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Radiation Therapy in Carcinoma of the Vulva
A Review of Fifteen Patients†

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외음부 암의 방사선 치료

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외음부에서 발생하는 악성종양은 부인과 영역의 악성종양중에서는 드물게 발생하는 것으로 알려져 있으며 치료에 있어서도 수술 또는 방사선치료 단독의 경우보다는 수술후 보조적으로 방사선 치료를 시행하는 것이 더 효과적이고 치료율도 높은 것으로 알려져 있다. 이에 1971년 1월부터 1985년 4월사이에 연세대학교 의과대학 치료방사선과에서 외음부 악성 종양으로 진단되어 방사선 치료를 받았던 15예에 대하여 후향성 분석을 시행한 바 다음과 같은 결과를 얻었기에 보고하는 바이다.

1. 15예의 외음부 종양 환자중 4예는 수술요법 시행후 보조적요법의 방사선 치료를 받았으며, 1예는 수술전 방사선 치료를 받았고, 나머지 10예는 근치적 목적의 방사선 치료를 받았다.

2. 방사선치료만을 시행한 群과 방사선치료 및 수술요법을 병행한 群과의 국소제어율을 비교하여 본 결과, 전 15예의 국소제어율은 53%(8/15)였으며, 단지 방사선 치료만을 시행한 群에서는 40%(4/10), 방사선 치료 및 수술요법을 병행한 群에서는 80%(4/5)의 국소제어율을 보였다.

3. 치료 실패율은(국소적 잔존+국소재발 또는 원격전이) 단지 방사선 치료만을 시행한 群에서는 70%(7/10), 수술후 방사선치료을 시행한 群에서는 40%(2/5)의 성적을 보였으며, 치료실패 호발부위는 원발병소(외음부)였다.

ABSTRACT

This study analyzes fifteen patients who underwent a course of radiation therpy for their vulva cancer in the Department of Radiation Oncology, College of Medicine, Yonsei University from January, 1971 to April, 1985.

Four patients had initial surgery for their vulva cancer and were subsequently treated by a course of adjuvant radiation therapy. Eleven patients were given radiation therapy as the initial course of therapy, and one of these was in adjuvant setting before radical surgery.

Treatment in each instance was individuilzed and usually consisted of some components of exte-

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rnal beam, brachytherapy, and/or electron beam therapy.

Primary local control rate in all cases was 53% (8/15), 40%(4/10) in the radiation therapy alone group and 80%(4/5) in the radiation therapy combined with surgery group. Treatment failures were noted in 7/10 in the radiation therapy alone group and 2/5 in the radiation therapy combined with surgery group.

The most common failure site was primary site failure(vulva).

INTRODUCTION

Prior to 1940, vulva cancer was not well understood. Treatment in most advanced centers was usually not effective; 5-year survival rates were 10~20%. Following the surgical principles espoused by Basset in France, Taussig in the United States and Way in Briatain demonstrated 5-year survival rates of 60% to 70%, utilizing a radical enbloc dissection of the vulva and regional node. In spite of the decrease in the mortality rate using radical surgery, operative morbidity was still high. The most frequent problems were wound necrosis, infection, leg edema and the collection of serous fluid. Generally, irradiation is not desirable as primary therapy for patients with vulva cancer since the area has a poor tolerance to radiation because of friction and moisture.

High dose irradiation to the vulva can cause painful acute reactions and also produce late complications such as ulcers that require prolonged local treatment and may also be quite painful. However, attempts have been made to circumvent this shortcoming by using brachytherapy* as a primary modality of treatment in certain cases in which surgery is regarded as undesirable. Moreover, the introduction of the supervoltage therapeutic machine and some equipped with electron beam, along with improved technique of delivering the beam, has made it possible to overcome some of the problems of limited tolerance of the vulva to ionizing radiation and radioresistance. Fortunately, we had an opportunity to study 15 patients of vulva cancer managed by radical or adjuvant radiation therapy. The purpose of this study was to evaluate the treatment plan, results and prognosis of 15 patients with vulva cancer who received various combinations of treatment in the Dept. of Radiation Oncology, College of Medicine, Yonsei University from January, 1971 to April, 1985.

The distribution of age, histology, stage, follow-up status, treatment failure pattern and complications subsequent to the treatment given to these patients were analyzed.

MATERIALS AND METHODS

From January 1971 to April 1985, 15 patients with vulva cancer were evaluated in the Dept. of Radiation Oncology, College of Medicine, Yonsei University.

All patients received routine pretreatment workups, including chest X-ray, intravenous pyelogram, cystoscopy, sigmoidoscopy in addition to a complete pelvic examination, blood count, urinary analysis and blood chemistries. Examinations of lymph node involvemnt were done by inspection and pelvic examination in 9 patients, by lymphangiogram in 5 patients and by postoperative survey in one patient. Biopsy was done on all cases.

The average age was 57 years ranging from 33 to 73 years old. One patient had documented leukoplakia, one condyloma accuminata in conjunction with the vulva cancer. One patient had VDRL positive.

Two patients had received TAH due to cervical cancer, one of the two patients had received intracavitary radium therapy. The presenting signs and symptoms in this group of patients were similar to those in other reports, and the most common ones were a lesion on the vulva with

* interstitial radium implant, surface radium applicators, combination of radium implant and surface radium applicators

Table 1. Histologic Findings in 15 patients with Vulva Cancer

Histologic Type	No. of cases
Epidermoid	13
Paget's disease	1
Anaplastic or Rhabdomyosarcoma	1
Total	15

pruritis, pain, discharge, or mass in the groin.

Histologic findings were made up of epidermoid carcinoma with no statement of differentiation 9 cases, moderately or well differentiated 3 cases, and poorly differentiated 1 case. There were one case of Paget's disease and one case of sarcoma or anaplastic cell type (Table. 1).

The distribution among the various stages (FIGO) was the following: stage 1, 1(7%); stage Ⅱ, 3(20%); stage Ⅲ, 9(60%); and stage Ⅳ; 2(13%). The TNM classification was used to define the local spread of the tumor(Table. 2,3).

Staging was retrospective and determined from clinical description, photographs, and pathology reports. There could be considerable errors in this method of retrospective staging.

The radiation therapy treatment modalities changed markedly over the time span of this study. Orthovoltage was used in the early 1970's, by which one patient was treated.

Cobalt teletherapy, Megavoltage, and electron beam therapy have been used for external radiation therapy ramaining 14 patients. Tandem inserted mold with RALSTRON(Co-60) has been used for contact therapy.

The midline pelvic tumor dose with these modalities varied from 3,000 to 6,000 cGys through anterior only, or parallel opposed anterior and posterior portals to cover the primary site and the inguinal and external iliac nodes with 2 : 1 or 3 : 1 loading tumor dose in contact therapy varied from 2,100 to 3,900 cGys(Table 2,3).

The surgical approach methods were also variable from wide excision to radical vulvectomy and inguinal node dissection. 13 patients have been followed for a maximum 130 months. 2 patients were lost to follow up after treatment(Table 2,3).

Table 2. Cases Summary in Radiation Treatment Alone Group

	Stage			Radiation treatment(cGy)		Primary control	Follow-Up status (Month)
	Age	TNM	FIGO	Ext.	CT		
1	73	T3N1Mx	3	4,500		N	A+9M
2	61	T2N3Mx	4	5,000	3,000	Y	D-18M
3	57	T2N2M1	4	4.000*1		N	A+41M
4	55	T3N1Mx	3	4,800	2,100	Y	A+35M
5	64	T3N2Mx	3	4,000*2	3,000	N	D-4M
6	33	T3N1Mx	3	6,000		N	D-24M
7	64	T3N0Mx	3	6,000*3		N	D-9M
8	50	T2N1Mx	2	3,400		Y	A+59M
9	59	T3N0Mx	3	4,000*4		Y	F-U lost
10	46	T3N0Mx	3	4,200		N	F-U lost

Ext.: External radiation treatment
CT: Contact treatment with surface mold
A: Alive
D: Death
* 1 boost on 2,000 cGys
* 2 boost 6,000 cGys on inguinal failure and 3,000 cGys on perineum
* 3 boost 3,000 cGys
N: No Y: Yes

Table 3. Cases Summary in Radiation Treatment with Sugery Group

	Stage			Operation	RT (cGy)	Primary control	Follow-up status (Month)
	Age	TNM	FIGO				
1	47	T2N1Mx	2	Simple V.	5,000	Y	A+55M
2	48	T1N2Mx	3	Simple V.	5,000	Y	A+65M
3	72	T3N1Mx	3	Wide excision	3,000	N	D-26M
4	62	T1N1Mx	1	Radical v. with inguinal lymphadencectomy	4,400*1	Y	A+130M
5	62	T2N0Mx	2	Modified radical v.	4,000*2	Y	D-26M

RT: radiation treatment
V: vulvectomy
*1: boost 1,200 cGy
*2: 4,000 cGy on perineum with inguinal node preoperatively, boost 3,900 cGy postoperatively

Table 4. Tumor Size and Node Involvement

	N0	N1	N2	N3	
<4 cm	1	4	2	0	7
>4 cm	3	3	1	1	8
Total	4	7	3	1	15

Table 5. Treatment Failures Patterns

Failure Site	RT* alone group	RT* combined with surgery
Vulva	2	1
Jnguinal lymph node	1	0
Perineum with inguinal	—	—
Lymph node	2	1
Pelvic lymph node	0	0
Distant mtastases	2	0
Total	7/10	2/5

RT: Radiation treatment

RESULTS

The relationship between tumor size and node metastses are listed in Table 4. In over 50% of the patients(8/15) were above 4 cm in size of mass. This may be due to delayed diagnosis and treatment suspectively. Nodal descriptions were retrospectively determined from inspection, pelvic examination, lymphangiogram and postoperative confirm. There could be considerable errors in these variable methods. Clinical assesment of inguinal lymph nodes is helpful, although false-positive and false-negative rates of 25 to 30% may be expected.

The disease was not under control at the completion of radiation therapy in 6 of the 10 patients in radiation therapy alone group nor 1 of the 5 patients in radiation therapy combined with surgery group. Thus primary local control rate in all cases was 53%(8/15), 40%(4/10) in radiation therapy alone group and 80%(4/5) in radiation therapy combined with surgery group. Treatment failures patterns are listed in Table 5. Postradiotherapy failures occured either in primary site or in an adjacent areas of the vulva, with concurrent nodal involvement. The most common failure site was primary failure(vulva). Three patients developed nodal metastasis without local recurrence, one of these patient had evidence of distant metastasis on L-spine.

Treatment failures ocurred 7 of the 10 patients in radiation therapy alone group and 2 of the 5 patients in radiation therapy combined with surgery group.

All patients who were treated aggressively by irradiation had varing degress of complications related to the treatment. What was observed during the course of the external beam therapy was skin reaction, but was recovered moderately well prior to brachytherapy.

DISCUSSION

Carcinoma of the vulva accounts for only a small fraction of all female genital neoplasm (3~5%), but despite this apparent infrequency, it is the 4th most common frequent cancer involving the female genitalia, being exeed by cervix, ovary, and endometium. Most lesion occurs on the labia majora, the labia minora is the next common site. Less common sites include the clitoris and perineum. In our cases, we cannot accurately describe the site of origin due to loss of descriptions and huge mass of unknown primary. We experienced only one patient invading the clitoris. The characteristic neoplasm, squamous cell carcinoma of the vulva is a disease of late life, with an increasing incidence in each decades. Green reported that in his experience, the vulva cancer amounted to 5% of all patients with gynecologic malignancies seen from 1927 through 1961, but in the next 12 years it increased to 8%. He believed that this increase in incidence was a result of the continued rise in the average age of the female population in recent years, causing an increase in the number elligible to develop the disease[4].

Over the years the possible association of vulva cancer and veneral or granulomatous lesion of the vulva has been noted. The incidence tend to higher in the old literature and much lower in the most recent roports, probably reflecting to a certain degree a lower incidence of syphilis in recent past[3]. The association of condyloma accuminatum with vulva cancer is well known, but no cause-end effect relationship has been delineated. In our cases, one patient had documented leukoplakia, one condyloma accuminata, and one VDRL positve in conjunction with the vulva cancer.

The association between cervical cancer and vulva cancer has led to speculation that a common pathogen (HSV-2) may be involved[7]. We experienced two patients had received TAH due to cervical cancer. Lymphatic drainage of the vulva is a very progressive systemic mechanism. Fundamental to the understanding of treatment for invasive cancer of the vulva is proper knowledge of the lymphatic drainage of vulva. All authors agree that the superficial inguinal lymph nodes are the primary nodal group for the vulva and can serve as the sentinel lymph nodes of the vulva. The deep femoral nodes are the secondary nodal receipients and are involved before drainage *into the deep pelvic nodes occurs*. The Cloquet's node is the last node on the deep femoral group and is located just beneath the poupart ligament. Attempt to determine the necessity for pelvic lymphadenectomy from the presence of metastases in inguinal lymph nodes or Cloquet's node have been utilized without general acceptance[3,10]. The overall incidence of lymph node metastases in vulva cancer is about 30%[3]. This figure, derived from reports since 1970, is much lower than the 61% reported by way in 1960 and reflects the trend earlier diagnosis and small lesion. Collins, Butledge, Morley et al reported a similar experience, But in our cases, we experienced clinically No(4), N1(7), N2(3), N3(1) patients may be due to delayed diagnosis. There were 31.0~47.6% of groin and positive pelvic nodes in their experiences[2,12,13,16].

The various prognostic indicators-particulary stage, node involvement have repeatedly been decumented over the past 4 decades. The relationship between size of lesion, node metastasis, and survival are very important. Monagham J.M. et al reported that there were 16.4% of groin nodes (+) and 0% of pelvic nodes(+) when size of

tumor was under 4 cm, 37.5% of groin nodes(+) and 6.8% of pelvic nodes(+) above 4 cm[11]. They insisted that survival was probably closely related to the node metastasis rate. Collins C.G. et al reported that expected size of lesion plays a major role in survival was 3 cm. They reported there were 20% of nodes(+) and 76.5% of survival when size of tumor was under 3 cm, 76% of nodes(+), 38.2% of survival above 3 cm[2]. Rutledge F. et al reported the incidence of nodal metastasis was determined according to the size of the tumor and whether it extended beyond the vulva; 2-fold increase in nodal metastasis in those patients with lesion greater than 2 cm(T1: 13%, T2: 22%). Disregarding size, lesions which invaded the anus, urethra, or vagina had an increased incidence of(+) nodes from 24~43%[16]. Hacker et al attained the corrected actuarial five-year(survival for patients with negative nodes was 96%, whereas it was 94% for patients with one pasitive node, 80% for those with two positive nodes, and 12% for those with three or more positive nodes[5,6]. Green T.H et al reported that there was no difference in the 5-year cure rates of stage I and II, but curability decreased with each incresing stage thereafter[4]. Others have reported a poor correlation between the FIGO clinical stage and the cure state. For example, Rutledge et al indicated that involvement of clitoris carried a poor prognosis because of a greater frequency of nodal metastases and incidence of recurrence, but in the FIGO classification, disease in the clitoris is included in T1 or T2. They also did not find that involvement of perineum was associated with any greater risk than involvement of the vulva. Only when it was associated with anal or vaginal lesions did perineal involvement indicate a poor prognosis[16]. A reevaluation based on the accumulation and pooling of more data from a number of institutions may lead to improvements in the current system.

Treatment failures are also related to above prognostic indicators. Collins C.G. et al reported that the most frequent failures were local persistence or recurrence[2]. MDAH reported two separate analyses of the patients treated and established that the prognosis was worse when the cancer extended beyond the vulva to involve the vagina, distal urethra, regardless of the size of the lesion, and the regional nodes were positive for tumor. In both groups of patients, local recurrence within the vulvectomy incision or the adjacent skin, urethra, or perineal area was common[16]. Podratz et al reported that treatment failure was also related to stage of disease. Rates of treatment failure increased with advancing stage of disease-from 14% for stage I to 71% for stage IV. The rate of local vulva recurrence was 18%, which was about three times greater than the recurrence rates for the groin, pelvis, and distant sites[15]. In our studies, postradiotherapy failures ocurred in primary site or in an adjacent areas of the vulva, usually with concurrent nodal involvement and the most common failure site was primary site failure(vulva).

This tendency for recurrence within the surgical field provides the rationale for considering adjunctive irradiation, either preoperatively or postoperatively. But the role of radiation treatment in the primary treatment of invasive carcinoma of the vulva was probably limited since the results were not favorable and the vulva tissues responded poorly to this type of exposure.

Shermon stated that as little as 3,000 cGy over four or five weeks caused an extreme vulva skin reaction with wet desquamation[7]. But in our studies, it was recovered modertely well prior to brachytherapy except I patient. Many authors reported overall survival rate in radiation treatment alone group where all stages are included were as low as 8.3% and as large as 47.5%[8,9,14]. There dose, however, appear to be an indication for its use in the far advanced lesion mainly as a palliative therapeutic procedure[1]. In our small series we have found that the vulva can be irradiated safely if basic precautions are taken.

We also havo found that the radiation treatment is effective in decreasing tumor mass. Which in

some cases will disappears completely. In the future, possibly one should consider radical surgery for the external disease involving the vulva and the groin lymph node and radiation treatment of pelvic lymph nodes bearing tissue be indicated.

In the present over the four decades treatment choice in vulva cancer was radical vulvectomy with bilateral inguinal node dissection with or without deep pelvic nodes dissection. In the past, many gynecologic oncologist consider[4] a pelvic node dissection as a routine part of the radial surgical treatment of invasive vulva cancer currently, this concept has been altered by most authorities since vulva cancer is now being diagnosed at an early stage, a less radical surgical approach to the disease is involving in an effort to decrease morbidity and disfigurement, and since, involvement of this chain of nodes is so infrequent, when these are involved, the prognosis is guarded even though an adequate pelvic lymph nodes dissection had been performed. Hacker et al reported that no patient with less than 3(+) unilateral groin nodes had positive pelvic nodes, or developed pelvic recurrence[5,6]. Some authors have reported that no positive pelvic node involvement in the absence of positive groin nodes, however Green et al postulated that even if pelvic lymph nodes were histologically negative. submicroscopic disease might be present in up to 20% of cases, so the pelvic lymph adenectomy would be therapeutic for these patients[4]. Because of above controversy in early stage vulva cancer treatment, Hacker et al insisted that individualization of the extent of lymphadenectomy for all patients must be performed[5]. Finally, our experience also indicates that a degree of individualization in the treatment of vulva cancer can be achieved with acceptable results. Selection of the patients with vulva cancer for curative intent treatment is important.

Close long term follow up is essential for the patient after finishing the primary therapy, to prevent the far advanced recurrent vulva cancer.

* Treatment failures(local persistance+local or distant recurrence)

CONCLUSION

15 patients who underwent a course of radiation therapy for vulva cancer were analyzed retrospectively at Dept. of Radiation Oncology, College of Medicine, Younsei University during Jan. 1971-April 1985.

Primary local control rate in all cases was 53% (8/15), 40%(4/10) in radiation therapy alone group and 80%(4/5) in radiation therapy combined with surgery group.

Treatment failures were noted in 70%(7/10) in radiation therapy alone group, 40%(2/5) in radiation therapy combined with surgery group.

The most common failure site was primary site failure(vulva).

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