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Testicular Cancer Treated in a Minor General Oncology Department

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The question of where to treat testicular cancer and by whom has been debated in several medical journals over the last few years. Here we present data from 98 patients (47 seminomas, 51 non-seminomas) treated between January 1985 and March 1993 at the Department of Oncology, University Hospital of Tromsø, Norway. During a 4-year median follow-up period 2 patients died of progressive disease. Our results are similar to those of major specialised oncology centres. We argue that within the context of multicentre cooperative studies or treatment protocols, patients with testicular cancer can be treated in a small general oncology centre with the same expectations of cure and treatment-related mortality and morbidity as achieved in major centres.

Key words: testicular cancer, treatment, general oncology unit
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INTRODUCTION

TESTICULAR CANCER has changed from a frequently fatal disease in the 1960s to a highly treatable tumour over the last two decades. The great majority of patients can now be cured by surgery, chemotherapy or radiotherapy. Currently, no stage of disease can be considered beyond cure. This fact has led to a debate on where testicular cancer should be treated and by whom. It has been documented that patients treated within the framework of clinical trials have a better prognosis than patients treated outside such trials [1]. Several studies refer to better prognosis after treatment of cancer in cancer centres rather than in peripheral hospitals [2, 3]. However, it is still not clearly defined whether patients with testicular cancer should be treated in general oncology units or in major specialised centres.

It has been argued that if the number of cases seen in the major centres continues to fall, the opportunities for conducting clinical trials to reduce morbidity and mortality of treatment and improve the cure rate will be frustrated [4, 5]. However, clinical trials can be performed on a multicentre cooperative basis between smaller centres, assuring a continuous evaluation of the treatment results at each centre and an up-to-date treatment procedure.

We report here treatment results from such a small general oncology unit serving the most northern part of Norway.

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MATERIALS AND METHODS

Since 1985, diagnosis, staging and treatment of testicular cancer have been performed at the University Hospital of Tromsø, Norway. The hospital serves a population of 500,000 inhabitants (11% of the Norwegian population) living in an area comprising 33% of Norway. Between January 1985 and April 1993, 100 patients (a mean of 13 patients per year) were treated for primary testicular tumours. Pathological classification was based on the WHO classification system [6]. Staging was performed according to the Royal Marsden staging system [7]. There were 47 seminomas, 51 non-seminomas, one malignant Sertoli cell tumour and one mesothelioma. The malignant Sertoli cell tumour and the mesothelioma were excluded from the study. Median follow-up time was 4 years (range 1–10). The values in the seminoma and non-seminoma groups were 4.0 and 4.4 years, respectively. Patients' characteristics are given in Tables 1 and 2.

Seminomas in stages I, IIA and IIB received radiotherapy to the ipsilateral external iliac, the bilateral common iliac, the paracaval and the para-aortic nodes (L field) using a 6-MV linear accelerator. One patient was treated with an inverted Y field because of bilateral testicular involvement. Doses employed initially were 36 Gy (stage I) and 40 Gy (stage II) using 2-Gy fractions. During the study period doses were altered to 30.6 Gy (stage I) and 39.6 Gy (stage II) using 1.8-Gy fractions. Seminomas stage IIC–IV were treated with four cycles of the BEP-20 (bleomycin, etoposide and cisplatin) regimen [8]. If there was residual tumour after chemotherapy, this was removed by surgery.

Table 1. Patient characteristics for 98 patients treated for testicular cancer at the University Hospital of Tromsø, Norway

	Seminoma (n = 47)	Non-seminoma (n = 51)
Age (years)		
Median	35	29
Range	22–73	16–61
Stage		
I	36	23
IIA	3	10
IIB	0	4
IIC	3	6
III	4	3
IV	1	5

Table 2. HCG, AFP and LDH levels in patients treated for testicular cancer at the University Hospital of Tromsø, Norway 1985–1993

	Seminoma (%)	Non-seminoma (%)
(U/l) HCG		
< 10	88	78
10–10 000	12	18
> 10 000	—	4
(μg/l) AFP		
< 10	100	58
10–1000	—	26
> 1000	—	16
(U/l) LDH		
< 450	82	84
450–1000	11	11
> 1000	7	5

AFP, α-fetoprotein; HCG, human chorionic gonadotropin; LDH, lactic acid dehydrogenase.

Non-seminomas stage I was initially treated with retroperitoneal lymph node dissection (RPLND) only. In 1991, stage I patients were subdivided into high, intermediate and low risk according to tumour cell invasion of vascular structures in the testis, and pre- and postoperative AFP levels. Low risk patients underwent surveillance only, intermediate risk had unilateral RPLND, and high risk patients received three courses of the BEP-20 regimen. Stage IIA patients were treated with three cycles of the BEP-20 regimen after RPLND, while stage IIB–C received four cycles of chemotherapy followed by RPLND. Stage III–IV were given four cycles of chemotherapy followed by RPLND and a consideration of resection of all residual tumour tissue according to the SWENOTECA (Swedish and Norwegian Testicular Cancer Project) guidelines. Stage IIB–IV patients with vital tumour tissue revealed by surgery were given two further cycles of the VIP regimen (VP-16, ifosfamide, cisplatin) [9].

The Microsoft Excel version 4.0 for personal computers was used for the final database and SPSS for Windows version 6.0 for statistical calculations. Patients with unknown value for a particular variable were excluded from analysis involving that variable. Statistical calculations were performed by bivariate correlation analysis with Pearson's correlation coefficient. All P values are two-tailed and considered statistically significant when $P < 0.05$.

RESULTS

All the 98 patients obtained complete remission. Treatment results are summarised in Table 3. 12 patients (four seminomas, eight non-seminomas) relapsed within 5–32 months (median 11 months). The relapsing patients had initially stage I (8 patients), stage II (1 patient), stage III (1 patient) and stage IV (2 patients) disease. 3 patients died during follow-up, 1 by suicide and 2 (one seminoma, one non-seminoma) from progressive disease. Both patients with disease-related deaths initially had stage IV disease. The 5-year cancer corrected cumulative survivals according to the Kaplan–Meier method were 0.9787 and 0.9804 in the seminoma and non-seminoma groups, respectively.

A statistically significant correlation between stage of disease and human chorionic gonadotropin (HCG) (seminoma $P = 0.021$, non-seminoma $P = 0.005$), lactate dehydrogenase (LDH) (seminoma $P = 0.003$, non-seminoma $P = 0.070$) and α-fetoprotein (AFP) in non-seminoma ($P < 0.001$) were found.

DISCUSSION

In a series of 1058 consecutive patients registered with the Danish Testicular Cancer Study Group (DATECA) (1976–1980) [10], the median ages at presentation were 40.5 and 31.7 years for seminomas and non-seminomas, respectively. The difference in median age at diagnosis was only 6 years in our study (35 versus 29 years). Seminomas tend to present with early stage disease. In seminoma patients documented in Denmark between 1976 and 1980, 77% had stage I, 21% stage II and 3% stage III and IV disease [11]. Compared with these data, there is a slightly increased frequency of stage III and IV disease in our seminoma patients (77% stage I, 13% stage II, 11% stages III and IV). In a study from the Norwegian Radium Hospital of 161 non-seminomas, 50% had stage I, 15% stage IIA, 12.5% stage IIB–III and 22.5% stage IV disease [12]. From our data, there is a lower frequency of stage IV disease (45% stage I, 20% stage IIA, 25% stage IIB–III, 10% stage IV).

6 patients (26%) with non-seminoma stage I relapsed in this study. The frequency reported by Klepp and colleagues [13] of 204 PSI patients in the SWENOTECA programme was 14.7% (30 patients). In our study 1 of 5 patients (20%) with stage IV non-seminoma died. He had a very bulky disease with liver and thoracic wall engagement. Our results are similar to the data from the Testicular Tumour Unit at the Royal Marsden Hospital reporting a 5-year actuarial survival of 81% in 320 patients treated for metastatic non-seminomatous testicular cancer between 1976 and 1985 [14].

The correlation between clinical stage and HCG/AFP levels

Table 3. Treatment results in 98 patients treated for testicular cancer at the University Hospital of Tromsø, Norway

	Seminoma (n = 47)		Non-seminoma (n = 51)	
Complete remission (PR)	47		51	
Relapse	4	(8.5%)	8	(15.7%)
Deaths				
Total	2	(4.3%)	1	(2.0%)
Death of disease	1	(2.1%)	1	(2.0%)

in our study is similar to the results in the DATECA study [15]. The correlation between LDH and stage of disease is not surprising since LDH is known to be correlated to tumour burden and a poorer prognosis [16, 17].

However, our excellent treatment results are similar to those of major oncological centres [10, 12, 18]. The results are of great interest in the debate on where testicular cancer should be treated and by whom. As the survival of testicular cancer has improved, more patients are being treated at general oncology units. Bagshawe and colleagues [3] report specialised centres to have the highest survival rate. Stiller [1] voiced concern that this message has not got through to all involved. In view of the success of highly specialised centres, should regional oncological departments be treating this rare tumour or should all new cases with testicular tumours be referred to highly specialised centres? There may always be a better prognosis in specialised centres caused by selection of patients. Patients not transportable to specialist centres have to be treated in the local general oncology unit, causing unfavourable statistical results. According to Naysmith and Berry [19], it would be an advantage to the patient if satisfactory treatment of testicular tumours could be provided locally, rather than in a highly specialised centre, particularly in view of the severe psychosocial problems associated with this disease and its treatment [20]. However, others [3] disagree, and argue that the extra travelling to a specialised centre is more than compensated for by the emotional security patients feel when treated by a specialised team of doctors and nurses.

Some authors worry that reversal of the policy of centralisation will slow down the scientific evaluation of new treatment regimens. None of the current therapy schedules is beyond improvement. Clinical trials to further improve survival and to reduce treatment-related morbidity and mortality are still of importance. There is a risk of reduced accrual rate for clinical studies as well as overtreatment and deviations from accepted therapeutic methods when testicular cancer patients are treated in small centres. However, this tendency can be counteracted by optimising the cooperation between oncological units by creating multicentre cooperative programmes. In Norway, the SWENOTECA project has played an important role in the co-ordination of the treatment of testicular cancer. Almost all treatment centres in Norway treat their patients according to the same protocols. This ensures a high standard of diagnosis, staging and treatment of testicular cancer. We also believe this way of treating testicular cancer is cost-effective in a country covering a large geographical area with few inhabitants (387 000 km^2 and 4.3 million inhabitants).

Within the context of multicentre cooperative studies or treatment protocols, patients with testicular cancer can be treated in a small general oncology unit with the same expectations of cure and treatment-related morbidity and mortality as is achieved in larger specialist centres. The objectives of improving survival and reducing treatment-related mortality/morbidity will not be compromised.

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