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Exocrine function of testis with germinal testicular tumour

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Abstract

Semen collected immediately before or soon after therapeutic unilateral orchidectomy from 86 men with germinal tumours of the testis was analysed. The mean sperm count was 65·6 ± SEM $10·3 \times 10^6$ per ejaculate. This was significantly different from that in a control population, in whom the mean was $165·2 \pm 12·9 \times 10^6$ per ejaculate. The difference appeared to be due to a subpopulation of 32 patients with counts of 20×10^6 per ejaculate; the distribution of counts in the remaining patients was similar to that in the controls.

The cause of this abnormality of exocrine function is unknown: it may either be due to the tumour or its treatment, or both, or, alternatively, it may predate the events of the malignant transformation, possibly even acting as an inducing or promoting factor.

Introduction

Dramatically improved survival of patients with germ cell testicular tumours has focused attention on other criteria for outcome of treatment.[1] Most patients are of reproductive age so that preservation of fertility is important. Treatment is often multidisciplinary with surgical procedures, including unilateral orchidectomy and retroperitoneal lymphadenectomy, plus abdominal irradiation or systemic combination chemotherapy, or both. Each modality affects potential fertility.[2] Less well understood is the state of spermatogenesis in these patients before treatment.[3] The occasional detection of a tumour during investigation of infertility and the low sperm density often found in patients referred for sperm banking have suggested that testicular exocrine function may be abnormal in the presence of germinal tumours before treatment. If correct, this observation might have fundamental biological importance as the germ cell line is thought to produce the stem cell of these tumours. Furthermore, pretreatment counselling would be improved if the impact of treatment was established from prospective data in individual patients. We therefore undertook a study of the quality of semen before treatment in patients with testicular tumour.

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Patients, methods, and results

Freshly ejaculated semen was collected immediately before or soon after therapeutic unilateral orchidectomy from 86 men with germinal tumours of the testis. Routine analysis was performed to assess semen volume and sperm density, motility, and morphology.[4] Density was measured by means of a haemocytometer chamber with visual counting.

Thirty five patients had classical seminomas and 51 non-seminomas. Control semen specimens were provided by members of the house staff and patients of a similar age admitted electively for minor surgery. All had been abstinent for two or more days, and the patients with testicular tumour denied ejaculation in the interval from orchidectomy to analysis.

The total number of sperm per ejaculate in the 86 semen samples provided by the patients with tumours was 65·5 ± SEM $10·5 \times 10^6$. This was significantly different from the mean of $165·2 \pm 12·9 \times 10^6$ in the 101 controls. The mean in the 35 patients with seminomas ($60·5 \pm 11·5 \times 10^6$) was not significantly different from the mean in the 51 patients with non-seminomas ($68·9 \pm 15·6 \times 10^6$). The mean count in all the patients was not significantly different from one half of the mean in the controls. Calculations using sperm density (which does not allow for variation in volume) produced similar results.

A subpopulation of 32 of the patients with tumours (37%) had under 20×10^6 sperm per ejaculate; such low values were present in only two (4%) of the controls (table). The distribution of sperm counts in the remaining 54 patients was similar to normal. The distribution of counts was similar in patients with seminomas and those with non-seminomas.

The mean sperm count in seven patients studied before orchidectomy ($45·3 \pm 14·8 \times 10^6$ per ejaculate) was less than the mean after orchidectomy ($66·2 \pm 11·1 \times 10^6$) (figure). Two patients studied before

and after orchidectomy showed only minor changes only in sperm density. Only a few of the patients had attempted conception by the time of diagnosis, so that data on fertility were not meaningful.

Discussion

In this study 32 out of 86 patients with germinal testicular tumours were found to have sperm counts below 20×10^6 per ejaculate before treatment other than hemicastration compared with two out of 101 normal controls. In the remaining patients the distribution of counts was similar to that in the controls. Thus these data suggest that the distribution of sperm counts in patients with germinal testicular tumours is bimodal. The cause of these abnormalities of exocrine function is unknown. They may be due to the tumour or its treatment, or both, or, alternatively, they may develop before the events of malignant transformation, possibly even acting as an inducing or promoting factor.

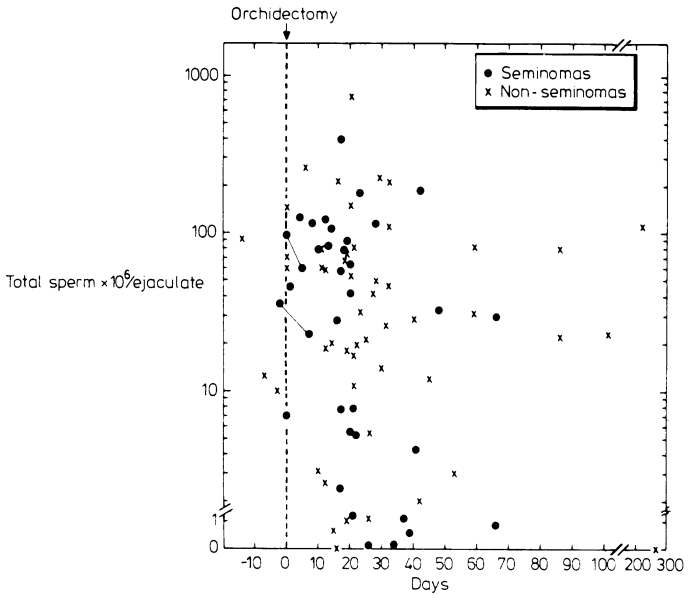
Human testes appear to have little ability to undergo compensatory hypertrophy or hyperplasia, so that unilateral orchidectomy would be expected to result in a sperm count of 50% normal after several ejaculations have emptied the ipsilateral vas deferens, ampulla, and seminal vesicle.[4-7] Although the mean count in our patients was not significantly different from one half of the count in the controls, the reduction appeared to be due to the patients in whom counts were below 20×10^6 per ejaculate. Furthermore, the mean of the sperm counts obtained in seven patients before orchidectomy was similar to the mean obtained after orchidectomy, and the counts in two patients studied before and after surgery did not change. These findings suggest that orchidectomy and subsequent ejaculation cannot alone explain the frequent low sperm counts and that a bilateral abnormality of testicular function must be present.

Immunological and hormonal influences may be important. Antitesticular tumour activity has been reported in the serum of some tumour bearing patients that cross reacts with sperm.[8] Hormonal changes occur in patients with tumours that produce human chorionic gonadotrophin. Cochrane *et al* reported increased concentrations of 17-oestradiol, which may be due to peripheral aromatisation of testosterone and androstenedione by tumour tissue in these patients.[9] Few of our patients had significantly increased concentrations of human chorionic gonadotrophin.

The alternative hypothesis that the abnormalities of spermatogenesis are present before malignant transformation occurs is difficult to test. The well known relation of tumours of the testis to cryptorchidism, however, indicates that testicular abnormalities may predate neoplastic change.[10] While we have not yet defined whether the suppression of spermatogenesis frequently seen with tumours of the testis exists before neoplastic transformation or develops as a result of the tumour, the abnormality is bilateral and often profound. Our data suggest, however, that the overall distribution is bimodal, the distribution of sperm counts being normal in 63% of patients. A potentially sterilising treatment may have a greater impact on already abnormal germinal tissue, and the application of sperm banking may be limited by the often poor quality of the semen at diagnosis.

Distribution of sperm count in patients and controls (figures are numbers (%) of subjects)

Sperm count $\times 10^6$/ejaculate:	0–5	– 10	– 20	– 40	– 80	– 160	– 320	– 640
Controls (n = 101)	0	0	4 (4)	7 (7)	16 (16)	35 (35)	24 (24)	15 (15)
Patients with tumour (n = 86)	18 (21)	5 (6)	9 (10)	12 (14)	17 (20)	17 (20)	6 (7)	2 (2)
Non-seminoma (n = 51)	9 (18)	1 (2)	9 (18)	8 (16)	11 (22)	8 (16)	3 (6)	2 (4)
Seminoma (n = 35)	9 (26)	4 (11)		4 (11)	6 (17)	9 (26)	3 (9)	



Sperm count in patients with testicular tumour by intervals from unilateral therapeutic orchidectomy. Two patients were studied before and after orchidectomy.

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