THERAPEUTIC EFFECT OF ABRIN AND RICIN ON HUMAN CANCERS

Preliminary Report

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(Received for publication, September 25, 1971)

Abrin and ricin are highly toxic proteins and have been isolated and crystallized from *Abrus precatorius*[1] and *Ricinus communis*[2-4] respectively. In our earlier studies, the crystalline abrin and ricin showed remarkable inhibitory effects on the growth of Ehrlich ascites tumor when they were administered intraperitoneally and immediately after inoculation of the tumor cells.[5,6]. The toxic proteins were also able to suppress the growth of the tumor cells when they were administered intraperitoneally in the mice bearing 8-day and 5-day-old tumor respectively[7]. The mechanism of their antitumor activity investigated at molecular level was that the toxic proteins possess a strong inhibitory effect on protein biosynthesis and moderatly inhibitory effect on DNA biosynthesis but no effect on RNA biosynthesis[8,9]. Nevertheless, their dramatic effects on the animal malignant tumor encouraged us to make clinical trials in human cancers.

MATERIALS AND METHODS

Abrin was isolated from *Abrus precatorius* by extracting the kernels with 5% cold acetic acid and then was subjected to ammonium sulfate fractionation. The proteins which were obtained between 45 and 100 percent saturation of ammonium sulfate were pooled and heated at 60° for 30 minutes. After the denatured proteins had been removed, the extracts were fractionated with a DEAE-Sephadex 50 A column and eluted with 0.005 M sodium acetate. The protein peak with high toxicity was pooled and concentrated by ammonium sulfate. After dialyzing the precipitates at 4° against 0.005 M phosphate buffer, pH 6.5, containing 10^{-5} M cupric sulfate rod-shaped crystals of abrin were obtained[1].

Ricin was isolated on a similar method for isolation of abrin except that ricin was precipitated between 0 and 50 percent ammonium sulfate. The toxic protein obtained by DEAE-Sephadex 50 A column chromatography was further fractionated with a CM-cellulose column. The toxic protein eluted with 0.02 M phosphate buffer was pooled, and then concentrated with ammonium sulfate and dialyzed against 0.005 M phosphate buffer, pH 6.5, containing 10^{-4} M cupric sulfate at 4°. After 24 hours dialysis rod-shaped crystalline ricin was obtained[2].

The LD_{50} of crystalline abrin and ricin was found to be 0.020 and 0.013 mg per Kg body weight of mice respectively. The molecular weight of abrin and ricin was found to be 65,000.

The purity of crystalline abrin and ricin was tested by electrophoresis, chromatographic analysis and sedimentation velocity analysis with an analytical ultracentrifuge[10]. Both toxic proteins were free from hemagglutinating activities.

In view of the extremely high toxicity of the phytotoxic proteins and the possibility of inactivation by the liver, I.V. or I.M. administration was precluded from our clinical trials

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and only topical application was taken into consideration; the following modes of administration have therefore been adopted.

1) Local administration of abrin or ricin in ointment

50 mg of crystalline abrin or ricin proven to be homogenous by the above-mentioned tests was dissolved in 5 cc of 0.1 M acetate buffer, pH 4.3, and then 1,000 units of hyaluronidase in 2 cc of normal saline was added. Addition of 5 cc of polyethylene glycol to this mixture enabled the water soluble proteins to dissolve homogenously in 75 g of terramycin ointment 'Pfizer' (each gram contains oxytetracycline HCl equivalent to 30 mg oxyteracycline, 10,000 units of polymixin B sulfate, white petrolatum and liquid petrolatum). This ointment was kept in a refrigerator and was used within one week. Depending on the size of the tumor or crater 1-5 g of this ointment was applied on the surface of the tumor or crater.

2) Intratumorous Administration

0.1 mg-0.2 mg of abrin (0.1 cc. of 0.1 M acetate buffer solution, pH 4.3, 1 cc containing 1 mg of abrin which was filtered through Chamberland and lyophilized) was diluted in 500 cc of normal saline to which 600 units of hyaluronidase was added. 10-20 cc of this solution with 2 cc of 1% xylocain added directly before using was injected into the tumor and adjacent tissues.

Because the substance to be absorbed at individual administration is expected to be small, repetition of local administration of abrin or ricin in ointment and intratumorous injection of abrin was prolonged until complete regression of the tumor was attained. Therefore, the total period of treatment was extended 1-2 months or more.

3) Intraperitoneal and Retroperitoneal Administration

0.1 mg of Chamberland-filtered and lyophilized abrin was dissolved in 500 cc of normal saline to which 600 units of hyaluronidase was added. The total dose of this solution was dripped daily through a polyethylene tube (I. V. set) inserted intra-or retroperitoneally and fixed to the abdominal skin. At the completion of the dripping the tube was closed with a stopcock and kept in sterilized dressing. The dripping was repeated daily until 1.0-1.3 mg of abrin was used.

4) Intra-arterial Administration

An umbilical artery catheter 'Alde' (Cat. No. Mar 1602-5, size 5 Fr. Length 15″) was inserted each to the bilateral internal iliac artery at the ventral site between the proximal ligature and distal clamp and transfixed to the vessels. The two catheters were brought out retroperitoneally to the abdominal wall, where they were connected to a Y-shaped glass adapter through a 3-way stopcock and then further connected to a SIP-11 pump through a silicon tubing. 0.2 mg of crystalline lyophilized abrin was dissolved in 500 cc of normal saline to which 600 units of hyaluronidase and 40 mg of heaprin were added. The speed of dripping was adjusted so as to infuse constantly 27 cc of the solution in an hour. The intra-arterial continuous infusion was continued until 1.5 mg of abrin in total was used.

REPORT OF CASES

A) Administration of Abrin

a) Primary uterine cervical cancer

In the primary cases of uterine cervical cancer the course of recovery has been recorded with color photography of the primary lesion and in the total number of cases the effects of abrin have been proved clinically.

1) Case L. S., age 56. Stage I uterine cervical cancer of epidermoid type. A thumb-sized papillomatous outer growth on the posterior lip was seen. Several days after administration of abrin, superficial hemorrhagic spots were observed in the tumor and the whole tumor changed its color from pink-reddish to liver color, then shrank gradually

and then completely flattened out 10 days after the onset of administration and 4 days thereafter the tumor completely disappeared. The surface of the base of the tumor showed erosion with a tendency to contact bleeding for a week and then was covered with normal mucosa 4 weeks after the onset of therapy. Repeated Papanicolaou's tests were negative. Biopsy done one month after the therapy showed only questionable carcinoma in situ in two out of five specimens, although the cervix showed normal appearance to the naked eye (Figs. 1, 2, and 3). Administration of abrin ointment to the endocervix has been instituted.

2) Case C. S. J., age 46. Stage I uterine cervical cancer of adenocarcinomatous type. A fungoid necrotic tumor of overhenegg-size fully occupied the vaginal lumen. 3 weeks after the onset of therapy the tumor flattened out and the external os could be made out. In this case a particular mode of administration was adopted, that is, a diaphragm (contraceptive) painted with 2.0 g of abrin ointment applied on the cervical tumor was tightly packed and pressed with gauzes. Now, 6 weeks after the onset of therapy, the cancerous tissue has almost disappeared and the cervix shows a broad severe type of papillary erosion with cervical hypertrophy (Figs. 4, 5, and 6).

3) Case L. S. C., age 56. Endocervical cancer, Stage II-b, epidermoid type. Endocervix formed a thumb-sized crater with involvement of upper third of the vagina. 2 weeks after the onset of therapy vaginal lesion cleared up and one week later the crater has diminished in size and the crater wall has been gradually cleansed. A tendency to contact bleeding is still noted.

4) Case H. S. Y., age 46. Stage II-b. Markedly anemic and cachectic. Epidermoid type. Speculum examination reveaied an overheneggsized necrotic crater involving the cervix and upper half of the posterior vaginal wall with papillomatous outer growth still protruding at the edge of the crater just like a dyke. Rectal examination revealed an apple-sized tumor fully occupied the pelvis compressing the anterior rectal wall and the paramatrial infiltration was about to reach the bilateral pelvic wall. However, the rectal mucosa was still intact. Corporeal involvement was indicated by the enlargement of the uterus with its fundus 12 cm above the symphysis. One month's application of abrin ointment resulted in the lowering of the uterine fundus to 7 cm above the symphysis, and the decrease of the size of the pelvic tumor from apple to heneggsize. Spontaneous bowel movements, which she had never had before therapy, have become possible owing to the decrease of rectal compression. The anemia and general condition have greatly improved.

b) Recurrent or persistent uterine cervical cancer.

1) Case Y. L. Y., age 58. Persistent cancerous lesion at the vaginal stump after radical operation. Papanicolaou's tests were positive. Pathological examination of the operative specimens also revealed posterior vaginal cuff with its distal section line was carcinomatously involved. Epidermoid type. After 2 weeks' administration of abrin ointment the cancerous lesion has been replaced by granulation tissues as proved histopathologically.

2) Case L. C. C., age 53. Epidermoid carcinoma. Recurrent lesion in the right lateral vaginal wall which was removed and irradiation followed. 3 months later biopsy still disclosed degenerated cancer cells. After local administration of abrin ointment for 2 weeks the cancer cells disappeared, as proved by Papanicolaou's tests as well as biopsy.

c) Intraperitoneal Administration of Abrin.

1) Case C. Y. S. L., age 44. Primary papillary cystadenocarcinoma of bilateral ovaries

with 5,000 cc of ascites and visceral dissemination. Underwent operation on September 1, 1971. From Sep. 1 to Sep. 14, 300 γ of abrin in saline solution was administered intraperitonealy at 3-day intervals and in total 1,780 γ of abrin was used. After the third administration no more accumulation of ascites has been observed and general condition has been greatly improved. On Sep. 27, 1971, a second-look operation was performed. The abdominal cavity was free from cancerous lesions except for 700 cc of ascites and only 2 tiny grayish degenerated nodules, which were removed and sent to the laboratory for examination. Cytologic examination revealed no cancer cells in ascites and pathological examination revealed the two tiny nodules to be fat tissues. 100 γ of abrin in 500 cc normal saline solution was administered daily from Sep. 27 and up to date 1,300 γ of abrin has been used. The patient is doing very well.

2) Case C. W. S., age 44. Recurrent ovarian cancer developed giant metastatic lesion in the liver after irradiation, which was proved by X-ray (elevated diaphragm) and radioisotope scanning. After evacuation of 2,500 cc. of ascites 100 γ of abrin was administered intraperitoneally every day. The liver tumor palpable 3.5 finger-breadth below the costal margin before the treatment has become almost inpalpable within one week after the onset of therapy (Fig. 7). The accumulation of ascites has become less marked and neuralgia radiating to the shoulder has greatly alleviated, necessitating narcotics only once a day after treatment, while the patient requested narcotics every two hours before the therapy. Repetition of radioisotopic examination will be attempted in the near future.

d) Intratumorous Administration of Abrin.

1) Case C. U. Y., age 44. Recurrent tumor in the pelvis and vaginal stump after anterior evisceration for Stage IV uterine cervical cancer, epidermoid type. Markedly anemic and cachectic. As described above, 2-4 γ of abrin was injected into the tumor. Several injections resulted in a remarkable shrinkage of the tumor and alleviation of neuralgia. General condition has also been improved.

2) Case H. M., age 59. Recurrent and metastatic adenocarcinoma of the right inguinal nodes. Several injections of 2-4 γ of abrin caused a remarkable shrinkage of the tumor.

e) Retroperitoneal Administration of Abrin.

Case W. C. C. M., age 47. Epidermoid Cancer. Retroperitoneal dripping of 100 γ abrin through polyethylene tube was performed daily for the purpose of destroying the cancer cells possible left over in the pelvis after anterior evisceration for Stage IV uterine cervical cancer. In spite of the extensive spread of cancer, the patient is doing very well.

f) Continuous intra-arterial Infusion of Abrin.

1) Case L. A. S., age 49. Stage IV uterine cervical cancer with hemorrhagic ascites, disseminations on uterine serosa, vesicouterine reflexion, Douglas pouch, rectum and intestinal serosa, thumb- to ping-pong ball-sized metastatic lesions in the bladder wall, extensive pelvic lymph nodes metastases as proved by biopsy at laparotomy, and over-henegg-sized gyri-like cervical tumor. Epidermoid carcinoma. Contiunous intra-arterial infusion with 200 γ of abrin was instituted immediately with the technique described above. Up to date 1,500 γ of abrin has been used. Speculum examination on the following day revealed the overhenegg-sized gyri-like outer growth of the cervix decreased in size (hen egg) with profuse serous and slimy discharge in the vagina, and on the second day the tumor became small henegg size. The tumor decreased in size gradually,

restored almost to its original size and shape with its external os discernible but still with some papillomatous outer growth around the latter. It was very interesting that the tumor had been anemic and friable throughout the whole course of infusion. The slimy discharge was replaced by blood-tinged discharge from the external os from the 5th postoperative day. No hematologic change, and no changes in blood chemistry. Mild fever was caused by E. Coli infection of urinary tract which was well controlled by Wintomylon. No dizziness. The patient is doing very well. We will perform retroperitoneal dripping for the metastatic nodes after completion of intra-arterial infusion (Figs. 8, 9, and 10).

B) Administration of Ricin

1) Case L. Y. S., age 75. Epidermoid cancer of the uterine cervix with tumorous involvement and crater formation of upper half of the posterior vaginal wall. Severe hemorrhage was seen. 1 week after administration of ricin a remarkable shrinkage of the crater and the tumor was observed.

2) Case H. M., age 59. Recurrent adenocarcinomatous lesion with a big crater at the vaginal stump. Necrosis was marked. Right inguinal region revealed a tumor of overhenegg size which was proved to be metastases histopathologically. In the crater at the vaginal stump ricin ointment was applied and into the iliac and inguinal tumor intratumorous injection with abrin was done. Local and general condition have been greatly improved.

COMMENT

Our experiences, though still limited, would seem to indicate the beneficial effects of abrin and ricin on human cancers and in particular, the applicability of this substance in the cases of radioresistant and advanced inoperable cancer, thus adding a new powerful therapeutic tool in the treatment of cancer. Varying modes of administration have been proposed and tried. Anticancer effect appeared slowly in the cases treated with topical administration of abrin or ricin ointment while it appeared to be most rapid and dramatical in the cases of intra-arterial continuous infusion and I. P. administration. However, no side effects were observed in the former while dizziness, transient fever and a trace of proteinuria were frequently encountered in the cases of I. P. and intratumorous administration. It is noteworthy that a case of intra-arterial continuous infusion did not show any side effects. Emphasis should be placed on the fact that as compared with other anticancer chemicals, these drugs possess no appreciable systemic side effect (either hematology or blood chemistry) and as compared with irradiation cause no damage to the normal adjacent tissues. It is very interesting to note that a remarkable increase of reticulocytes (from 3 to 16 to 36%) has been observed in some cases of I. P. and retroperitoneal administration (Case Y. S. L., W. C. C. M., C. W. S.). In case C. Y. S. L. the last two I. P. administrations in the first course of abrin treatment, and each I. P. administration in the second course were followed by moderate or high transient fever. Therefore, we suspected that antigen-antibody reaction was evoked by abrin. However, in this case no antibody production was confirmed by immuno-elelectrophoresis.

Owing to the limit of time and manpower, in the present study ricin was used only in the form of ointment. However, the clinical course of Case L. Y. S. and Case H. M. is also as satisfactory as with abrin.

Our limited experiences obtained from the cases decribed above are that pathological changes are always sluggish after therapy not keeping pace with the relatively rapid clinical improvement. This might be related to the mechanism of the anticancer action of abrin or ricin which is different from

other anticancer chemicals at molecular level. We shall not go further into this point in the present paper and shall publish this elsewhere.

SUMMARY

Proper modes of administration have enabled us successfully to apply two plant proteins—abrin and ricin—clinically in spite of their extremely high toxicity and to confirm their strong anticancer effects on human cancers. However, how long the complete remission can be maintained, and whether or not any difference of sensitivity to these proteins exists between various human cancers should await further energetic investigation.

AKNOWLEDGEMENTS: We thank Dr. K. H. Ling of this Institute for his valuable suggestions and discussion. We are also indebted to Mr. S. T. Ju, Miss S. Y. Yang of this Institute and Dr. C. H. Roan of Department of Gynecology, Provincial Chung-Shing Hospital for their technical assistance. We are in particular indebted to Prof. Wang and Prof. Chen, The National Taiwan University Hospital for their generous assistance in radioisotope scanning of the clinical cases. This investigation was supported by National Council of Science, Republic of China.

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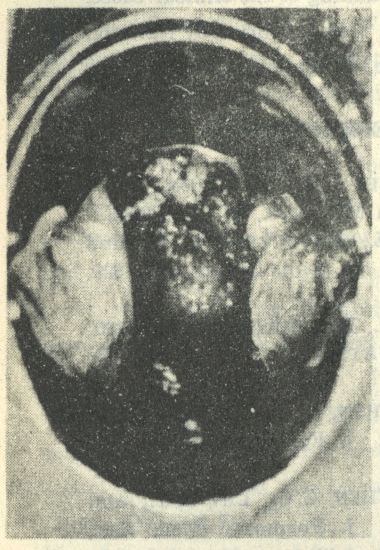

Fig. 1, Case L.S.,
Cervical finding before treatment. A thumb-sized papillomatous outer growth is seen.

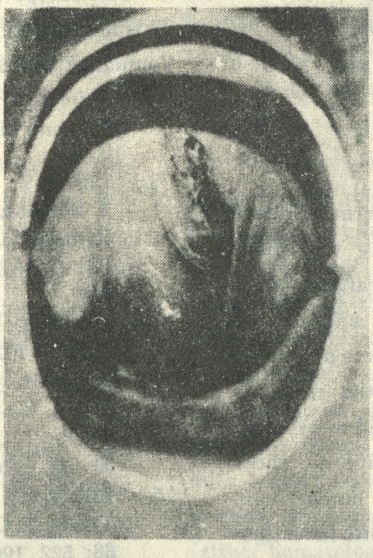

Fig. 2, Case L.S.,
Cervical finding 4 weeks after treatment. papillomatous outer growth almost disappeared.

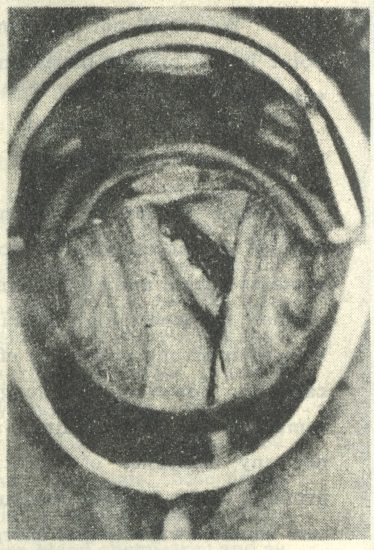

Fig. 3, Case L.S.,
Cervical finding 6 weeks after treatment. papillomatous outer growth disappeared.

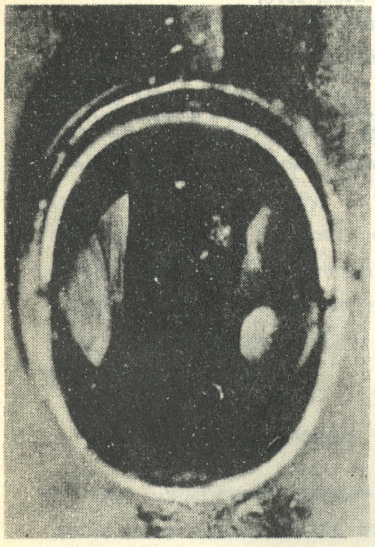

Fig. 4, Case C.S.J.,
Cervical finding before treatment. A large fungoid necrotic tumor occupied the whole vaginal lumen.

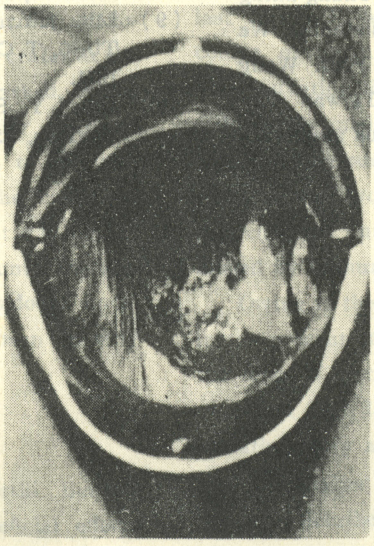

Fig. 5, Case C.S.J.,
Cervical finding 3 weeks after treatment. The fungoid mass diminished in size and is going to flatten out.

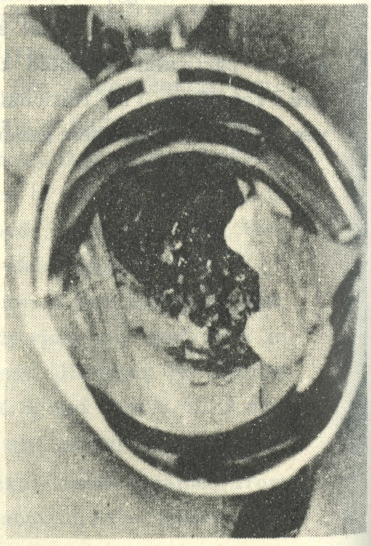

Fig. 6, Case C.S.J.,
Cervical finding one month after treatment. The cervix almost restored its shape and size, however, still presenting a picture of broad papillary erosion with a tendency to outer growth.

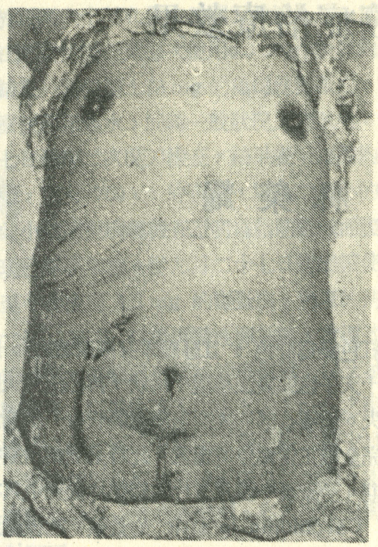

Fig. 7, Case C.W.S.,
shows the course of regression of liver tumor after treatment.

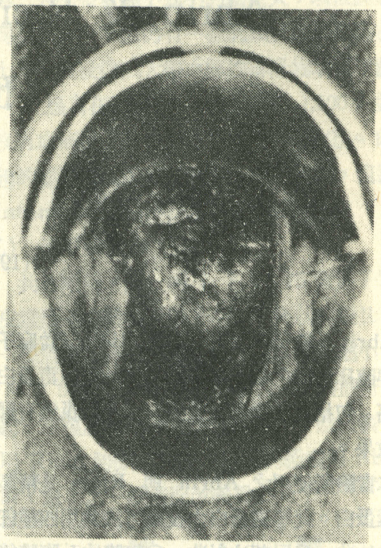

Fig. 8, Case L.A.S.,
The cervical tumor before intraarterial infusion.

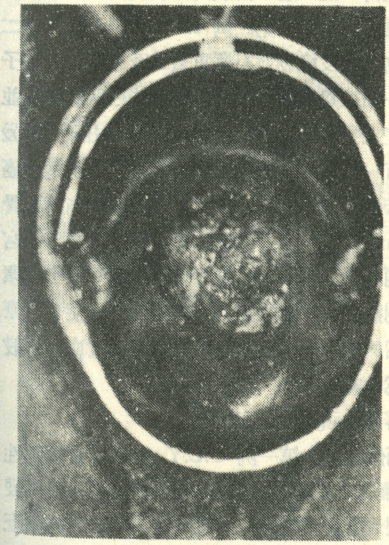

Fig. 9, Case L.A.S.,
The cervical tumor regressed 3 days after intraarterial infusion. The vaginal lesion of the upper third of the posterior vaginal wall also started regressing.

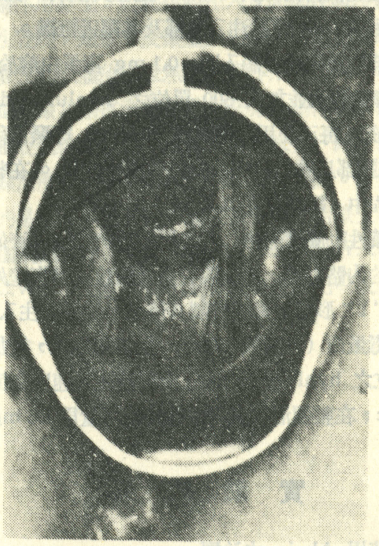

Fig. 10, Case L.A.S.,
The cervical tumor showed marked regression 7 days after intraarterial infusion. The vaginal lesion has almost cleared up.

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Abrin 及 Ricin 對人體癌症治療效果

預　報

董大成　徐千田　林榮耀

(1971年9月25日受理)

Abrin (鷄母珠毒蛋白) 與 Ricin (蓖麻子毒蛋白) 經臨床實驗的初步結果顯示，此兩種毒蛋白對子宮頸癌 (包括表皮樣癌及腺癌) 以及卵巢癌有顯着的治療效果。

本實驗所使用之 Abrin 與 Ricin 是精製的結晶性毒蛋白。此等毒蛋白之投藥方法共用四種即：①局部塗抹法，②局部注射法，③腹膜內及腹膜後注射法，④繼續性動脈灌流法。

局部塗抹法：用 50 mg 之 Abrin 或 Ricin 以少量醋酸緩衝液溶解後再加入 75 g 的羥四環素藥膏 (藥膏含有 2.25 g 之羥四環素)。塗抹患部時每次使用上述製成的軟膏 1 到 5 g，每天早晚各塗抹一次。

局部注射法：把 0.1 mg 的結晶毒蛋白先溶於少量醋酸緩衝液再稀釋於 500 cc 生理食鹽水，取此溶液 10 到 20 cc 直接注入患部及其鄰近組織。

腹部內及腹膜後滴入法：0.1 mg 毒蛋白溶於500 cc 生理食鹽水並加入 600 單位之 hyaluronidase 製成試液。每天使用此種試液 500 cc 經聚乙稀管 (固定在腹部皮膚上) 滴入腹膜內或腹膜後。在整個治療過程中，總共使用 1.0 到 1.3 mg。

繼續性動脈灌流法：各使用一隻臍動脈導管使插入兩側的內髂動脈，並使導管由後腹膜連到腹壁外，再接一"Y"形管用幫浦控制其流速，使每天注入 0.2 mg 的毒蛋白 (先溶於 500 cc 生理食鹽水，後加入 600 單位之 hyaluronidase) 並維持注入速度在每小時 27 cc，在整個治療過程中總共使用量爲 1.5 mg。

實驗結果

(甲) 使用 Abrin 之治療：

(1) 初期子宮頸癌共有四例，第一例爲 56 歲的病人 (L. S.) 是第一期表皮樣型的子宮頸癌。在子宮頸後唇有一大拇指大小的乳頭狀癌。經使用 Abrin 軟膏外敷後數天，癌組織有出血點出現其後腫瘤的顏色也由粉紅色變爲肝色，且腫瘤本身漸漸萎縮。開始治療後十天子宮頸表面呈現平滑狀，再經過四天腫瘤完全消失。腫瘤基部的表面呈現糜爛狀有一星期之久。隨後完全被正常粘膜所覆蓋。此時是開始治療後第四個星期。治療後一個月五片病理切片檢查中只有二片呈現 Carcinoma in situ 的景像。此後毒蛋白軟膏繼續使用於子宮頸內。第二例：CST, 46 歲是第一期子宮頸腺癌。腫瘤之大小比鷄蛋還大用毒蛋白軟膏塗抹過的避孕套蓋住患部，三週後癌組織漸漸消失，六週後子宮頸只留下乳頭狀糜爛及子宮頸肥大，第三例爲 LSC，56 歲屬第二期 -b 型子宮頸內癌 (表皮樣型)。子宮頸內有一大拇指大小的杯狀病變。病變已侵犯到陰道的上三分之一處，經二週治療後陰道病變消失再，經一週子宮頸內杯狀病變的大小減少，同時輪廓變爲清楚，第四例 H. S. Y. 46 歲爲第二期 b 型子宮頸表皮樣癌並有嚴重貧血及惡病質。在子宮頸上有一個比鷄蛋還大且已呈壞死的杯狀病變，並在陰道後壁上半部有乳頭狀瘤狀物突出。由肝門診發現骨盆內有一蘋果大小的腫瘤壓迫着直腸的前壁。癌已由子宮旁侵犯達骨盆壁。子宮變大其底部高達恥骨上方 12 cm。經一個月的塗抹毒蛋白軟膏後，子宮底部降低到恥骨上方 7 cm 處而骨盆腫瘤的大小由蘋果大縮小到鷄蛋大。治療前病人不能自行排便，治療後由於腫瘤的縮小，病已人能自行大便。貧血及一般狀況也大爲改善。

(2) 再發及頑固性子宮頸癌

共有兩個病例，第一例 Y.L.Y. 58歲。是頑固性子宮頸癌(屬表皮樣型)此病人是曾經根治開刀後再發者。經二週治療後糜爛性的癌組織經病理組織的檢查證明爲肉芽組織所取代。第二例 L.C.C. 53 歲表皮樣子宮頸癌。病變發生在右邊陰道側壁，該處曾經接受根治開刀治療，開刀後三個月發現仍有變性的癌細胞。經毒蛋白油膏塗抹後兩星期，由 Papanicolaou's 試驗及病理切片檢查皆證明癌細胞已消失。

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(3) 腹膜內滴入法

共有二例，第一例C.Y.S.L.，44歲，在兩側卵巢有初發性乳頭狀囊腺癌且腹腔有 5,000 cc. 的腹水，於民國六十年九月一日開刀並於九月一日到九月十四日之間每隔三天每次使用0.3 mg作腹膜內滴入治療，結果一共使用 1.78 mg 的鷄母珠毒蛋白。於第三次治療後卽無腹水，同時一般狀況大爲改善。於九月二十七日做第二次開刀檢查，結果表示腹腔內已無癌性病變，只有 700 cc 的腹水，以及二個小的變性結節。此小結節經病理檢查證明爲脂肪組織而腹水經檢查發現已無癌細胞。從九月二十七日起繼續使用毒蛋白，至今共使用 1.3 mg 的毒蛋白，患者的情況良好，第二例 C.W.S. 44歲再發性卵巢癌，曾經接受根治開刀的治療，肝臟已有轉移的癌組織。每天抽出 2,500 cc 腹水後由腹膜內滴入法注入 0.1 mg 之毒蛋白，經一週治療後肝瘤已由肋下三個指廣大減少到不能被摸到，同時放射到肩部的神經痛也已減輕。本來在治療前要兩小時打一次的麻醉劑，在治療後只需一天打一次針卽可。

(4) 局部性注射法

共有二例，第一例 C. U. Y.，44歲再發性第四期子宮頸表皮樣癌。有嚴重貧血及身體虛弱的現象，注射 2-4 γ 之毒蛋白後腫瘤大爲縮小，神經痛也減輕，一般狀況進步，第二例， H. M. 59 歲右側腹股結節的再發性轉移癌。經毒蛋白 (2-4 γ) 注射後腫瘤顯著變小。

(5) 腹膜後滴入法

W. C. C. M.，47歲，第四期子宮頸癌，曾經切除恐癌細胞殘留於管盆內故續用毒蛋白治療，經治療後患者症狀良好。

(6) 繼續性動脈內灌流法

L. A. S.，49 歲，第四期子宮頸癌（表皮樣型）經開刀發現有出血性腹水。癌細胞散佈到子宮，及大小腸漿膜，膀胱有大拇指大到乒乓球大的轉移腫瘤，骨盆的淋巴腺也證實有癌組織的轉移，隨卽開始繼續性動脈灌流，每天 200 到 100 γ 之鷄母珠毒蛋白，第二天就發現子宮頸上比鷄蛋還大的腫瘤已消失到如鷄蛋大的腫瘤並在陰道上有多量漿性及黏性的排出物，第三天腫瘤更縮小到小的鷄蛋大，以後腫瘤繼續縮小到原來大小，但仍有一些乳頭狀組織殘留在子宮頸口上。灌流後第五天帶血絲的排泄物取代了黏性排泄物。此惠者在治療中，總共使用 1,500 γ 並在治療中沒有血液學上及血液生化學上的變化。由大腸菌引起的泌尿系發炎使病人有過輕度發燒，但迅速地被 Wintomylin 控制病人症狀改良很多。

(乙) 使用 Ricin 之治療

共有兩例，第一例 L. Y. S., 75 歲爲子宮頸癌，表皮樣型。在陰道後壁上半部有杯狀病變且有嚴重出血。經治療後杯狀病變以及腫瘤有顯著縮小。第二例 H. M.，59 歲，再發性子宮頸腺癌，陰道有大的杯狀突起，右腹股有鷄蛋大小的轉移瘤。陰道裏的杯狀病變用 Ricin 治療，腹股及腸管的腫瘤用 Abrin 局部注射，患者之一般情況改善很多。

結　　論

本實驗雖然規模不大，但初步結果顯示 Abrin 及 Ricin 對人體癌症頗爲有效，尤其是不宜開刀的末期癌症病人及對放射線治療有抵抗性之病人，使用 Abrin 或 Ricin有更良好的反應。用局部塗抹法其抗癌作用比較緩慢而使用繼續性動脈灌流法及腹膜內注入法則反應較快。在使用局部塗抹過程中，並無任何副作用發生。但在腹腔注入及局部注射時偶而有暫時性發燒，頭暈，及微量蛋白尿。值得注意的是使用繼續性動脈灌流法並無任何副作用，Abrin 及 Ricin 並不像其他抗癌藥品常有全身性副作用（在血液學及血液生化學上如白血球數目之減少）同時也沒有放射線治療所引起的破壞正常組織的缺點。此外相當有趣的是在某些腹腔內及腹腔後滴入的治療上有顯著的增加網織血球的現象（如 C. Y. S. L., W. C. C. M., 及 C.W.S. 三個病例）但是且沒有證明出有抗證的產生。