Treatment Of Stage I Seminoma Testis With Extended Field Adjuvant Radiation


Department of Radiation Oncology and Uro-Oncology, Tata Memorial Centre, Mumbai, India

Abstract

With an aim to analyze and document the outcome of Stage I Seminoma patients we undertook a retrospective analysis of patients treated between January 1990 and December 1998. The treatment charts of patients treated between January 1990 and December 1998 were reviewed. Patient and tumor characteristics, treatment details, relapse rates, late toxicities, or occurrence of second primary was noted. Royal Marsden Staging System was utilized because of its simplicity and wide-use in the above period. Out of 137 patients, 41 (30%) patients did not receive any further treatment, 96 (70%) patients received prophylactic radiotherapy to para-aortic and pelvic nodes. The observation group patients had a median follow-up 20 months, 9 patients had nodal relapse with 7 in retroperitoneal nodes and 2 patients in inguinal nodes. Of these, 7 patients received BEP chemotherapy and 2 patients Chemoradiation. Four patients had complete remission while remaining 5 patients had partial response. The histopathologies of all the 5 patients with partial response were reviewed to reconfirm the diagnosis.

Patients of prophylactic radiotherapy group had a follow-up of 33 months, 6 patients relapsed, RP nodal disease in 5 patients and distant metastasis in 1 patient. All these patients received BEP chemotherapy. One had complete response and remaining 5 patients had partial response. The group of patients under observation had a significantly higher relapse rate and lower disease free compared to the adjuvant radiotherapy group (73.5% vs. 91% at five years, p value 0.004). Disease specific survivals for the two groups were however similar (89% vs. 93%) at five years, p value 0.18).

We conclude that Stage I Seminoma patients treated with prophylactic radiation to para-aortic and pelvic region had better outcome.

Keywords

Seminoma, Observation, Adjuvant Radiotherapy.

Introduction

Seminoma testis is one of the curable cancers with cure rates in early stage disease confined to testis approaching 100%. Post orchidectomy prophylactic radiation to para-aortic and pelvic nodal region, adjuvant chemotherapy or surveillance has been tried with no definite consensus. Until recently, the majority of patients with Stage I seminoma were treated with prophylactic para-aortic and pelvic lymph nodal irradiation, also known as dogleg or spade shape portal. The results of such treatment are excellent with a long-term survival of approximately 95%\(^{1,2,3,4}\). Although chemotherapy is generally considered for more advanced diseases, single agent carboplatin has shown comparable results with radiotherapy in MRC trial\(^{5,6}\). Post orchidectomy surveillance has also been explored in a many studies \(^{7,8,9,10}\). However, surveillance needs more extensive, prolong follow-up and intense use of resources. Even motivated patients at times eventually become non-compliant \(^{11}\). The recurrence rate for patients with seminoma on surveillance is around 16% \(^{8,9,12}\). Also, there is no randomized test of adjuvant chemotherapy versus surveillance for patients in early stage disease.
trial to prove superiority of surveillance over prophylactic therapy. Evidences are strong from multivariate analysis and the Spanish Testicular Cancer Group that factors like size of tumour or invasion of rete testis are adverse risk factors for relapse requiring adjuvant therapy and surveillance can cause an unacceptable high risk of relapse of about 32% (13, 14).

With an aim to introspect the outcome of patients with Stage I Seminoma, we undertook a retrospective analysis and form the basis of this report.

**Methods and Materials**

The treatment charts of patients with Seminoma treated between January 1990 and December 1998 at the Department of Uro-Oncology Services of Tata Memorial Hospital were retrospectively reviewed. Patient and tumor characteristics, including computed tomography scan or Ultrasonography scan of the abdomen and pelvis, chest X-ray, tumor stage, treatment details including type of surgery, adjuvant treatment, radiation portals, doses, technique etc. relapse rates, any late toxicities, or occurrence of second primary were noted. Staging was done according to Modified Royal Marsden Staging System because it was simple and widely practiced during the above period. Post treatment follow-up status including physical examination, imaging, tumor markers if done and pattern of relapse were noted. Survival outcomes and analysis was done using SPSS Version 11. Patients with post orchidectomy Stage I Seminoma were classified into Group I, if patients were kept under observation and group II if patients received prophylactic nodal radiation.

**Group I: Patients after orchidectomy under observation:**

Patients who did not receive prophylactic radiation to nodal region underwent follow-up imaging (USG or CT scan Abdomen Pelvis) every 6 – 12 monthly. The decision of patients under surveillance was at the discretion of treating physician since there was no established guideline then.

**Group II: Patients undergoing prophylactic radiation:**

These patients received external beam radiation with Cobalt 60 gamma rays or 6MV X-rays by conventional dose fractionation and schedule of 180 - 200 cGy / Fraction, 5 Fr / week. All the patients received radiation to para-aortic and pelvic nodes by simple parallel opposing antero-posterior and postero-anterior beams. The decision to treat single ipsilateral pelvic field or bilateral pelvic fields was non uniform. To shape the radiation portals, customized blocks until 1995, and multi-leaf collimators subsequently were used. All these patients were reviewed weekly and acute toxicities if any were documented and managed conservatively.

**Results**

A total of 281 seminoma patients were treated at the Department of Uro-Oncology services of Tata Memorial Hospital during the period of 1990-1998. One hundred and thirty seven patients (49%) were Stage I. A detailed analysis of 137 patients with Stage I Seminoma was performed (Table 1) shows the patient characteristics. With a mean age of 36 years (median: 35 range 20-68 years), 72 patients (52.6%) had right sided, 63 patients (46%) left sided and 2 (1.4%) patients had bilateral seminoma respectively. Eleven (8%) patients had history of mal-descendent testis. One hundred and twenty one patients (88%) were referred after orchidectomy, 9 (6.6%) patients after adjuvant radiation for further treatment and 7 patients underwent surgery at

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Mean (Range)</th>
<th>37 years (20 - 68 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side of testis</td>
<td></td>
<td>Right 72 (52.6%)</td>
</tr>
<tr>
<td>History of mal-descendent testis</td>
<td></td>
<td>Absent 126 (92%)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td>Inguinal orchietomy 102 (74.5%)</td>
</tr>
<tr>
<td>Presentation to TMH</td>
<td></td>
<td>Sx 121 (88.3%)</td>
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<tr>
<td>Histopathology</td>
<td></td>
<td>Classic seminoma 133 (98%)</td>
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<tr>
<td>Adjuvant therapy</td>
<td></td>
<td>Observation arm 41</td>
</tr>
</tbody>
</table>

Table 1: Patient Characteristics of 137 patients
A Retrospective Analysis Of Stage I Seminoma Patients, U. Mahantshetty, et. al.

our institution. One hundred and two (74%) patients had undergone inguinal orchidectomy and 35 (26%) scrotal orchidectomy. Out of 137 patients, 41 (30%) patients did not receive any further treatment (Group I), 96 (70%) patients received prophylactic radiotherapy to para-aortic and pelvic nodes (Group II). In 71 patients only ipsilateral pelvic fields were included (dog leg portals) and in 25 patients bilateral pelvic fields were irradiated (spade shaped portal). Mean radiation doses delivered was 30 Gy (Median: 30 Gy; Range: 20-45 Gy) by conventional dose, fractionation and schedule, (1.8 -2 Gy per fraction, five fractions per week) one patient who received 20 Gy of EBRT defaulted at that dose after having chicken pox and other 4 patients who did not completed total dose of 30 Gy due to social reasons. Two patients had already received 40 Gy and 45 Gy of radiation in a peripheral rural center before presenting to our hospital.

For 41 patients under observation, with a median follow - up 29 months (Mean: 55 months; Range 8 - 218 months), 9 patients had nodal relapse with 7 in retroperitoneal nodes and 2 patients in inguinal nodes, both of them underwent scrotal violation. Of these, 7 patients received BEP chemotherapy and 2 patients received chemotherapy followed by radiation to the residual nodal mass. Four patients had complete remission and were disease free at the time of last follow up. While remaining 5 patients had partial response. Of these 5 patients, 4 patients died of disease and one patient was alive with disease at last follow up. Two other patients died of unrelated cause. For 96 patients who underwent prophylactic radiation, with a median follow-up of 34 months (mean 51 months; range 9- 226 months), 6 patients relapsed (RP nodal disease in 5 patients and distant metastasis (lung) in 1 patient). Of these five patients with nodal failure, three patients received 20-25 Gy. The patient with lung metastasis relapsed within 9 months of treatment completion and all patients with relapse underwent CT thorax to rule out lung metastasis). All these patients received BEP chemotherapy. One had complete response and was cured of disease. The remaining 5 patients had partial response to salvage. 4 patients died of disease and one patient was alive with disease at 18 months of follow up. All the blocks and slides of these five patients were reviewed.

Five years Disease free survival (DFS) [Figure 1] and Disease specific survival (DSS) [Figure 2] was 73.5% and 89% for Group I and 91% and 93% for Group II patients respectively. The p value by log rank test was significant for DFS between the two arms (0.004) but not of any statistical significance for DSS (0.18). We could not find any prognostic factor of significance like age, laterality of tumour, size of the tumour, invasion of the spermatic cord or vascular invasion in our study.

We had a maximum follow-up period of 19 years and no case of any second primary cancer was reported from our patients. None of our patients had any late Grade III radiation toxicity reported so far.
**Discussion**

The options for Stage I Seminoma patients are surveillance, radiotherapy (which may be extended or limited field) or short course of chemotherapy all being equally effective (15). However, there is no level I evidence to date comparing these treatment options. Also, there is a persistent difficulty in detecting early relapse in these patients because of lack of any specific markers. Since stage I seminoma is potentially curable disease in our setting prophylactic therapy scores over surveillance. However, the type of adjuvant therapy is determined by i) tumour characteristics ii) age of patient iii) patient preference and the cost of treatment. Currently no studies from India are available addressing the issue of prophylactic therapy vis-à-vis surveillance. To address this issue in Indian setting, we undertook this retrospective analysis.

In our study, stage I accounted for 50% which is less than that reported in western literature (70%) suggesting that advance stages at presentation are common in our setting (16). Our study reflects that seminoma testis is equally distributed among both side of testis and mal-descendent testis is a risk factor for testicular tumours. We had 11 patients (8%) of the patients with history of maldescendent testis. This corresponds well with literature that 6.5-14.5% of germ cell testicular tumors are associated with past (corrected) or present cryptorchidism (17). Also, in our group of patients 35 patients (24.5%) underwent scrotal violation of them 2 patients had inguinal relapse in further course.

The observation group had a higher relapse rate and though all the patients were treated by BEP only four out of nine patients were salvaged with BEP chemotherapy. This may be due to the fact that most of the relapsed cases were detected when they presented with symptomatic relapse of disease rather than detected on routine radiological surveillance.

Group receiving radiotherapy had a much better results and is comparable with reported literature (18). Of the 5 patients who had retroperitoneal nodal relapse, three patients received 20-25 Gy as compared to a mean/median radiotherapy dose of 30 Gy in the larger group. Although MRC trial suggests that 20 Gy is good enough dose as compared to 30 Gy in terms of recurrence rates (19), our patients receiving more than 20 Gy had better control rates.

The study shows that the group of patients under observation had a significantly higher relapse rate and lower disease free (73.5% vs. 91% at five years, p value = 0.004). Disease specific survivals for the two groups were similar (89% vs. 93%) at five years, p value=0.18) which is comparable to the reported literature (18, 20).

All the patients have received extended field radiation as it was the institutional practice at that time, gradually with time the radiotherapy portals have been reduced and currently with stage I seminoma we practice only para-aortic field radiation. However, all patients treated with para-aortic radiation therapy require follow-up computerized tomography of the pelvis due to risk of nodal recurrence in pelvis (19,20), an investigation that is not needed in patients treated with extended-field radiation therapy. Recurrence in seminoma always occurs outside the irradiated field (16). Neither of these modified treatments will probably completely eliminate the risk of second malignancy and any associated risk reduction remains unknown. Thus, although para-aortic radiation therapy to a minimum dose of 20 Gy in 2 Gy fractions is the radiation therapy option that may best reduce acute toxicity, because of concerns about the additional follow-up needed and pelvic relapses, extended-field radiation therapy may still be appropriate (18,20). Besides repeated CT scans to abdomen and pelvis also carries substantial risk of second radiation induced cancer (21, 22). Some groups advocate for a risk based approach which is not accepted by most uro oncologists. (16)

Relapse rate with one single course of carboplatin at 3 yr was 5.2% and a considerable number of the relapses occurred after >2 yr. Hence we need to be cautious in interpreting the encouraging results of single-agent carboplatin therapy (20). The late sequelae of carboplatin treatment (induction of malignancies, treatment response of recurrences, fertility) and the impact on quality of life compared to observation or adjuvant irradiation are yet to be addressed.
Conclusion

In our retrospective analysis patients with stage I seminoma (post orchiectomy) under observation are associated with higher relapse rates and poor salvage results. In our series, the disease free and disease specific survivals of 73.5% and 91% at 5 years in the observation group is inferior to 89% and 93% at 5 years respectively for patients receiving prophylactic nodal radiotherapy. The role of prophylactic chemotherapy cannot be ascertained from our study. Also, we could not identify the obvious high risk factor(s) for our patients who would benefit from prophylactic radiotherapy rather than surveillance.

References