对 Meb 的疗效并无明显影响，提示 Meb 抗细粒棘球蚴的疗效不依赖于宿主的免疫水平，这与文献[2]报道 BCG 可增强 Meb 抗泡球蚴的疗效有所不同. 这种差异可能主要是与虫种不同有关，即细粒棘球蚴因刺激宿主组织反应，形成了包围虫体的外囊(ectocyst)，这外囊的内侧与细粒棘球蚴的外侧角质层相紧邻，但无任何血管联系[4]，它和角质层起着屏障和过滤作用，从而使宿主的淋巴细胞和特异性抗体难以进入囊内参与杀虫[5]，而泡球蚴是通过无外囊性浸润生长，形成以分隔性增殖为主的囊泡[6]，这种增殖特征可能使宿主的淋巴细胞和特异性抗体易与囊的生发层相接触而参与杀虫.

本文结果表明，Meb 对感染时间长的小鼠疗效较感染时间短的差，这种差异可能是感染时间长，宿主体内的囊较大，囊壁增厚，从而使扩散进入囊内的药量减少，也可能是此时的生发细胞具有较旺盛的增殖作用，经药物作用后，残留的或受损较轻的生发细胞易于修复和增殖.

由于感染宿主的免疫水平对 Meb 的疗效无明显影响，因此，需进一步寻求高效的抗细粒棘球蚴药物.

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九种抗癌药物对人胃腺癌裸小鼠移植瘤 MKN-28 的治疗作用

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Therapeutic effects of 9 antitumor drugs on stomach adenocarcinoma (MKN-28) in nude mice

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ABSTRACT Therapeutic effects of 9 antitumor drugs were studied on nude mice inoculated with transplanted human stomach tumor (MKN-28). When cisplatin, cyclophosphamide, chlormethine, 5-fluorouracil or mitomycin C was given ip to nude mice bearing MKN-28 at respective dose of 3, 100, 40, 80 and 2 mg / kg once weekly for 3 wk, the tumor inhibition rates of the former 3 drugs were over 80%, while the later 2 were 70-77% . Cytarabine 200 mg / kg twice or thrice weekly for 3 wk gave an inhibition rates of 68-72% . Hydroxycamptothecin 20 mg / kg twice weekly for 3 wk showed a better therapeutic effect than that given at 40 mg / kg once weekly for 3 wk, the tumor inhibition rates were 65

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and 32% respectively. No apparent effect of vincristine and methotrexate on MKN-28 was seen.

Histopathological observation indicated that in cisplatin group, numerous necrotic areas of tumor cells as well as sparse infiltration of inflammatory cells were found.

KEY WORDS stomach neoplasms; nude mice; antineoplastic agents

提要 本文报道9个临床常用抗癌药物治疗人胃管状腺癌裸小鼠移植瘤MKN-28的结果. 其中盐酸尼氮芥(ACNU), 环磷酰胺(CTX)和顺铂(cis-DDP)对MKN-28具有较高的肿瘤抑制率, 而长春新碱(VCR)和甲氨蝶呤(MTX)则无效. 病理切片的结果显示, 有效组的瘤组织中有坏死瘤细胞和中性白细胞散在, 对照组中则无上述现象.

关键词 胃肿瘤; 裸小鼠; 抗肿瘤药

影响胃癌药物治疗的因素较多, 其中不同病理类型及不同分化程度的癌组织对药物敏感性可能不同. 人癌裸小鼠移植瘤作为筛选抗癌药物模型的研究已取得一定进展. 对于给药后移植瘤瘤组织的病理观察虽有报道[1-3], 但却均未见病理变化. 我们用高分化的人胃管状腺癌裸小鼠移植瘤作实验, 观察9个常用抗癌药物对此类型胃癌的治疗效果和给药后瘤组织的病理变化, 以供临床参考.

MATERIALS AND METHODS

裸小鼠 人胃管状腺癌移植瘤的传代保种用NC品系裸小鼠, 鼠龄3-5 wk, 实验治疗用swiss品系裸小鼠,鼠龄6-8 wk,共132只, 均由本研究室提供. 体重22.5±SD 0.6 g, 小鼠均置于带有过滤罩的透明笼具内饲养. 笼具, 饲料, 垫料和饮水均经高压消毒, 室温24-27 ℃.

人癌模型 将体外培养的人胃管状腺癌MKN-28细胞[4]接种于NC小鼠右侧腋部皮下, 形成皮下型移植瘤模型. 接种后约20 d, 小鼠皮下长出直径约1 cm的瘤块, 取此瘤组织进行传代.

实验治疗 用10-20代MKN-28移植瘤按报道[5]的方法将瘤块接种在小鼠的右侧腋部皮下. 接种4 d后分笼, 称重, 每笼4鼠为一组, 按照不同的给药方案(Tab 1)进行ip治疗. 接种22 d后解剖称瘤重, 并与对照组比较, 计算肿瘤抑制率. 实验全程23 d. 实验用药是盐酸尼氮芥(chlormethine, ACNU, 日本三共株式会社); 丝裂霉素C(mitomycin C, MMC, 日本协和发酵工业株式会社), 顺氯氨铂(cisplatin, cis-DDP, 中国齐鲁制药厂); 羟基喜树碱(hydroxycamptothecin,HC, 上海药物所); 盐酸阿糖胞苷(cytarabine, Arac), 环磷酰胺(cyclophosphamide, CTX), 甲氨蝶呤(methotrexate, MTX), 长春新碱(vincristine, VCR)和5-氟尿嘧啶(5-fluorouracil, 5-FU)均由上海十二制药厂生产.

瘤组织病理检查 瘤组织HE染色, 光镜观察瘤细胞和瘤组织结构的变化, 同时也做AB-PAS染色, 检查粘液反应.

RESULTS

实验治疗 MKN-28是高分化的人胃管状腺癌移植瘤, 各代接种成活率100%, 移植瘤生长稳定. 在上述实验治疗中, 对照组的平均瘤重在1.7 g以上, 所试的9个抗肿瘤药物对MKN-28的实验治疗结果表明, 以cis-DDP, CTX及ACNU的效果最显著, 肿瘤抑制率均在80%以上. 其次为5-FU, Arac, MMC和HC抑制率为55-77%. 在不同给药方案治疗中, 用剂量相同的Arac每周间隔仅给药2或3次的治疗效果相似, 而HC治疗组的结果以每周间隔给药2次的治疗效果明显优于每周仅给药1次的, 在9个抗肿瘤药物中MTX及VCR对MKN-28无治疗作用(Tab 1).

瘤组织的病理观察 对照组的瘤组织中血管丰富, 纤维间质少, 瘤细胞呈编织状排列, 瘤细胞大, 呈椭圆形, 胞浆丰富, 胞核大而色

Tab 1. Effects of Chlormethine (ACNU), mitomycin C (MMC), cisplatin (cis-DDP), hydroxycamptothecin (HC), cytarabine (Arac), cyclophosphamide (CTX), methotrexate (MTX), vincristine(VCR) and 5-fluorouracil (5-FU) on nude mice bearing MKN-28. $n=4$ (treated groups), $n=8$ (control). $\bar{x} \pm$ SD. $^{*}P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ *vs* control.

Drug	Dose mg/kg	Schedule in each wk for 3 wk	Mice Initial/Final	Body wt (g) Initial/Final	Tumor wt (g) Treated/Control	Tumor wt inhibition rate (%)
ACNU	40	once	4/4	22.1/20.5	0.5±0.4/3.9±1.5	87.2***
	50	〃	4/4	24.5/23.0	0.7±0.4/3.9±1.5	82.1***
Arac	200	d1,4	4/4	23.3/29.8	1.6±0.8/5.0±1.8	68.0***
	200	d1,3,5	4/4	21.3/22.9	0.57±0.25/2.0±1.0	71.5**
cis-DDP	2	once	4/4	23.3/24.5	1.7±0.8/2.2±0.9	22.7*
	3	〃	4/4	22.5/23.6	0.14±0.12/2.0±1.0	93.0***
CTX	100	〃	4/4	22.6/23.9	0.23±0.10/1.7±0.5	86.5***
5-FU	60	〃	4/4	22.5/24.5	1.7±1.2/3.9±1.5	56.4**
	80	〃	4/4	24.3/24.7	0.9±0.7/3.9±1.5	76.9***
MMC	1.5	〃	4/4	22.5/31.5	3.0±2.2/5.0±1.8	40.0*
	2	〃	4/4	21.0/23.6	0.6±0.4/2.0±1.0	70.7**
MTX	150	〃	4/4	21.3/23.0	1.8±0.8/2.8±0.9	35.7*
	200	〃	4/3	22.5/22.0	2.2±0.4/2.8±0.9	21.4*
OPT	20	d1,4	4/4	20.9/23.5	0.8±0.6/2.15±0.17	68.8***
	40	once	4/4	21.6/23.8	1.46±0.26/2.15±0.17	32.1*
VCR	1	〃	4/4	22.5/26.9	3.5±1.5/5.0±1.8	30.0*
	1.5	〃	4/3	23/22	2.39±0.25/4.8±1.0	50.2*

深，核分裂相多(Fig 1 A).在高抑制率组(如cis-DDP,ACNU 及 CTX 的瘤组织中，瘤细胞小而狭长，其核浆比相对地比较小，纤维间质相对地多，在整个切面上可看到散在的，呈点状分布的变性或坏死瘤细胞，这此瘤细胞呈现出胞浆中有空泡，核膜崩解，核结构模糊或核固缩，核仁消失等现象. 在这些坏死瘤细胞周围可见炎性细胞浸润，主要为中心白细胞(Fig 1 B). 上述现象在中度及中度以下抑制率组(如 HC)的瘤组织中不太明显.

对瘤组织的石腊切片作 AB-PAS 染色处理，各组均呈阴性，说明瘤组织无粘液分泌.

DISCUSSION

人癌裸小鼠移植瘤是高度接近于临床的模型，用此类模型筛选抗癌药物能给于临床治疗癌症提供可信赖的参考. 我们用高分化的人胃管状腺癌裸小鼠移植瘤 MKN-28 对 9 种临床常用抗癌药物进行实验治疗的研究结果与临床应用的情况[6]基本相符. 由于本文所采用的模型为单一病理类型，而临床上胃癌的病理类型较为复杂，因此本文结果可为临床制定胃腺癌类癌症治疗方案时提供参考，从而能提高此病理类型胃癌的治疗效果.

本文的研究还表明，HC 以每周间隔给药 2 次的效果较每周给药 1 次的明显为好，这一结果可为临床给药方案研究时参考.

化学药物治疗后瘤组织病理观察结果表明：药物对瘤组织形态的影响与药物对肿瘤生长抑制的程度有密切的关系. 这提示我们：组织形态学的观察对药物的全面评价具有意义.

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维拉帕米、硝苯啶及尼卡地平的抗炎作用[1]

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Anti-inflammatory effects of verapamil, nifedipine and nicardipine[1]

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ABSTRACT Anti-inflammatory effects of calcium antagonists verapamil (Ver), nifedipine (Nif) and nicardipine (Nic) were compared. They all produced significant inhibitions in acute and chronic inflammatory models in a dose-dependent manner. The ED_{30} in the capillary permeability were: Ver 18, Nif 12 and Nic 8 mg/kg, respectively. In the xylene-induced swelling of mouse ears, the ED_{30} were: Ver 39, Nif 14, and Nic 25 mg/kg, respectively. In the carrageenan paw edema of mice, and in the acetic acid-induced pleurisy and cotton granuloma of rats these drugs inhibited inflammatory responses at 5 or 10 mg/kg. Nif showed a greater effect than Ver and Nic on the paw edema, and Ver showed greater effects than Nif and Nic on the pleurisy and granuloma. At 10 mg/kg they depressed the PGE_2 content measured by radioimmunoassay in inflammatory tissues of carrageenan paw edema of mice.

KEY WORDS verapamil; nifedipine; nicardipine; non-steroidal anti-inflammatory agents; prostaglandins E

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提要 钙拮抗剂维拉帕米(Ver)、硝苯啶(Nif)及尼卡地平(Nic)ig给药，以剂量依赖方式对多种急慢性炎症模型产生明显抑制作用.降低毛细血管通透性，Nic作用强；抑制炎性肿胀，Nif作用较强；抑制肉芽增生及急性胸膜炎，Ver作用较强. 3种药物还显著降低炎症组织中PGE_2含量.

关键词 维拉帕米；硝苯啶；尼卡地平；非甾体抗炎剂；前列腺素E类

炎症反应的许多环节受Ca^{2+}的调控，包括毛细血管的通透性，炎症介质的产生与释放[1-3]. 本文的目的是观察钙拮抗剂维拉帕米(verapamil, Ver)、硝苯啶(nifedipine, Nif)及尼卡地平(nicardipine, Nic)是否具有抗炎作用.

MATERIALS

小鼠由新疆计划生育研究所动物室提供，大鼠由新疆医学院动物室提供，♀♂兼用. Ver针剂(Finland Orion). Nif及阿司匹林(aspirin, Asp)粉剂(新疆制药厂)，临用前以10%的淀粉配成混悬液，Nic粉剂(南京医药工业研究所)，临用前以蒸馏水配制. 地塞米松针剂