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TESTICULAR GERM CELL TUMOURS IN DENMARK 1976–1980

Pathology of 1058 consecutive cases

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Abstract

In the first five-year period of the Danish Testicular Carcinoma Study (DATECA) 1058 consecutive testicular germ cell tumours were examined. Of these, 554 were seminomas comprising 515 of typical type, 26 anaplastic and 13 spermatocytic; 497 were non-seminomas comprising 145 pure tumours and 352 mixed tumours of various types. Among the various subtypes of non-seminomas embryonal carcinoma (EC) was recorded in 87 per cent, endodermal sinus tumour (yolk sac tumour; EST) in 22 per cent, teratoma (T) in 55 per cent and choriocarcinoma (CC) in 17 per cent. Only very few tumours were pure EST or pure CC. Five tumours were recorded as 'others or uncertain'. The tumours were graded with regard to various histologic features. Moderate and severe necrosis, bleeding, and a large number of mitoses were significantly more frequent in non-seminomas. The presence of tumour tissue at the resection margin was also more frequent in non-seminomas. Tumours with a largest diameter of less than 2.5 cm had already caused metastases in 16 per cent of the seminomas and 29 per cent of the non-seminomas. Increasing size of the tumours was associated with increasing frequency of metastatic disease but this association was not directly proportional. Distribution of the various histologic types according to the stage of disease varied. Thus, 78 per cent of the seminomas presented in stage I while 54 per cent of the non-seminomas had localized disease. Anaplastic seminomas were distributed similarly to the non-seminomas while all spermatocytic seminomas, with one exception, were recorded as stage I. Of non-seminomatous subtypes pure EC was associated with the highest frequency of stage III, followed by mixed tumours containing CC components. Although the present series is large the heterogeneity of germ cell tumours demands further investigation of larger numbers to confirm some of the findings.

In the first five-year period, 1976 to 1980, of the Danish Testicular Carcinoma Study (DATECA), 1058 males with testicular germ cell tumours were participants in the study. The organization of this investigation has been described previously (15). The present report describes the results of the patho-anatomic evaluation of the tumours.

Material and Methods

In Denmark, patients with testicular tumours undergo orchiectomy at the surgical department of the local hospital. Afterwards, they are referred to the regional oncologic centre for further evaluation and therapy.

The orchiectomy specimen is forwarded to the local department of pathology where it is handled and sectioned according to the recommendations for the DATECA study (14). After fixation in 10% buffered formalin for 24 to 72 hours the size of the testis is recorded in three planes. The testis is cut sagittally towards the mediastinum and the tumour is measured in the largest single plane using two perpendicular diameters, which permits a rough estimate of the proportion of the testis with tumour involvement (<25%, <50%, >50%, <75%, >75%). The sectioning follows a standard procedure. Sections are taken from the margin of resection, the proximal

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cord, the epididymis, the mediastinum, the tumour, and the adjacent testis parenchyma. At least five sections are taken from the tumour. The sections are embedded, cut and stained according to the routine procedures of the local department of pathology.

Since Jan. 1, 1976 the primary report and the slides have been forwarded to one of the five DATECA pathologists, who perform the final pathologic evaluation which is reported to the central registry of DATECA.

The tumours were classified according to the WHO typing of testis tumours (9), with slight modifications. In mixed tumours each tumour component was recorded separately. A rough estimate of the relative amount of the various tumour components was given on a four grade scale, as were the extent of necrosis and bleeding. Mitoses were counted in high power fields ×400 (HPF) with the most pronounced mitotic activity and recorded on a four grade scale, i.e. 0 = no or few mitoses, 1 = maximum 3 mitoses per HPF, 2 = maximum 5 mitoses per HPF, and 3 = more than 5 mitoses per HPF. Seminomas with more than 5 mitoses per HPF and/or considerable nuclear variation without differentiation were recorded as anaplastic seminomas. The number of lymphocytes and granulomas were additionally recorded on a four grade scale. Giant cells were not recorded separately until mid-1980. Local invasive properties were recorded using the same simple four grade scoring system. Invasion of the rete testis, the tunica albuginea, the epididymis, the proximal funicle and the resection line were recorded as follows: 0 = no, 1 = slight, 2 = moderate, and 3 = severe invasion.

The slides were not circulated routinely among all the member pathologists but uniformity of judgement was maintained by regular meetings of the pathology committee.

Staging was performed at the oncologic centres using a clinicoradiologic staging system which was a slight modification of the system originally proposed (1, 15, 16).

The chi-square test was used to test any association between the various groups of the series.

Results

The annual numbers for the 1058 patients registered are shown in Table 1 and the number of various tumour types in Table 2.

Table 1

Annual number of patients with testicular germ cell tumours registered in the Danish Testicular Carcinoma (DATECA) Study in 1976–1980

Year	Patients with				
	Seminomas		Non-seminomas		Total* No.
	No.	Per cent	No.	Per cent	
1976	103	(51.8)	96	(48.2)	199 (1)
1977	100	(49.5)	102	(50.5)	202 (1)
1978	117	(54.7)	97	(45.3)	214
1979	123	(53.5)	107	(46.5)	230 (3)
1980	111	(53.4)	97	(46.6)	208
Total	554	(52.6)	499	(47.4)	1 053 (5)

* Numbers in parentheses indicate number of tumours classified as 'others and uncertain' that are not included in the figures.

The mean age of patients with seminomas was 40.5 years (range 19–84) and of patients with non-seminomas 31.7 years (range 14–72). This did not change in either group during the period under review. The mean age of patients with anaplastic seminomas was 39.1 years (range 20–80) and of those with spermatocytic seminomas 58.8 years (range 35–80). For the various stages of seminomas the mean age was as follows: I: 39.9, II: 41.3, III: 49.1 years, and for the non-seminomas it was I: 32.6, II: 31.0 and III: 29.9 years.

Table 3 gives the mean largest diameter of the primary tumours for each of the five years. It appears that seminomas were larger than non-seminomas at the time of orchiectomy and that the size of both tumour types has decreased since the start of the DATECA study. The decrease in the size of seminomas has been accompanied by a significant increase in stage I tumours ($p<0.05$) while this has not occurred for non-seminomas. In the various stages of the disease the mean largest diameter of seminomas I: 4.9, II: 6.0 and III: 7.7 cm, while that of non-seminomas was I: 3.9, II: 4.7 and III: 5.7 cm.

In Table 4, the frequencies for seminomas and non-seminomas of various sizes are given in relation to the stage of the disease. As expected, increasing size of tumours was associated with increasing frequency of metastatic disease. Tumours with a largest diameter of less than 2.5 cm had, however, already caused metastases in 16 per cent of the seminomas and 29 per cent of the non-seminomas.

Table 2

Number of the various tumour types in 1053 cases of testicular germ cell tumours

Seminomas n=554)	
Typical	515
Anaplastic	26
Spermatocytic	13
Non-seminomas (n=499*)	
Pure tumours (n=145)	
EC	109
EST	3
T	31
CC	2
Mixed tumours without ST (n=209)	
Two types	123
EC+EST	15
EC+T	90
EC+CC	13
EST+T	2
EST+CC	0
T+CC	3
Three types	71
EC+EST+T	39
EC+EST+CC	6
EC+T+CC	26
EST+T+CC	0
Four types	15
EC+EST+T+C	15
Mixed tumours with ST (n=137)	
One type + ST	77
EC	55
EST	0
T	20
CC	2
Two types + ST	40
EC+EST	9
EC+T	22
EC+CC	7
EST+T	0
EST+CC	0
T+CC	2
Three types + ST	15
EC+EST+T	12
EC+EST+CC	1
EC+T+CC	2
EST+T+CC	0
Four types + ST	5
EC+EST+T+CC	5
Mixed tumours with SA (n=6)	
EC	3
T	1
EC+T	1
EC+T+CC	1

*Two non-seminomas were not further specified because of extensive necrosis.

Abbreviations: ST = typical seminomas, SA = anaplastic seminoma, EC = embryonal carcinoma, EST = endodermal sinus tumour (yolk sac tumour), T = teratoma, CC = choriocarcinoma.

Table 3

Primary size of testicular germ cell tumours and distribution of tumours in relation to stage of disease

Year	Size of primary tumour (mean largest diameter, cm)		Stage of disease (%)			
			Seminoma		Non-seminoma	
	Seminoma	Non-seminoma	I	II+III	I	II+III
1976	5.7	5.1	70	30	52	48
1977	5.4	4.8	71	29	53	47
1978	5.2	4.2	77	23	58	42
1979	4.9	4.0	83	17	51	49
1980	4.8	4.0	78	22	68	32

Seminomas with a largest diameter of 2.5 to 4.5 cm and 4.5 to 8.5 cm did not differ with regard to frequency of metastases, neither did the frequency of non-seminomas of such sizes.

When the distribution of the tumours was considered in relation to the estimate of the proportion of the testis involved it emerged that when <25 per cent was involved 24 per cent of seminomas and 29 per cent of non-seminomas were associated with metastases while 28 per cent of seminomas and 51

Table 4

Number and frequencies of testicular germ cell tumours of various sizes in relation to stage of disease (per cent in parentheses)

Size*	Seminoma**				Non-seminoma***			
	Stage of disease			Total	Stage of disease			Total
	I	II	III		I	II	III	
<2.5	62 (84)	9 (12)	3 (4)	74 (100)	71 (71)	21 (21)	8 (8)	100 (100)
2.5–4.5	106 (79)	28 (21)	0 (0)	134 (100)	86 (57)	43 (28)	23 (15)	152 (100)
4.5–8.5	152 (81)	33 (18)	3 (2)	188 (100)	79 (52)	48 (32)	24 (16)	151 (100)
>8.5	23 (45)	22 (43)	6 (12)	51 (100)	7 (24)	9 (31)	13 (45)	29 (100)
	343	92	12	447	243	121	68	432

* Largest diameter of primary tumour in cm.
** Anaplastic and spermatocytic seminomas are excluded and 71 patients were not registered due to insufficient information.
*** 64 patients were not registered due to insufficient information.

per cent of non-seminomas involving more than 75 per cent had metastasized.

Of the 554 recorded seminomas 515 (93.1%) were typical, 26 (4.7%) were classified a anaplastic and 13 (2.3%) were spermatocytic as shown in Table 2.

Of 497 non-seminomatous tumours 145 (29%) were pure tumours and 352 (71%) mixed tumours. Embryonal carcinoma (EC) was recorded in 431 (87%) non-seminomas. Endodermal sinus tumour (yolk sac tumour; EST) occurred rarely as a pure tumour but as a tumour component in 104 (30%) mixed tumours, i.e. EST was recorded in 22 per cent of all non-seminomatous tumours. Teratoma (T) occurred in pure form in only 31 cases, but as a tumour component in 241, i.e. 55 per cent of all non-seminomas. Choriocarcinoma (CC) was rare as a pure tumour, but was present in 84 mixed tumours, comprising 17 per cent of non-seminomatous tumours.

Seminoma of typical type and anaplastic seminoma occurred in combination with various tumour components in 137 and 6 tumours, respectively (Table 2). Where typical seminoma was combined with another tumour component EC was the most frequent tumour type. Where seminoma was combined with two tumour elements EC and T were the most frequent combination. These were also the tumour components that occurred most frequently in combination with anaplastic seminoma. EST was not seen in combination with anaplastic seminoma.

Five cases in this investigation were recorded as 'others and uncertain'; these comprised two cases of gonadal tumours in hermaphrodites, one of microinvasive carcinoma, one of burnt-out testicular tumour, and one case with no orchiectomy performed.

Table 5

Distribution of testicular germ cell tumours in relation to various histologic features

	Frequency of tumours	
	Seminoma	Non-seminoma
Histologic features (grade 2 + 3)		
Necrosis	22.2	54.1
Bleeding	9.3	36.7
Mitoses	31.3	67.3
Lymphocytes	46.4	14.0
Granulomas	1.2	0.5
Invasion of (grade 1 + 2 + 3)		
Rete testis	59.8	56.1
Tunica albuginea	53.6	51.0
Epididymis	21.0	22.3
Proximal funicle	10.3	14.3
Tumour tissue at resection margin	4.8	8.1

The frequency of various histologic features appears in Table 5. The frequency of tumours with moderate (=grade 2) and severe (=grade 3) necrosis and bleeding and a high number of mitoses was significantly higher in non-seminomatous tumours than in seminomas ($p<0.05$), while moderate and severe infiltration with lymphocytes was more pronounced in seminomas ($p<0.05$). The presence of granulomas did not differ significantly between the two tumour groups. Table 5 also shows that the

Table 6

Distribution of typical, anaplastic and spermatocytic seminomas and non-seminomas in relation to stage of disease (per cent in parentheses)

Tumour type	Stage of disease		
	I	II	III
Typical seminoma*	398 (78)	99 (19)	15 (3)
Anaplastic seminoma	14 (54)	10 (38)	2 (8)
Spermatocytic seminoma	12 (99)	1 (1)	0 (0)
Non-seminoma**	270 (54)	137 (28)	90 (18)
Not classified	2		3
Total	696 (66)	247 (24)	110 (10)

* Three tumours were not staged.
** Two tumours were not staged.

Table 7

Distribution of various types of testicular germ cell tumours with and without a seminoma component in relation to stage of disease (per cent in parentheses)

Tumour type	Stage of disease		
	I	II	III
EC	47 (43)	33 (30)	29 (27)
EC+ST	35 (64)	15 (27)	5 (9)
T	17 (57)	8 (27)	5 (16)
T+ST	13 (65)	7 (35)	0 (0)
EC+T	61 (68)	21 (24)	7 (8)
EC+T+ST	13 (59)	7 (32)	2 (9)
EC+T+EST	28 (72)	7 (18)	4 (10)
EC+T+EST+ST	5 (42)	4 (33)	3 (25)

For abbreviations see Table 2.

Table 8

Distribution of 107 testicular germ cell tumours containing an endodermal sinus tumour component in relation to stage of disease (per cent in parentheses)

Tumour type	Stage of disease			
	I	II	III	Total
EST	1	0	2	3
EST+EC	8	3	4	15
EST+EC+ST	2	4	3	9
EST+T	0	2	0	2
EST+EC+T	28	7	4	39
EST+EC+T+ST	5	4	3	12
EST+EC+CC	2	3	1	6
EST+EC+CC+ST	1	0	0	1
EST+EC+T+CC	9	4	2	15
EST+EC+T+CC+ST	1	1	3	5
	57 (53)	28 (26)	22 (21)	107
EST + any other combination − ST	48 (60)	19 (24)	13 (16)	80
EST + any other combination + ST	9 (33)	9 (33)	9 (33)	27

For abbreviations see Table 2.

frequency of local invasive growth in the two tumour groups did not differ significantly. Only the presence of tumour tissue at the resection margin was more frequent in non-seminomatous tumours than in seminomas ($p<0.05$).

The distribution of the histologic main groups of tumours in relation to the stage of the disease is shown in Table 6, from which it appears that 78 per cent of the patients with pure seminomas presented in stage I, while only 54 per cent with non-seminomatous tumours had localized disease. Patients with anaplastic seminoma showed almost the same stage distribution as those with non-seminomatous tumours.

Tables 7, 8 and 9 show the distribution of some pure and mixed non-seminomatous tumours with and without a seminoma component in relation to the stage of the disease. Pure EC was associated with the highest number of patients in stage III. The combination of EC with seminoma reduced the overall frequency of metastatic stages significantly ($0.01<p<0.05$), due in particular to a pronounced reduction of the frequency of metastatic III disease. The combination of EC with T also reduced the frequency of stage III tumours, and this frequency was even less than that of pure T. The occurrence of seminoma or EST in combination with EC + T did not change the frequency of such tumours in stage II + III significantly compared with EC + T alone, although the presence of seminoma was associated with a tendency to increase the number of patients with metastatic II + III disease. Patients with EC + T + EST had metastatic disease in 28 per cent of the cases compared with 58 per cent of such patients who in addition had a seminoma component in the tumour, and this difference was statistically significant ($0.025<p<0.05$). When all tumour combinations containing EST were compared in relation to the presence or absence of seminoma, the overall frequency of metastatic disease was also found to be significantly higher in patients with a seminoma component than in those without ($p<0.05$). With

these exceptions the presence of seminoma in any tumour type was, however, associated with either an unchanged or a decreased percentage of patients with metastatic disease compared with patients with the same tumour type without seminoma.

Of the patients with a CC component in the tumour 55 per cent had metastatic disease while this frequency for all patients with non-seminomas was 46 per cent (Table 9). The overall stage distribution of tumours with CC did not change significantly whether a seminoma component was present or not. However, within some of the subgroups occurrence of seminoma changed the stage of the disease considerably. Thus 31 per cent of patients with CC + EC had localized disease compared with 71 per cent of patients with the same tumour type combined with a seminoma component.

In summary, non-seminomatous tumours with the highest frequency of localized stage I disease were: EC + T + EST (72%), EC + CC + seminoma (71%), and EC + T (69%), while tumour types with the lowest frequency of stage I disease were: CC + EC (31%), CC + EC + T (42%), EC + T + EST + seminoma (42%) and EC (43%).

Table 9

Distribution of 85 testicular germ cell tumours containing a choricocarcinoma component in relation to stage of disease (per cent in parentheses)

Tumour type	Stage of disease			
	I	II	III	Total
CC	1	0	1	2
CC+ST	0	1	1	2
CC+EC	4	5	4	13
CC+EC+ST	5	0	2	7
CC+T	1	0	2	3
CC+T+ST	1	1	0	2
CC+EC+T	11	7	8	26
CC+EC+T+ST	2	0	0	2
CC+EC+EST	2	3	1	6
CC+EC+EST+ST	1	0	0	1
CC+EC+T+EST	9	4	2	15
CC+EC+T+EST+ST	1	1	3	5
CC+EC+T+SA	0	0	1	1
	38 (45)	22 (26)	25 (29)	85
CC + any other combination − ST	28 (43)	19 (29)	18 (28)	65
CC + any other combination + ST or SA	10 (50)	3 (15)	7 (35)	20

For abbreviations see Table 2.

Discussion

A standardized handling and evaluation of all or almost all specimens of testicular germ cell tumours from a whole population in a well-defined geographic area for a consecutive number of years has not been undertaken before. Since only a very small number of patients did not enter the study the reported data describe aspects of the disease in its entirety in the Danish male population during the cited 5-year period.

The age distribution of the patients showed that the mean age for those with non-seminomatous tumours was approximately ten years less than that for patients with seminomas. The size of the seminomas decreased during the five-year period, which means that they were diagnosed earlier than previously, although the mean age of these patients did not change. It is to be noticed that the mean age of patients with anaplastic seminomas was equal to that of patients with seminomas although the distribution of anaplastic seminomas according to stage of disease followed that of non-seminomas.

As expected, the frequency of metastatic disease in patients with small tumours was less than that associated with large tumours. The frequency of metastatic disease was, however, not directly proportional to the size of the tumour since the frequency of metastases in tumours of 2.5 to 4.5 cm and 4.5 to 8.5 cm differed neither in seminomas nor in non-seminomas. This may explain why delayed diagnosis and treatment does not change the prognosis significantly for such patients (4). The figures also indicate that in order to reduce the frequency of patients with metastatic disease considerably, the tumours should be diagnosed when they are almost impossible to recognize at palpation.

Although a standardized handling of the orchiectomy specimens was effected, the specimens were examined less uniformly than could have been achieved by a single pathologist. In particular, this may have influenced the evaluation of the invasive properties of the tumours. With regard to the tumour classification it is well known that sampling errors are frequent if only one or a few sections are cut from the germ cell tumours. We believe that this error was minimized in the present investigation by the examination of a minimum of five tumour sections. The difference in frequency of the various tumour components reported in previous series of

testicular germ cell tumours is in our opinion more likely to have been due to differences in interpretation of the morphologic patterns. Reduction of discrepancy within this series was accomplished by frequent meetings of the rather small group of participating pathologists.

Previous investigations on testicular germ cell tumours have usually been based on material from selected cases. The report of FRIEDMAN & MOORE (4) on 922 cases comprised tumours collected from patients of military age serving in the US Armed Forces. The report by PATTON & MALLIS (10) dealt with 510 cases seen at the Walter Reed Army Hospital from 1940 to 1956. MOSTOFI (8) based his investigation on 6000 testicular tumours registered at the Armed Forces Institute of Pathology during 25 years. The large series of testicular tumours, 2739 cases, analyzed by the British Testicular Tumour Panel (BTTP) in the years 1958 to 1973 represented less than one third of the total number registered in the United Kingdom within those years (13), and in addition it was stated that this series contained an unduly high proportion of some of the more unusual and rare tumours. In contrast, TEPPO's study (19) of 131 malignant testicular tumours comprised all the cases registered in Finland during the years 1953 to 1961.

Seminomas in the various series comprised from 35 to 60 per cent of germ cell tumours (4, 7). The percentage of seminomas in the present series did not differ from that published by the Danish Cancer Registry from previous five-year periods (2), and it was equal to the percentage in the less selected series published previously (19).

In addition to variation in selection of patients differences in histologic classification make comparison between the various series difficult. However, certain groups of tumours can be compared. EC or undifferentiated malignant teratoma according to the BTTP classification is the tumour component most frequently present in non-seminomatous testicular germ cell tumours in all series. It is also agreed that CC is a very rare pure tumour and that it occurs more frequently as a tumour component in mixed tumours. EST is rarely reported as a pure tumour, but in recent years EST has been increasingly recognized in adult mixed testicular germ cell tumours (12, 17). Yet it is not included in all the major systems of classification. TEILUM (18), who has given the most detailed description of the EST, did not state the incidence of this tumour component in mixed tumours. In a retrospective study of 122 testicular tumours classified as teratomas according to the BTTP classification WURSTER et coll. (21) found that 37 per cent of the tumours included EST. In a recent investigation, GRIGOR (5) found 152 (66%) tumours with EST elements in male patients with teratomas (BTTP), and of these, 32 were recorded as pure EST in adults. In one retrospective and one prospective study of non-seminomatous testicular adult germ cell tumours TALERMAN (17) found EST elements in 28.7 and 44.4 per cent of the cases, respectively. He emphasized that detection of EST elements depends on thorough sectioning, judicious sampling, careful histologic examination and familiarity with the various histologic patterns of the EST.

In the present investigation the number of EST elements recorded increased with increasing awareness of the variegated pattern of the EST. Although the various patterns of the EST were described in detail many years ago the recognition of these patterns has developed only very slowly, despite their being distinctive and fairly easily recognizable when once realized. Within our group of pathologists initial discrepancies in recognizing this tumour element have been overcome and the fact that EST was reported with increasing frequency in later years in the DATECA series was a result of this development, rather than a true increase of this tumour component in the germ cell tumour. The number of EST elements for the whole period of this series are thus minimum figures.

It should be noted that apart from a few pure EST and two tumours with EST + T it seems as if EST is invariably associated with EC. It may be that pathologists hesitate to designate a tumour EST without EC, or that some components of the solid type of EST may be interpreted as EC. However, T is also found in a very few combinations without EC.

Variations of the frequencies of certain tumour combinations in mixed tumours with and without seminoma are interpreted as a random variation until a larger number of patients is recorded in the various subgroups.

From a clinical point of view it is important to distinguish seminomas from non-seminomas. Seminomas may be further subdivided into typical, anaplastic and spermatocytic types. Various criteria of anaplastic seminoma have previously been proposed. Using more than five mitoses per HPF defines, however, a group of seminomas that, with

regard to the stage of the disease, is distributed as non-seminomas, indicating a different biologic behaviour compared with typical seminomas. This is also in accordance with the experience of VON HOCHSTETTER (6), who recommended six mitoses per HPF as the arbitrary criterion until a more reliable one is found.

In the BTTP classification the non-seminomas are subdivided with regard to degree of differentiation, which has been shown to be of prognostic significance. In the WHO classification the impact on prognosis of the various subtypes is not known with certainty. It is known that CC as a pure tumour as well as a tumour component of mixed tumours implies a poor prognosis and it has been reported that EST is also associated with a poor prognosis (11, 17). The possible prognostic significance of various tumour types and histologic features in the present series are dealt with in the report by VÆTH et coll. (20). However, investigation of the prognostic significance of the various histologic subtypes has been rendered highly difficult by the success of combination chemotherapy and only very great differences can be expected to stand out clearly.

At the time of diagnosis, patients with testicular malignancy have harboured their tumour for some time, frequently for more than one year (3). Thus it might be expected that tumour components and tumour combinations with a grave prognosis would be apparent already at this time through a high frequency of metastatic disease. The various tumour types were therefore compared with the stage of the disease at the time of diagnosis. Patients with pure EC and with mixed tumours with CC had a higher frequency of metastatic disease than the group as a whole.

It is notable that EST was not associated with an especially high frequency of patients with metastatic disease. One group of patients with EST in the tumour (EC + T + EST) even had the highest frequency of stage I among patients with non-seminomatous tumours. In the series of PARKINSON & BEILBY (11) the combination of EST elements with seminoma improved the prognosis significantly, which was interpreted as a modification of EST malignancy by seminoma. By contrast, addition of a seminoma component to germ cell tumours containing EST in the present series caused a displacement of the patients towards a higher frequency with metastatic disease. A small group of patients with EC + T + EST + seminoma actually had the same high frequency of metastatic disease as patients with pure EC. Whether this is a general phenomenon will remain uncertain until a larger series has been examined.

Although the present series was large the heterogeneity of germ cell tumours demands further investigation of a larger number of patients in order to clarify other aspects of the disease.

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