Radiation Therapy of Testicular Seminoma

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=Abstract=

Purpose : Testicular seminomas are radiosensitive and adjuvant radiation therapy after orchiectomy results in long term survival in early stage diseases. Ten year results of radiation therapy after orchiectomy and results of definitive treatment of recurrent seminoma are presented.

Materials and Methods : Between August 1980 and February 1990, 32 patients with testicular seminomas were treated at the Department of Therapeutic Radiology, Seoul Natoinal University Hospital. Twenty-seven patients received radiation therapy after orchiectomy and 5 patients for treatment of recurrent tumors. Two of postoperatively treated patients and 2 of recurrent patients were excluded from the study because of incomplete treatment. Of the patients treated postoperatively, 18 were stage I, 5 were stage IIA, one was stage IIB, and one was stage IIC. There were 4 ipsilateral and 2 contralateral cryptorchids. Preoperatively, β-HCG levels were elevated in 5 patients. Median dose to pelvic and paraaortic lymph node area was 2900 cGy (1550-4550 cGy). One patient with stage I, 4 with stage IIA, and 1 with stage IIB received prophylactic mediastinal irradiation. Two patients were treated with chemotherapy before radiation therapy. Median follow-up period was 104(3-144) months.

Result : Local control rates were 100% at 5 years after orchiectomy. Five year survival rates were 94.4% in Stage I and 100% in Stage II patients. One patient with stage I disease died 3 months after surgery due to mediastinal metastasis. All the 3 patients treated for recurrent disease are alive without disease.

Conclusion : Postorchiectomy radiation to the pelvis and para-aortic area remains the treatment of choice for patient with early stage testicular seminoma. Radiation therapy is also an excellent treatment modality for recurrent seminoma.

Key Words : Seminoma, Postoperative radiotherapy, Recurrent seminoma

INTRODUCTION

Testicular cancers are uncommon but represent the most common malignancy in men from the ages of 15 to 35 years, and pure seminoma represents nearly 50% of testicular tumors[1]. This cancer has an excellent prognosis following treatment with orchiectomy and radiation therapy. Because of high sensitivity to radiation, survival rates for patients with early stage seminomas are reported in the range of 80% to 97%[2,3]. In spite of these excellent results, controversy exists over the role of radiation therapy in the management of the various stage of seminoma.

This review of 10 year experience of the outcome of radiation therapy in 25 postoperative patients and 3 recurrent testicular seminomas

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evaluates the results of treatment.

MATERIALS AND METHODS

Between August 1980 and February 1990, 27 patients with testicular seminoma and 5 patients with recurrent diseases were treated at the Department of Therapeutic Radiology, Seoul National University Hospital. Most patients had undergone orchiectomy elsewhere and were referred for postorchiectomy management. Two patients with primary and 2 patients with recurrent disease were excluded from the study because of incomplete treatment(less than 1500 cGy).

Eighty percent of the patients were between ages 21 to 50 years inclusive, with 36% of the patients being between 31 and 40 years(Table 1). The age groups were evenly distributed among the stage grouping. Older patients did not have a preponderance of Stage II presentation(Table 2).

Table 1. Patients Characteristics(n=25)

Characteristic	No. of pts(%)
Age	
11–20	1(4)
21–30	7(28)
31–40	9(36)
41–50	4(16)
51–60	3(12)
61–70	1(4)
Stage	
I	18(72)
IIA(D≤2)	5(20)
IIB(2<D≤5)	1(4)
IIC(5<D≤10)	1(4)
Side of primary tumor	
right	8(32)
left	17(71)
Presence of cryptorchidism	
ipsilateral	4(28)
contralateral	2(8)
no	19(76)
Pathology	
classic	11(44)
anaplastic	2(8)
mixed	2(8)
not stated	10(40)

Table 2. Distribution of Stage by Age

Age	Stage				Total
	I	IIA	IIB	IIC	
11–20	1				1
21–30	4	3			7
31–40	6	2	1		9
41–50	3			1	4
51–60	3				3
61–70	1				1

All the patients were staged retrospectively using the available information according to the modified Royal Marsden Hospital system[4]. Eighteen (72%) patients were stage I and 7 (28%) were stage II. Among the patients with available pathologic data 11 had classic type, 2 had anaplastic type, and 2 had mixed type. There were no patient with spermatocytic type. There were 6 patients with undescended testis. Four had ipsilateral and 2 had contralateral cryptorchidism. Seventeen of 25 patients (71%) had their primary tumor on the left side(Table 1).

Five of 25 patients had elevated β-HCG levels prior to orchiectomy. Values ranged between 38 and 96 mIU/ml. The level of β-HCG came to normal postoperatively in every patient.

Clinical features of 3 recurrent testicular seminomas are shown in Table 3. One patient was ipsilateral and one was bilateral cryptorchids. Two patients had reccurent disease in paraaortic lymph nodes and one had disease in intraabdominal and inguinal areas in addition to paraaortic lymph nodes. Initial treatment of all the 3 patients were orchiectomy without adjuvant treatment. Data about their initial stages and pathologic types were not available.

Following the initial surgical procedure, all the patients received megavoltage irradiation using anterior and posterior parallel opposing fields to the para-aortic nodes and ipsilateral pelvic nodes. Usually the fields extended superiorly to the interspace between the 10th and 11th thoracic vertebra, inferiorly to the bottom of the obturator formen, and included the ipsilateral renal

Table 3. Clinical Features and Outcome of Recurrent Testicular Seminoma

Case	Initial stage	Initial Tx	Recurrent site	Tx after recur	Dose(cGy)	Follow-up(Mo)	State at last FU
1	n.s.	op	PAN	op & RT	4480	110	NED
2	n.s.	op	PAN, RLQ, inguinal	op & RT	4860	100	NED
3	n.s.	op	PAN	chemoTx & RT	3960	100	NED

Abbreviation: PAN-paraaortic lymph node, NED-no evidence of disease n. s. -not stated, RLQ-right lower quadrant
chemoTx: cisplatin+vincristine+bleomycin

Table 4. Radiation Field by Tumor Stage

Field	Stage I	IIA	IIB	IIC
PEL+PAN	17	1	0	1
PEL+PAN+MED	1	4	1	0

PEL: pelvic lymph node, median 3000cGy (1500-3500 cGy)
PAN: paraaortic lymph node, median 2760 cGy (2275-4550 cGy)
MED: mediastinum, median 2450 cGy (1980-2550 cGy)

hilum. Lateral extent of field was to encompass the bony margins of the ipsilateral pelvis with 1-2cm margin. Doses ranging from 1550-4500 cGy, five fractions per week were delivered. In early 1980's, there was tendency to use higher dose. Recently, however, most patients with early stage testicular seminoma receive about 2500 cGy. Whole abdominal irradiation was initially done in one patient with stage IIB disease and shrinking field technique was used. Total dose to this patient was 4550 cGy. Prophylactic mediastinal and supraclavicular irradiation was not used routinely although six patients received such treatment. They include 1 Stage I, 4 Stage IIA, and 1 Stage IIB patients. Dose ranged 1980 cGy to 2550 cGy and 2 Stage IIA patients received supraclavicular boost of 800 cGy and 900 cGy (Table 4).

Two of 25 patients received chemotherapy after radical orchiectomy. Both patients received chemotherapy at the other hospital. Their characteristics and outcome of treatment are shown in Table 5.

Treatment of recurrent disease were mass excision and postoperative radiation therapy for 2 patients and chemotherapy and radiation therapy for 1 patient. Radiation doses ranged 3960 cGy to 4860 cGy to recurrent site.

Patients were followed routinely after treatment with a physical examination, chest X ray, α-fetoprotein, and β-HCG examination.

Median follow up period was 104 month, ranging from 3 month to 144month.

Survival rates were calculated using the actuarial method.

RESULTS

The 5-year actuarial survival rate for all patients was 96.0%. Only one Stage I patient died at 3 month after orchiectomy due to mediastinal metastasis. There was no in field recurrence. Thus, no patient who received para-aortic irradiation relapsed in nodal area below the diaphragm. The 5-year actuarial survival rates were 94.4% with Stage I and 100% with Stage II patients(Fig. 1). Five patients who had elevated β-HCG level prior to orchiectomy are alive without evidence of disease.

Table 5. Patient who received chemotherapy

Pt.	Age.	Stage.	Agents.	Cycles.	Status.
1	35	IIB	VCR+CTX+ACT-D	#1	NED at 125Mo
2	43	IIC	VBL+Bleo+C-DDP	#4	Ned at 79Mo

VCR: vincristine, CTX: cyclophosphamide, ACT-D: actinomycin D, VBL: vinblastine, Bleo: bleomycin, C-DDP: cisplatin

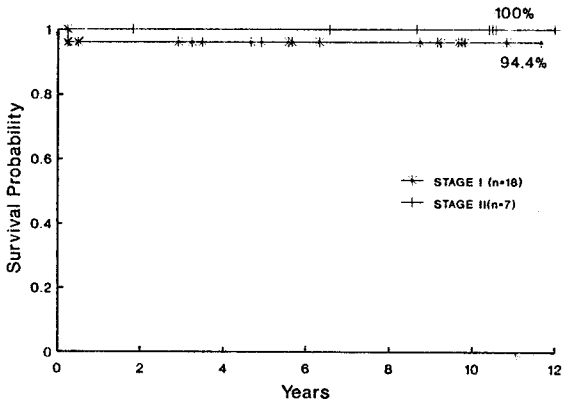

Fig. 1. Survival of early stage testicular seminoma

Table 6. 5 Year Survival (percent) for Stage I and Stage II Testicular Seminoma with Orchiectomy and Radiation Therapy.

Series	Survival(%)	
	Stage I	Stage II
Werf-Messing (n=132) 1976[5]	100	75
Cionini et al (n=121) 1978[6]	98	80
Dosoretz et al (n=160) 1981[7]	97	92
Willan and McGowan (n=171) 1985[8]	98	70
Zagars and Babaian (n=211) 1987[9]	95	85

The outcome of treatment of recrrent disease are shown in Table 3. All the 3 patients are alive without disease at 100 to 110 months.

Long-term radiation-related complication was noticeably absent. No patient developed any recognizable delayed radiation-induced complication affecting small bowel, large bowel, large bowel, bladder, kidney, liver, spinal cord, skin or subcutaneous tissues. Acute toxicity was not quantitated in this report.

DISCUSSION

In the literature, reported overall cure rates for patients with seminoma range from 70 to 100% (Table 6.) and this series documents an overall cure rate of 94.4% for stage I and 100% for stage II seminoma. This success is probably a result of a combination of three factors: the marked radiosensitivity of this tumor, its orderly spread to adjacent lymph node areas, and the tendency for most patients to present without disseminated disease.

Table 7. Distribution of Patients by Stage (%)

	MD Anderson	Royal Marsden	Princess Margaret
I	56	63	76
IIA	18	19	9
IIB	16	8	10
III	10	8	5

Despite this success there remain certain areas of controversy and uncertainty in the management of patients with seminoma of the testicle. Surveillane as a management approach has been increasingly applied to Stage I nonseminomatous tumors and results show that in 70% to 80% of these patients orchiectomy alone is curative[10-13]. A similar approach might be justified for seminoma and has been implemented by some[11,12]. The surgical data on the incidence of occult nodal disease is limited: however, the avilable information suggests that less than 10% of the patients with clinical stage I seminoma have paraaortic lymph node involvement[14]. The exact magnitude of the risk for relapse in unirradiated patients with Stage I seminoma is not known but has been estimated to be 15% to 20%[15-17], and the main site of relapse in many studies were the retroperitoneum alone (85% of relapses)[18-21]. The major virtue of surveillance is that it would spare the majority of patients unnecessary treatment. However, surveillance is approporiate only if survival is not compromised. But theoretical long-term side effects of radiotherapy have proven to be insignificant.

The majority of patients in this series were disignated as Stage I (72%), as compared to other series in which Stage I patients ranged from 56% to 76% (Table 7). In a large series reported from the United Kingdom in which lymphography was used routinely, 63.6% of the

patients had Stage I disease compared with 72% in this series[22]. We can infer from this that between 10 and 20% of patients with retroperitoneal disease in the current series were downstaged and therefore classified as having Stage I disease. The inclusion of such patients in Stage I might be expected to lower the survival of patients with stage I disease. Because of small number of patients in current series, however, it is difficult to evaluate the result.

The significance of elevated β-HCG level in seminoma is controversial. Some reports have shcwn a modest adverse effect of elevated β-HCG[23-25], whereas others have found this to be of no prognostic value[7,8,26-29]. In the current series, 5 patients had elevated β-HCG levels and all survived without disease. In these patients all the values returned to normal level following orchiectomy. If the β-subunit does not return to normal after time has been allowed for the circulating serum HCG to be cleared following orchiectomy, mor extensive disease may be present, and further therapy may be indicated. The value of postoperative HCG titers in predicting prognosis and formulating therapy remains an area for future investigation.

There are some adbocates of prophylactic mediastinal irradiation for patients with Stage I seminoma[30]. In one series, four of six patients who developed mediastinal recurrence were not salvaged[31]. A policy of prophylactic mediastinal irradiation could possibly have prevented death in these patients, but it would have required unnecessary irradiation of the mediastinum in the majority of other patients who never received prophylactic mediastinal irradiation and who never recurred in this site. The possible gain in survival from prophylactic mediastinal irradiation in Stage I would have been 1.2% to 2%[9,31], assuming that such treatment would be accompanied by no long term risks. One report in the literature suggests that patients receiving such treatment may be at higher risk for the development of second malignancies and bone marrow hypoplasia than those receiving irradiation to the abdomen and pelvis only[15]. In keeping with the findings of numerous other reports[7,8,15,31], we believe that prophylactic mediastinal irradiation is not advisable for stage I patients.

prophylactic mediastinal irradiation for all patients with stage II seminoma has been the accepted method of treatment in most centers treating this disease[6,22,33,32,33]. The presence of palpable abdominal disease prior to treatment is of major prognostic importance[31] so that the analysis of the role of mediastinal irradiation is more meaningful if stage IIA and remaining stage II patients are considered separately. From the literature, recurrent mediastinal disease is not a problem for patients presenting with stage IIA disease[6,31,33]. In one series, stage IIB-D patients had a greater chance of developing an isolated first recurrence in the mediastinum when prophylactic mediastinal irradiation had not been given than did either the stage IIA or the Stage I patients[31]. But the theoretical survival benefit from a policy of routine prophylactic mediastinal irradiation would have been 6.5% in theat series. This irradiation would have no curative benefit for 93.5% of the other patients. Moreover, recent studies report that primary and salvage treatment with combination chemotherapy have the gain exceeding the possible extra cures obtainable from the routine use of prophylactic mediastinal irradiation. Thus, unneccessary initial prophylactic irradiation of the mediastinum will only compromise bone marrow tolerance of systemic therapy in those patients requiring chemotherapy for relapse[34-36].

In current series, 6 patients had tumor arising from undescended testis. In the literature, appropriate treatment of these tumors results in an excellent outcome equivalent to that observed for the more usual scrotal seminomas and there was no significant prognostic difference between seminomas arising in a cryptorchid testis and those arising in normal testis[37].

From the data in current series we cannot deduce a dose-control relation. However, the uniform control of microscopic disease with doses

in the range of 25–35 Gy suggests that 25Gy is adequate for subclinical disease.

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=국문초록=

고환 정상피종의 방사선 치료 성적

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연구목적 : 고환의 정상피종은 방사선치료에 매우 민감한 종양으로서 초기 정상피종에 있어서 근치적 고환절제술 후 보조적 방사선치료로 좋은 결과를 얻을 수 있는 것으로 알려져 있다. 10년간 서울대학교 병원 치료방사선과에서 치료를 받은 28명의 환자를 대상으로 치료성적의 분석을 실시하였다.

대상 및 방법 : 1980년 8월에서 1990년 2월까지 서울대학교병원에서 치료를 받은 고환 정상피종 환자 32명을 대상으로 후향적 분석을 하였다. 27명의 환자는 근치적 고환절제술 후에 그리고 5명은 재발 후에 방사선치료를 받았는데 각군에서 2명씩은 불완전한 방사선치료로 연구대상에서 제외되었다. 고환절제술후 치료를 받은 환자들의 병기별 분포는 I기 18명, IIA기 5명, IIB기 1명 IIC기 1명이었다. 재발 후 방사선치료를 받은 3명은 첫 진단시 병기를 알 수 없었다. 전체 환자 중 6명 환자에서 동측 고환, 2명에서 반대편 고환, 그리고 1명은 양측에서 잠복고환이 관찰되었다. 후복막 및 골반 임파절에 대한 방사선치료 선량의 중앙치는 2900cGy (1550-4550cGy)이었다. 종격동조사를 시행한 환자는 I기 1명, IIA기 4명, IIB기 1명 그리고 재발된 환자가 1명이었다. 항암화학요법은 IIB기 1명, IIC기 1명, 재발된 1명에서 방사선치료 전에 시행되었다. 환자들의 중앙추적기간은 104개월 (3-144개월) 이다.

결과 : 전체 국소치유율은 5년에 100%를 보였고, I기 환자 1명에서 종격동 전이로 인한 사망을 보여 생존율은 5년에 I기 94.4%, II기 100%, 그리고 재발한 경우에서 100%를 보였다.

결론 : 고환 정상피종에 있어서 방사선치료는 근치적 고환절제술 후의 보조적 목적뿐 아니라 국소적으로 재발한 경우에 있어서도 우수한 치료방법으로 생각된다.