

天花粉治疗19例恶性滋养叶肿瘤的临床观察

南京妇产医院 黄跃兰

内容提要 本文报告了用中药天花粉加手术治疗恶性滋养叶肿瘤19例,除2例Ⅱ、Ⅲ期绒癌并恶病质死亡外,17例得以根治。通过临床观察及实验室验证,天花粉可直接作用于绒毛滋养叶细胞,使之变性坏死,并可提高机体的免疫功能。提示天花粉可作为治疗恶性滋养叶肿瘤的选用药物之一。

恶性滋养叶肿瘤是一种常见的恶性程度很高的肿瘤,包括绒毛膜上皮癌(简称绒癌)及恶性葡萄胎(简称恶葡)。仅以手术切除原发病灶容易转移或复发。近年来国内外筛选了几种化学药物,采用大剂量冲击疗法,治愈了不少患者,成为目前最有希望治愈的恶性肿瘤之一。但化疗副反应大,疗程长,费用高。在我院用天花粉引产5000余例中,发现该药能选择性地作用于绒毛滋养叶细胞,由此设想用天花粉治疗恶性滋养叶肿瘤。自1970年起之九年间用天花粉加手术治疗19例,经8~16年随访,疗效较好,报告如下。

临床资料

19例患者中,绒癌5例,恶葡14例。全部病例均经临床、实验室、病理及X线检查确诊。临床检查包括病史、体检;实验室检查包括尿蟾蜍试验,尿或血HCG测定;病理检查按Novak⁽¹⁾等提出恶葡与绒癌之标准诊断。临床分期按北京协和医院所制订标准判定⁽²⁾。绒癌5例,Ⅰ期2例,Ⅱ期2例,Ⅲ期1例;发病年龄在29~43岁,其中4例足月产后,1例良性葡萄胎后。恶葡14例均系良性葡萄胎后恶变,Ⅰ期10例,Ⅱ期2例,Ⅲ期2例。发病年龄23~47岁,其中8例在30~47岁。19例发病至就诊时间在1月至1年之间。

治疗方法及结果

一、治疗方法:

我们采用两种天花粉制剂,天牙冻干粉

(简称天牙粉)及注射用天花粉。前者系1965年我院由民间引产方中筛选出天花粉、牙皂两味,主药是天花粉,牙皂助其吸收。两药经快速冷冻干燥制成10%合剂,置入胶囊,每枚剂量由0.25g~0.5g,经阴道给药。注射用天花粉,1971年由上海生产,供肌肉注射及静脉滴注用。使用前先做天花粉皮试,阴性后始能给药。本组16例用天牙粉治疗,其中绒癌5例,恶葡11例(Ⅰ期8例,Ⅱ期2例,Ⅲ期1例),以温开水冲洗阴道,排除积水后将天牙粉胶囊放入后穹窿,卧床8小时。剂量由0.25g开始,间隔5~7天上药一次,如用药后反应轻微,每次可增加药量0.025g。16例总治疗次数为2~6次。2例用注射用天花粉,溶于5%葡萄糖500ml内由静脉缓滴,首次剂量为5mg,每隔3~5天滴注1次,每例各滴注6次,总剂量各为38mg。另1例恶葡Ⅲ期用天牙粉9次及注射用天花粉1次。如皮试阳性或间隔一段时间再用时需做天花粉脱敏注射。两药一般使用7次。

本组有11例先做子宫加附件切除术,其中9例术后5~10天给天牙粉治疗,1例术后22天开始用药,1例术后2月行天牙粉治疗。3例先用天牙粉阴道上药2~4次后手术;2例滴注天花粉1次后手术。3例单用天牙粉治疗2~10次,未手术。全部病例均未用化疗药物。

二、结果:按1969年8月全国肿瘤会议制定的标准评定,本组19例中除2例绒癌一般情况极差,入院后病情迅速恶化死亡外,17例均痊愈,平均住院48.75天,出院时均做尿TT或

HCG测定阴性。出院后均未进行治疗,随访8~16年无一例复发。1例恶葡1期治愈后生三个健康子女。

讨 论

天花粉治疗恶性滋养叶肿瘤之可能机制是对滋养叶细胞之直接作用及增强机体之免疫功能。国内已将天花粉作为引产药物之一,由引产后胎盘的病理检查观察到胎盘绒毛的变性坏死。通过对天花粉蛋白(Trichosanthin, TCS)进行药理、免疫功能及临床的系统研究,证明TCS对胎盘滋养叶细胞有明显之抑制作用。杨秉炎报告天花粉首先作用于绒毛的合体滋养叶细胞^[9]。上海实验生物研究所利用荧光抗体追踪天花粉素作用,发现8小时后底蜕膜与海绵区之间滋养层呈现明显的荧光,认为天花粉对绒毛滋养层细胞有选择性作用^[10]。我们在多次先用天花粉而后手术的绒癌及恶葡标本中,亦发现滋养叶细胞明显坏死。上述事实可证明天花粉对滋养叶细胞有选择性的直接作用。天花粉是高分子植物蛋白,有极强的抗原性,可引起机体严重的过敏反应以致死亡。上海国际妇幼保健院测定用天花粉后的血清内有抗体长期存在^[11]。作为抗原,天花粉可刺激免疫系统引起非特异性免疫反应,表现为白细胞总数、嗜中性及单核细胞增高,我们发现天花粉甚至可使化疗后骨髓抑制而下降的白细胞增高。郭峰等实验报告天花粉还可以刺激特异性免疫反应,增强T细胞之功能,故认为天花粉是一种免疫增强剂^[12]。免疫功能在恶性肿瘤的治疗中有其特殊的地位,残留的癌细胞要通过机体的免疫机制来清除,这可能是天花粉治疗绒癌与恶葡的另一机制。

天花粉治疗较化疗周期短,副反应轻。化疗是通过影响细胞的有丝分裂而起治疗作用,其副作用表现在造血功能障碍、消化道反应、口腔溃疡、腹痛腹泻、药物中毒性肝炎、皮疹、脱发等,如发生并发症可致死亡。天花粉用药1~2天后发热(多在38.5℃以下),关节肌肉痛,白细胞升高,食欲增进,个别出现严重过

敏反应可死亡。自1970年制出天花粉皮试针剂后,通过严格选择病例,密切观察病情,及时治疗过敏反应,天花粉使用还是安全的。我院用于引产及治疗异位妊娠、恶性滋养叶肿瘤数百例,未出现过敏及其他严重反应。

天花粉治疗绒癌与恶葡有一定的局限性,因个体对它的敏感性有一定的差异,且初用天花粉疗效明显,再用出现“耐药”现象,通常用药7次为度,尚不足以治愈广泛转移的晚期病例。但天花粉配合化疗却可相得益彰,一般情况很差者先用天花粉,待情况改善后再化疗及手术;化疗与天花粉同时使用可减轻化疗的副反应,常能按期完成化疗,增加了化疗的安全性并减轻了病人的经济负担。我们由临床观察天花粉可通过血脑屏障,脑转移时以天花粉静脉滴注配合化疗有明显的效果。因此,我院把天花粉列为治疗脑转移的常规用药及化疗的辅助用药。

天花粉为我国传统中药,它具有药源丰富,造价低廉,治疗周期短,副作用较轻的特点,可作为治疗恶性滋养叶肿瘤的选用药物之一。

参 考 文 献

1. Novak El Gynecologic and obstetrics pathology, 8th ed, London W. B. Savnoers Company 1979: 651—660.
2. 宋鸿钊, 廿年806例绒癌和恶葡化学治疗经验总结. 中华妇产科杂志 1979; 14(4): 255.
3. 杨秉炎, 等. 天花粉引起胎盘功能与形态的变化. 生殖与避孕 1980; 12: 16.
4. 杨宜弟, 等. 天花粉及天花粉素中期妊娠引产的胎盘形态变化观察. 中华妇产科杂志 1980; 15(1): 36.
5. 庄晋琪. 天花粉针剂用作中期妊娠引产后对血清抗体效价的观察. 中华妇产科杂志 1979; 14(2): 122.
6. 郭 峰, 等. 天花粉引产的几项免疫指标观察. 中华妇产科杂志 1981; 16(3): 188.

• 书 讯 •

由《山东医药》杂志编辑部编辑的《内科疑难症笔谈》第二集, 于本月由山东大学出版社出版。每册定价: 2.7元(另加邮资0.2元)。欲购者请与济南市青年路1号《山东医药》编辑部邹伟联系。购50册以下者一律从邮局汇款, 50册以上可从银行信汇(帐号: 3089113, 开户济南市历下区办事处)。

Clinical Observation of Adult Diabetes Mellitus Treated with Jiang Tang Jia Tablet (降糖甲片)

— Left Ventricular Functional Determination in 38 Cases

Lin Lan (林 兰), Zhang Hong'en (张鸿恩); Wang Yuzhong* (王毓钟), et al
Guang An Men Hospital; *Central Laboratory, China Academy of TCM, Beijing

The clinical application of non-invasive left ventricular determination has proved that the systolic time interval (STI) was a good parameter in evaluating the ventricular function and the pharmaceutical effect of the drugs. Jiang Tang Jia tablet consisted of *Astragalus membranaceus*, *Polygonatum sibiricum*, *Pseudostellaria heterophylla*, *Rehmania glutinosa* and *Trichosanthis kirilowi* had been used in treating 38 cases of diabetes mellitus with deficiency of Qi (气) and Yin (阴) syndrome. Their left ventricular function was checked. Results: As the lowering of blood and urine sugar, the heart functions improved, the left ventricular ejection time (LVET) has been extended from 286.62 ± 9.48 ms to 298.18 ± 10.65 ms. It showed that before treatment, the heart ejection time was shortened, heart output reduced, it recovered to a certain degree after the therapy. The pre-ejection period (PEP) decreased from 118.41 ± 11.54 ms to 107.20 ± 14.00 ms, which denoted that before treatment, the cardiac function was markedly deteriorated, but enhanced somewhat after medication, the ratio of PEP/LVET was less than 0.38, it is generally accepted as the most reliable criteria in evaluating the left ventricular function. In this group, the PEP/LVET lowered from 0.42 ± 0.07 to 0.40 ± 0.07 , it indicated that the myocardium impairment and cardiac function disturbance were significantly improved. It elevated the level of plasma insulin, improved the glucose tolerance, lowered the blood lipid, fibrinogen and its catabolic substance. This beneficial effect may be due to regulating the Yin-Yang (阴阳) of the body, replenishing the Qi and Yin, and thus enhancing the function of heart and islets of pancreas. (original article on page 148)

Clinical and Experimental Studies on Treatment of Peptic Ulcer with Jianwei Yuyang Tablets (健胃愈疡片)

Li Jiabang (李家邦), Jin Yiqiang (金益强), et al
The 1st Affiliated Hospital, Hunan Medical College, Changsha

This paper reports 37 cases of gastro-duodenal ulcer treated with Jianwei Yuyang (invigorate the stomach and cure the ulcer) tablets in comparison with a control group treated with placebo. The results proved that the cure rate for the treated group was 73% and the effective rate was 86.5%, while those of the control group were obviously lower. Based on syndrome differentiation, optimal effect was reached in treating "liver stagnation and spleen deficiency" syndrome, the cure rate was 100%. Our experimental results also showed that this drug neither affected the normal hepatic function nor reduced the value of hemoglobin and the count of WBC. Results of animal experiment showed that the mean ulcer index of Jianwei Yuyang tablet group was lower than that of control group ($P < 0.05$) and had a similar mean ulcer index both of proglumide group and of ranitidine group ($P > 0.05$). Through clinical observation and animal experiment, it showed that Jianwei Yuyang tablet has better therapeutic effects than others in promoting the healing of ulcer. (Original article on page 151)

A Clinical Study on Treatment of Malignant Trophoblastic Neoplasia with Trichosanthin

Huang Yuelan (黄跃兰)
Nanjing Hospital for Gynaecology and Obstetrics, Nanjing

Malignant trophoblastic neoplasia is a common but highly malignant tumor. Affirmative effect has been obtained through chemotherapy. The major problems are serious side effects, long course of treatment and high cost. In 5,000 induced abortion patients with trichosanthin (TCS), their histological degeneration and necrosis of villi has been observed, so TCS has been used for treating choriocarcinoma and invasive mole since 1970. From 1970 to 1978, 19 cases of choriocarcinoma and invasive mole were treated with TCS alone. 17 of them survived without additional treatment and recurrence after 8~16 years follow-up, the remaining 2 cases died of severe choriocarcinoma. It is speculated that the main pharmacological mechanism of TCS is its direct action on trophoblastic tissue and stimulates the immune function of organisms in controlling choriocarcinoma and invasive mole. TCS originated in China. It is characterized by rich resources, low cost, short treatment course and relatively mild side-effect, it may enhance the effect of chemotherapy and therefore TCS is recommended among the agents in treating malignant trophoblastic neoplasia. (Original article on page 154)