

Prospective study of follow up alone in stage I teratoma of the testis

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Abstract

In a prospective surveillance study of 45 patients with stage I teratoma of the testis 34 (76%) required no further treatment. Eleven patients relapsed but were salvaged by chemotherapy and radiotherapy. Seven patients relapsed within three months of the initial assessment and only one after more than 12 months.

These preliminary results suggest that a follow up policy in stage I teratoma of the testis is possible but only in a regional centre with facilities for close monitoring of patients.

Introduction

About 40-50% of patients with testicular teratoma have metastases at presentation that can be detected by clinical examination or chest radiology.¹ A further 20-30% have subclinical metastases in the para-aortic lymph nodes or micro-metastases in the lungs. Before the development of effective chemotherapy patients in whom metastases were not detected were treated after orchidectomy either by radiotherapy to the para-aortic nodes with or without scrotal irradiation² or (in the United States) by retroperitoneal node dissection. In a retrospective study of 167 patients treated by radiotherapy at this hospital during 1957-72 the five year survival was 70% (fig 1).

volume metastatic disease.⁶ We thought that routine postoperative radiotherapy could be stopped, and we began a prospective surveillance study in November 1979.

Patients and methods

Patients who were referred with a histological diagnosis of testicular teratoma after orchidectomy were assessed by clinical, radiological, and biochemical examination. Radiological examination consisted of radiographs giving three views of the chest and computed tomography of the abdomen. Computed tomograms that were considered to be equivocal were repeated after an interval of six to eight weeks. Some patients in the initial part of the series also underwent bipedal lymphography and computed tomography of the thorax. In all patients serum α fetoprotein (normal < 25 KU/l) and serum β human chorionic gonadotrophin (normal < 1 IU/l) concentrations were obtained at presentation and at weekly intervals if the first result was raised. Preoperative marker concentrations were not usually available. A standard biochemical profile and liver enzyme activities were obtained routinely. The histological material was reviewed in each case and classified according to the Testicular Tumour Panel and Registry.⁷

Patients were considered to be eligible for study (stage I) if the following criteria were fulfilled: (1) there was no clinical evidence of metastatic disease; (2) radiological investigations yielded normal results; (3) serum concentrations of α fetoprotein and β human chorionic gonadotrophin were normal; and (4) the patients had undergone inguinal orchidectomy and no tumour was present at the cut end of the spermatic cord.

All patients were followed up at this hospital. Visits were monthly in the first year and every two months in the second. Assessment at each visit included clinical examination, chest radiology, and estimation of serum concentrations of α fetoprotein and β human chorionic gonadotrophin. Other investigations were performed when clinically indicated. In the event of relapse computed tomography of the chest and abdomen was performed. Patients who relapsed were treated by chemotherapy alone or with radiotherapy according to the site and extent of disease.

Results

We studied 45 patients prospectively during November 1979 to June 1982. All were followed up for more than six months after the initial assessment, 37 for more than 12 months, 26 for more than 18 months, and 16 for more than 24 months (range six to 39 months). The primary tumour was right sided in 25 patients, left sided in 19, and bilateral in one. The mean age of the patients was 31.8 (range 17 to 56). The histological classification was: TD three patients, MTI 18, MTU 14, MTI/S six, MTU/S one, MTT one, MTI/YS/S one, and MTI TD/S one.

Eleven patients relapsed (24%). The time from initial assessment to recognition of relapse was three months or less in seven patients. One patient relapsed more than 12 months after the initial assessment. The table gives details of the patients who relapsed. The sites of relapse were para-aortic (two patients); lung (three); lung and para-aortic (three); para-aortic, mediastinum, and supraclavicular (one); and inguinal canal (one). In one patient raised marker concentrations were the only indication of relapse. The initial indication of recurrence was provided by a chest x ray film in four cases, estimation of marker concentrations in three, a computed tomogram of the lung in one, and clinical findings in three. One patient (case 7) had had a pulmonary embolus after orchidectomy, but on review the pulmonary metastases were also present on the initial computed tomogram of the lung. One patient (case 10) developed a supraclavicular node, and biopsy showed only seminomatous elements. This patient had mediastinal and para-aortic secondaries on computed tomography. At relapse only four

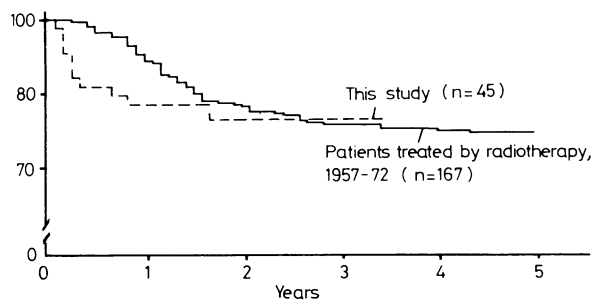


FIG 1—Survival of patients with no clinical evidence of metastases treated by radiotherapy during 1957-72 compared with relapse free survival of patients followed up in this study during 1979-82.

The present study was prompted by the observation that several long term survivors of testicular teratoma had been treated with orchidectomy alone.³ In addition, identification of subclinical metastases had improved with the development of computed tomography⁴ and estimation of tumour markers,⁵ and chemotherapy had become successful for patients with small

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Details of patients who relapsed

Case No	Side of tumour	Pathology	Time to relapse (months)	Site of relapse			Raised concentrations of:		First sign
				Para-aortic	Lung	Other	α Fetoprotein	β Human chorionic gonadotrophin	
1	Left	MTI	1½			Inguinal canal			Mass
2	Right	MTU	2						Marker
3	Left	MTI	2	+			+	+	Marker
4	Right	MTI/S	2	+	+				Chest x ray film
5	Left	MTU	3	+			+	+	Marker
6	Left	MTU	3	+	+				Chest x ray film
7	Left	MTI	3		+				Computed tomogram*
8	Left	NTI/YS/S	4		+				Chest x ray film
9	Left	MTI/S	8		+			+	Chest x ray film
10	Left	MTI/S	10	+		Supraclavicular,* mediastinum			Chest x ray film Mass
11	Right	MTU	20	+					Backache

* Pathology: seminoma.

† Metastases present on initial lung scan on review.

patients developed significantly raised concentrations of the markers (two β human chorionic gonadotrophin and two β human chorionic gonadotrophin plus α fetoprotein); two further patients had borderline concentrations of both markers.

Despite the usual predominance of right sided tumours only three out of 11 patients with relapse had right sided tumours. Comparison of relapse free survival (fig 2) showed a significant difference ($p=0.02$).

CHEMOTHERAPY

Patients requiring chemotherapy received it over a four year period, and this reflected the changes in policy regarding both the combination and duration of treatment. Thus the first six patients received a combination of PVBB (cisplatin 20 mg/m² intravenously on days 1-5, vinblastine 6 mg/m² on days 1 and 2, etoposide 100 mg/mg² intravenously on days 1 to 3, and bleomycin 30 mg weekly intravenously for

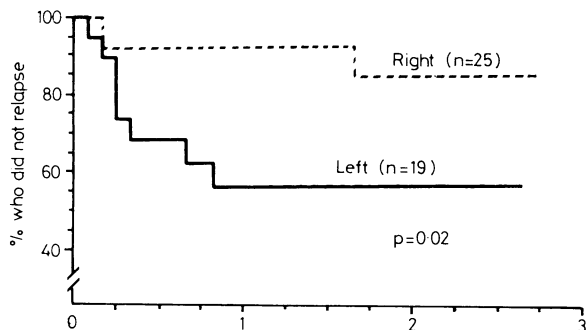


FIG 2—Relapse free survival in patients with right and left sided tumours.

12 weeks), a regimen that has proved effective in patients with bulk disease.⁸ The remaining five patients received a combination of VEP (vinblastine 6 mg/m² intravenously on day 1, etoposide 150 mg/m² intravenously on days 1 and 2, and cisplatin 100 mg/m² as a 24 hour infusion starting on day 1). This regimen has in our experience proved to be effective in eradicating small volume disease and was judged to be more appropriate for this particular group of patients.

The policy was to give two courses beyond remission of the hormone marker concentrations or a minimum of four courses if the concentrations had returned to normal after the first treatment; courses were repeated at intervals of three weeks, blood count permitting. For those patients in whom hormone marker concentrations were normal before treatment a total of four courses were administered, again at intervals of three weeks. Radiotherapy was given after chemotherapy to sites of previous nodal disease.

All patients achieved a complete remission, and the minimum period of remission after completion of treatment was four months (range 4-30 months). One patient (case 5) developed enlargement of the remaining testis 38 months after initial assessment. Orchiectomy showed a tumour, which was classified as MTU, similar to the original pathology. There was extensive tumour of the lower spermatic cord

and blood vessels. It was not possible pathologically to say whether this was a second primary tumour or a metastasis. Further chemotherapy in this patient induced complete remission.

Discussion

The current management of patients with teratoma of the testis in whom no metastases can be detected after orchidectomy is routine postoperative radiotherapy to the para-aortic nodes,² with chemotherapy being given subsequently for patients who relapse. All patients are therefore subjected to the morbidity of radiotherapy. In addition, radiation compromises bone marrow function, and chemotherapy is less well tolerated and may be less successful in patients who have received prior irradiation.

This study shows that a policy of surveillance in stage I malignant teratoma of the testis is possible in a large regional centre. Most of the patients (34/45) required no further treatment. This figure is similar to the previous survival of patients at this hospital treated by postoperative radiotherapy before salvage with chemotherapy became possible (fig 1). Relapse occurred in only 11 of the 45 patients (24%), and this is similar to the incidence of relapse (40/157; 25.8%) in patients treated by orchidectomy and radiotherapy reported on by Peckham *et al.*⁹ In seven of the 11 the time to recurrence was three months or less, and only one patient relapsed more than 12 months after assessment. All the patients were salvaged by chemotherapy and radiotherapy and were free of disease more than four months after the completion of treatment.

Although it may be argued that some of the patients who relapsed might not have required chemotherapy had prophylactic radiotherapy been given, only three patients appeared to have disease that would have been encompassed by a standard infradiaphragmatic radiotherapy field. Forty two patients (93%) might therefore have received unnecessary irradiation.

Relapse was detected by chest radiological examination, measurement of marker concentrations, and clinical examination. We adopted a less intense scheme of radiological follow up than Peckham *et al.*,⁹ but the incidences of relapse (11/45 (24%) *v* 9/53 (17%)) were similar ($p=0.95$). Relapse was due to lung metastases in five patients in this series compared with two in the series of Peckham *et al.* The efficacy of chemotherapy means that the earlier diagnosis of lung metastases by computed tomography of the lung and whole lung tomography may confer little advantage.

The decision not to use lymphography was based on previous experience at this hospital in Hodgkin's disease. In a study of 60 cases lymphography did not detect disease in any patient in whom computed tomography yielded negative results.¹⁰ In a study of 62 patients with malignant teratoma of the testis, Husband *et al.* found that computed tomography was superior to lymphography, and that no patient in whom computed tomography yielded negative results gave positive results on lymphography.⁴

In this series only four of the 11 patients who relapsed had raised concentrations of either or both markers. This compares with an earlier study at this hospital in which 80% of patients with metastatic disease had raised concentrations of either or both markers (G Read, unpublished observation). With the present scheme of follow up patients with tumours that do not produce markers and in whom the relapse occurs in the abdomen only might be at a disadvantage as the relapse might be diagnosed relatively late, but in this series only one patient fell into this category (case 11) and complete remission was obtained with chemotherapy. Routine estimation of preoperative marker concentrations would be helpful in identifying these patients.

Peckham *et al* found a predominance of patients with MTU tumours among those who relapsed,⁹ but this was not so in this series. Patients with left sided tumours, however, were significantly more likely to relapse. While further studies are required to confirm this finding, it is intriguing to note a comparison with the improved survival in patients with right sided malignant lymphoma of the testis.¹¹ Further studies are also required to provide more information on the pattern of relapse so that the optimum scheme for follow up of patients can be devised. Pathological studies may permit identification of particular patients at risk.

These preliminary results suggest that follow up alone in stage I teratoma of the testis is viable, but at present it is suitable only for large centres with access to specialised investigational techniques, and the optimum scheme for surveillance remains to be determined.

We thank Dr E Gowland, biochemistry department, Withington Hospital, for estimating the serum marker concentrations, Dr M K

Palmer for statistical analysis, and Mrs V Kelly for typing the manuscript.

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(Accepted 9 September 1983)

Patients with angina with normal and near normal coronary arteries: clinical and psychosocial state 12 months after angiography

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Abstract

The clinical and psychosocial states of 46 patients (26 men and 20 women) who had undergone cardiac catheterisation were examined prospectively. All of the patients had insignificant (< 50%) coronary lesions and had been told that no limitation of activity was necessary. Twelve months after angiography 19 of the patients continued to complain of chest pain. Twenty one reported phobic symptoms, and 13 were found by standardised clinical interview to have psychiatric morbidity. This had been evident at the time of catheterisation in 28. Twenty three patients had evidence of unexplained breathlessness, 13 were taking psychotropic drugs, 29 were continuing to

consult a doctor, and 11 were unable to work because of their symptoms.

Patients initially assessed as having high levels of psychiatric morbidity and raised neuroticism scores were more likely to complain of chest pain one year after angiography. The 19 patients with persistent pain also had significantly higher levels of psychiatric and social morbidity at one year than the 27 patients whose chest pain had lessened during the follow up period.

Those patients who fail to improve after being told that they have normal or nearly normal coronary arteries tend to be a chronically neurotic and socially maladjusted group in whom psychiatric disorder presents with predominantly somatic symptoms.

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Introduction

Among patients referred for cardiac catheterisation because of chest pain up to one third may have either normal coronary arteries or mild non-obstructive atherosclerosis.^{1, 2} The prognosis in these patients is favourable, the incidence of subsequent myocardial infarction and mortality not being increased above that in the population at large when measured 10 years after angiography.³ Several recent follow up studies have shown,