TESTICULAR CANCER AND INFERTILITY: PREDICTING SPERMATOGENESIS

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TESTICULAR CANCER AND INFERTILITY

Germ cell tumours are the most common malignancy in young men (15-40 years). The greatest incidence occurs during peak reproductive years[1].

RELATIONSHIP BETWEEN TC AND INFERTILITY:
- 50% of men with TC have normal sperm quality before treatment[1]
- 10-35% suffer from infertility[1]
- 6-24% are reported as azoospermic at diagnosis [2,3]

Figure 1. Testicular cancer impacts on spermatogenesis in 3 ways:

1. Testicular Hormonal Effect of Tumour
2. Local Chemotherapy Radiotherapy
3. Surgery Dysgenesis Syndrome

Spermatogenesis

1. TC patients have an inherent risk of infertility.
2. The tumour disrupts spermatogenesis.

TC is thought to share epigenetic and genetic aetiologies with abnormal spermatogenesis, cryptorchidism and hypospadias, as part of a phenomenon named testicular dysgenesis syndrome.

The tumour secretes hormones that disrupts the local testicular hormone balance and the hypothalamic pituitary axis.

3. Treatment options can cause infertility.

Impairment is either temporary or permanent depending on the regimen.

PROBLEM STATEMENTS
- There is no way to predict the likelihood of patient azospermia at diagnosis, or after treatment.
- Only 24% of men with TC cryopreserve their sperm[4]; broaching fertility preservation needs more emphasis at diagnosis.

AIMS

1. To assess the frequency of spermatogenesis in testicular cancer
2. To assess the characteristics of spermatogenesis (focal/ widespread & frequency of sperm at different distances from tumour)
3. To determine whether the following parameters can predict spermatogenesis:
   a. Tumour characteristics (type, TNM stage, size of tumour)
   b. Presence of tumour microtheliasis (TML)
   c. Raised tumour markers
   d. Age

METHODS

Retrospective review of 103 germ cell tumour orchidectomy specimens, obtained between 2011-2015 at Guy’s Hospital, London, United Kingdom

Inclusion
- Consecutive series of all radical orchidectomy specimens at Guy’s Hospital between 2011-2016
- 418 years
- 106 cases

Exclusion
- Non-germ cell tumours = 2 cases
- No spermatogenesis information available = 1 case

Final cohort
- 103 patients (19-76 years; mean 37.1 years)
- 63 seminomas, 19 non-seminomas, 21 mixed tumours

Specimens assessed by expert pathologist (CH)
- Tumour type, testicle size, tumour stage, presence of spermatogenesis and TML determined
- Tumour and testicle size measured- the percentage of testicle tumour occupation (PTT) was calculated
- Other data from electronic patient notes and correspondence documents

Statistical analysis
- Logistic univariate and multivariate analysis with backward elimination
- Statistical significance p<0.05

RESULTS: AIMS

1. Spermatogenesis present in 70% (72/103)
2. Spermatogenesis widespread in 62% (45/72) and focal in 38% (27/72). Figure 2 summarises the frequency of sperm found at different distances from the tumour
3. On univariate analysis both PTT and age can predict the likelihood of the presence of spermatogenesis (Figures 5 & 6)
   a. Neither tumour type or stage;
   b. The presence of TML, nor
   c. Raised tumour markers were found to predict spermatogenesis on univariate or multivariate analysis

RESULTS: TUMOUR SIZE (PTTO) & AGE AS PREDICTORS OF SPERMATOGENESIS

- For every 1% increase in the PPTO, patients were 4% less likely to have spermatogenesis (OR: 0.96 95% CI: 0.95-0.98).
- Patients with PTT >50% were 81% less likely to have spermatogenesis than those with <50% (OR: 0.19 95% CI: 0.07-0.48).
- Men above >50 years have <50% chance of spermatogenesis

Figure 2. Diagram to represent occurrence of spermatogenesis within, next to or away from the tumour

Figure 4. Chart to show the frequency of spermatogenesis in men with differing percentage tumour occupation

Figure 5. Graph to show the percentage of spermatogenesis present with increasing age

RECOMMENDATIONS FOR PRACTICE

1. Broach fertility preservation at diagnosis. Aim for assessment of testicular function and semen analysis
2. Assess patients’ PTT at diagnosis to predict the likelihood of infertility in azospermia
3. Azoospermic patients with PTT >50% and or >60 years should be counselled on <50% chance of spermatogenesis (rule of 50s)
4. Since spermatogenesis is focal in 38%, an onco-micro-TESE technique is the optimum choice for surgical sperm retrieval in the azospermic patient with TC


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