(9)在撞击部位胸壁上安装弹性软垫可有效地延长撞击力作用时间、减小瞬时撞击力、存储部位撞击能量，显著地减轻了损伤程度；通过增大撞击面积来减轻伤情的效果则不够理想。

关键词 胸部损伤；生物力学；呼吸力学；创伤评分 ；肺顺应性

中图法分类号 R655

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