

INTRALESIONAL INJECTION FOR CONDYLOMA ACUMINATUM

Intralesional Injection of a Small Amount of Bleomycin
for Condyloma Acuminatum

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SYNOPSIS-ABSTRACT

The therapeutic measures as surgical resection or cautery with drugs have been used in the treatment of condyloma acuminatum, but relapses are not infrequent. We obtained excellent therapeutic results in the treatment of 5 cases of condyloma acuminata grown in the vulva by intrafocal injection with a small dose of bleomycin which was found recently in Japan as an antitumor antibiotic against squamous cell carcinoma. Neither side effect nor relapse was observed.

Various methods of chemical, surgical and physical therapy have been employed in the treatment of condyloma acuminatum. However, these methods are not satisfactory, since recurrences are frequent. Considerable difficulty has been occasionally encountered upon the surgical resection of multiple condylomata, especially vulval condylomata.

We have recently obtained excellent therapeutic results to eradicate condylomata acuminata in 5 cases by intratumor injection of very small amount of bleomycin (BLM), an antitumor antibiotic, which was recently discovered in Japan by UMEZAWA *et al.*¹⁾.

BLM is an antitumor antibiotic produced by *Streptomyces verticillus* and was found by UMEZAWA *et al.* in 1962¹⁾. Its structural formula has not been determined, but it has a molecular weight of 1,400 and is a water-soluble basic polypeptide^{2,3,4)}.

It inhibits the activity of DNA polymerase by binding to DNA^{5,6,7)}. Excellent therapeutic results by bleomycin have been reported in the treatment of squamous cell carcinoma⁸⁻¹³⁾. Occasionally it has caused pneumonia-like symptoms or pulmonary fibrosis as a side effect but never has produced leukopenia¹⁴⁾.

TECHNIQUE OF INTRALESIONAL INJECTION

Fifteen mg of crystalline BLM contained in an ampule were dissolved in 9 ml of xylitol solution and preserved in a 10 ml vial, from which an appropriate amount was withdrawn when used. The solution contained 1.0 mg of BLM per 0.6 ml. Using a tuberculin syringe and a needle, the solution was injected into a tumor at several sites. Care was taken for the solution to remain only within the tumor. The dosage was adjusted to the size of the tumor. If tumor was so flat as not to allow the intratumoral injection, the injection was performed into the skin as close to the tumor as possible. Injections were repeated weekly for several weeks.

CASE REPORT

Case 1 A 26 years old woman had noticed the presence of several tumors in the vulva 6 months before. The tumors were resected by a surgeon, but relapse was noticed 10 days after the operation increasing in size. Then, when she was seen in our clinic she had the tumors localized at the posterior part of both labia minus pudendi and vaginal orifice, and sized smaller than a small finger tip. They were cockscomb-shaped with many fissures, glossy and soft tumors. After admission 0.5 mg of BLM were injected locally according to the technique described above every 5 days for 3 times. The condylomata showed rapid reduction in size after the first injection. After the third injection, the tumor almost disappeared leaving moderate erosion which healed 2 to 3 days later. Ten days after the third injection, she was released from the hospital after receiving another injection of 0.5 mg of BLM to prevent relapse. No relapse has been observed. None of the side effects was noticed

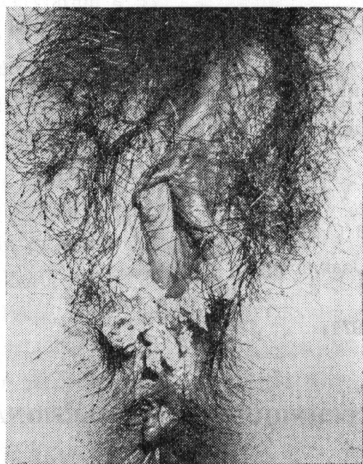


Fig.1 Case 1, vulval condylomata, before the treatment.

(Figs. 1 and 2).

Case 2 A 24 years old woman had found a number of tumors enlarging on the vulva about 3 months previous to her first visit. They located almost at the same area as that of Case 1. The papilliform tumors were glossy whitish and thumb tip in size. She was treated as an outpatient. A total of 6.5 mg BLM was injected over a period of 2 months. At first she received an injection of 1 mg every week for 4 weeks, then the weekly dose was reduced to 0.5 mg corresponding to reduction of the tumor in size and the medication was continued for following 5 weeks. Finally, the tumors disappeared completely leaving no scar. Neither relapse nor side reaction was observed.

Case 3 A 40 years old woman had found several small tumors in the vulva 3 months before. They were small glossy papilliform tumors from half of a rice grain to a red bean in size, and localized at the posterior half of both labia minus pudendi and at the vaginal orifice. A total dose of 3.0 mg BLM was injected locally in 3 divided 1 mg doses, resulting in complete disappearance of the tumors. Neither relapse nor side effect was noticed.

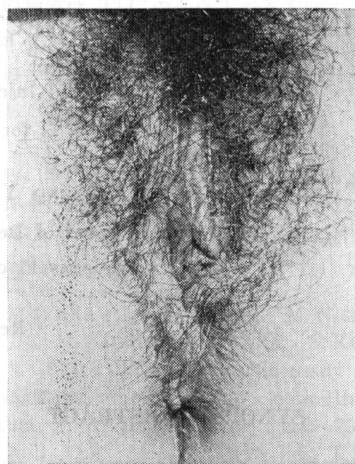


Fig.2 After the intralesional injection of BLM, the tumors disappeared completely.

Case 4 A 28 years old woman was seen with a complaint of many growing tumors of the vulva. They were ischemic, cockcomb-shaped and ranging up to a soy bean in size, localized on both labia minus pudendi. A total dose of 4.5 mg BLM was injected locally over a period of one month. For the first 3 weeks, weekly dose was 1 mg, then the dose was reduced to 0.5 mg for the following 3 weeks. Result was complete cure. Neither side reaction nor relapse was observed.

Case 5 A 25 years old woman found the presence of a number of small tumors in the vulva about 10 days before. While she received irrigation at a gynecological clinic because of a large amount of vaginal discharge, the tumors became larger and she visited our clinic. The tumors were localized on both labia minus pudendi and at the vaginal orifice. Five local injections of BLM 0.5 mg were performed with one week intervals. The site became eroded slightly at first, but after 2 or 3 injections it cured without leaving any scar. No relapse or side reaction was observed.

The results of treatment in the above 5 cases are summarized in the following table.

Case	Age	Sex	Site	Single injection dose	No. of injection	Total dose	Effect
1	26	F	Labia minus pudendi, vaginal orifice	0.5 mg	4	2 mg	Remarkable
2	24	F	"	1.0 0.5	4 5	6.5	"
3	40	F	"	1.0	3	3.0	"
4	28	F	"	1.0 0.5	3 3	4.5	"
5	25	F	"	0.5	5	2.5	"

DISCUSSION

It has been wellknown from a number of publications that BLM gives excellent therapeutic effect to malignant tumor of the skin, particularly squamous cell carcinoma⁸⁻¹³). It seems that the treatment of benign tumors with systemic administration of BLM has been hesitated because of its side effects^{12,14}) and of its expensiveness although its effectiveness is highly conceivable. Taking these into account, we tried local injection of a small amount of BLM directly into the affected focus. Five cases of condylomata acuminata were treated with the local injection of BLM and all of them responded well with complete disappearance of the tumors.

Even the total dose of BLM administered in this study ranged from 2.0 to 6.5 mg which are far smaller in amounts than a single dose of BLM used in systemic administration. It is well documented that BLM may cause fever or anorexia in a dose of less than 50 mg and pneumonia-like symptoms or pulmonary fibrosis which may lead to fatal outcome when given more than 250 mg^{12,14}). However, it has less harmful effect on the hematopoietic organs compared to other antitumor agents. Some degree of side effects might be permissible in a case of malignancy, but it should be avoided in the treatment of benign tumors like condyloma acuminatum. A single dose of BLM used ordinarily in intravenous injection is 15 mg. In the present study, such a small dose of 6.5 mg or less is sufficient to treat condyloma acuminatum when applied locally. Moreover, it might be expected that only small fraction of injected drug leaks into blood stream when the drug is administered into the tumor.

CONCLUSIONS

Five cases of condylomata acuminata were completely cured without relapse and side reaction by local treatment with BLM which was injected into the tumor in a dose of 0.5 to 1 mg each time. A total dose of 2 to 6.5 mg is less than a single dose of the routine intravenous injection. This treatment is considered to be one of the most effective therapeutic measures presently available.

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