

Wednesday 25 June 16.00–17.00

Poster Session 12: Andrology 2

Chairmen: T. Christmas and S. Wilson

P110

Molecular and cytogenetic characterisation of testicular cancer cell lines using 24-colour fluorescence *in situ* hybridization (FISH) and comparative genomic hybridization (CGH)-based microarrays

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INTRODUCTION

It has been estimated that 5–10 deletions of putative tumour suppressor genes are required before malignant transformation takes place, and that a variable degree of amplification in oncogenic material is required before metastatic potential is acquired. It is also possible that several chromosomal translocations act to form novel fusion genes, the significance of which has been shown clearly for CML. We used multiplex FISH and CGH-based microarrays to screen a series of 10 testicular cancer cell lines for aberrations in copy number of a series of 300 genes implicated in tumorigenesis, and to identify novel and recurrent chromosomal translocations which may have prognostic or diagnostic utility.

MATERIALS AND METHODS

A series of 10 testicular cell lines was acquired and cultured in RPMI with 10% fetal calf serum at 37°C. Metaphase spreads were

prepared by disrupting the spindle apparatus with colcemid, incubating cells in hypotonic KCl and fixing onto slides. The M-FISH probe and specimen were co-denatured and hybridised for 48 h. After counterstaining with DAPI, images were captured using a fluorescence microscope. DNA for microarray analysis was extracted according to manufacturers instructions. Sample and reference DNA was subjected to random primer labelling with Cy3 and Cy5 fluorophore, and co-hybridised onto arrays for 66 h. Images were captured using a Genocensor imaging station.

RESULTS

M-FISH analysis highlighted several novel chromosomal translocations. In addition to the isochromosome 12p [i(12p)] we identified several other novel recurrent translocations. The frequency with which these were detected suggest a potential role in the development or progression of germ cell

tumorigenesis. Breakpoint translocations have been FISH mapped and candidate genes identified. In addition, microarray analysis showed characteristic patterns of loss and gain of genes. The principle amplifications occur amongst genes on the short arm of chromosome 12. The amplification of KRAS2 oncogene was the most consistent and marked copy number change.

CONCLUSION

Microarray analysis reveals characteristic patterns of loss and gain of genes which are consistent across cell lines. As such they provide a genomic fingerprint of germ cell tumorigenesis which may be of prognostic or diagnostic significance. We also identified a series of novel and recurrent chromosomal translocations which, given their frequency, may be fundamental in either the initiation or progression of disease.

Funding: Orchid Cancer Appeal

P111

The role of retroperitoneal lymph node dissection in the management of stromal tumours of the testis

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INTRODUCTION

Although only 10% of testicular stromal tumours show malignant behaviour metastatic disease appears to be associated with a poor outcome. There is limited evidence to guide management. In this study the role of retroperitoneal lymph node dissection (RPLND) in managing both primary and metastatic stromal tumours of the testis is evaluated.

PATIENTS AND METHODS

We retrospectively reviewed 14 patients who underwent RPLND for Leydig/Sertoli cell

tumours of the testis between 1995 and 2002.

RESULTS

Nine patients had stage I disease and five had retroperitoneal masses on imaging, either at presentation (three) or during the follow-up (two). A median (range) of 8 (3–23) lymph nodes was resected. No pathological evidence of tumour was found in the nine patients with clinical stage I disease. At a median (range) follow-up of 7 (4–46) months these patients all remain disease-free. One of the five patients with retroperitoneal masses on imaging had only ganglion

tissue in the resected specimen. Of the four patients with metastatic disease in the RPLND specimen, three have recurrent extranodal disease and one has no evidence of recurrence, with a short follow-up of only 6 months.

CONCLUSION

Sertoli/Leydig tumours of the testis are potentially aggressive and biological behaviour is difficult to predict on clinical or pathological grounds. Resection of established metastatic disease does not appear to be curative. Early RPLND in patients with stage I disease should be considered.

P112

Incidence of second tumours in patients with testicular germ cell tumours on surveillance and after chemotherapy

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INTRODUCTION

An increased risk of second tumours after chemotherapy for testicular germ cell tumours (GCTs) is well documented. In this study the incidence of second tumours in patients managed by surveillance was examined.

PATIENTS AND METHODS

Data were collected prospectively from patients referred with testicular GCTs between 1978 and June 1997. The incidence of second tumours in patients managed by surveillance alone was compared with the incidence in patients receiving chemotherapy (cisplatin, vincristine, methotrexate,

bleomycin/etoposide, actinomycin-D, cyclophosphamide).

RESULTS

In all, 315 patients with stage I testicular GCTs were treated; 83 (26%) developed metastases and received chemotherapy or radiotherapy, 21 (7%) were lost to follow-up, 211 (67%) were assessable for second-tumour incidence on surveillance, and 18 (8.5%) developed a second tumour. Eleven patients (5.2%) had contralateral testicular GCTs and seven (3.3%) other primaries (three bladder, and one each stomach, oat cell, mycosis fungoides and basal cell carcinoma). During the same period, 298 patients with metastases were treated; 277 (93%) were assessable for second

tumours and 21 (7%) were lost to follow-up. Second tumours occurred in 23 patients (8%); three (1%) developed contralateral testicular tumours and 20 (7%) other primaries (four acute myeloid leukaemia, three renal, two each colon, stomach, melanoma, and one each lung, prostate, oesophagus, penis, bladder, glioma and lymphoma).

CONCLUSION

Patients with testicular GCTs may have a greater incidence of second tumours when managed by surveillance or chemotherapy. Effective chemotherapy appears to reduce the incidence of contralateral testicular tumours.

P113

Does the aetiology of obstructive azoospermia affect the outcome of intracytoplasmic sperm injection?

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*Assisted Conception Unit, Chelsea & Westminster Hospital, and *Charing Cross Hospital, London, UK***INTRODUCTION**

The aim of this study was to define whether the outcome of intracytoplasmic sperm injection (ICSI) using sperm surgically retrieved from men with obstructive azoospermia depends on the cause of the obstruction. We first analysed our data and then used a meta-analysis of published data (including ours) to compare the outcome of ICSI in obstructive azoospermia classified as congenital or acquired.

PATIENTS AND METHODS

Eighty-two couples underwent 127 ICSI cycles using surgically retrieved sperm. The cause was classified as congenital absence of

vas deferens (CBAVD) in 20, after vasectomy in 56, infective/inflammatory in 21, not infective in 24, and ejaculatory in five. Five reports (687 cycles) including ours were identified as suitable for meta-analysis.

RESULTS

Analysis of our data showed that fertilization (FR) and live birth rates (LBRs) were highest in men with previous vasectomy and non-infective causes (vasectomy 51%, LBR 23%; non-infective FR 53%, LBR 29%, respectively) and lowest in men with infective or inflammatory causes (LBR 6%). There was no difference in outcome if the sperm was fresh or frozen, or whether epididymal or testicular.

A meta-analysis comparing congenital (CBAVD) and acquired causes showed a significantly increased FR (95% CI 0.84–1) with acquired causes. A meta-analysis of three papers reporting the delivery outcome showed no difference in LBR but a significantly higher miscarriage rate in the congenital group (relative risk 2.67).

CONCLUSION

In ICSI cycles in men with obstructive azoospermia, the causes influences outcome, the FR is higher and miscarriage rate lower in acquired obstruction, and the outcome is not influenced if the retrieved sperm is fresh, frozen, epididymal or testicular.

P114

Clomifene: a new, noninvasive method of sperm retrieval for intracytoplasmic sperm injection in cases of unobstructive azoospermia – a multicentre study

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Clomifene (Clomid) is a well-established drug used empirically to treat idiopathic oligospermia. It increases endogenous GnRH secretion from the hypothalamus and gonadotrophin hormone secretion directly from the pituitary, thus increasing intratesticular testosterone concentration. Its benefits in the treatment of azoospermia have not been tested. With recent advances in assisted reproduction techniques, only one sperm is sufficient for fertilization with intracytoplasmic sperm injection (ICSI). The objective of this study is to determine if the application of Clomid in men with unobstructive azoospermia may result in sufficient sperm for ICSI.

PATIENTS AND METHODS

In this multicentre study, 42 patients with unobstructive azoospermia (age range 25–39 years) were evaluated with routine history, physical examination and hormonal assessment. Testicular biopsy showed maturation arrest in 43% and hypospermatogenesis in 57%. The Clomid dose was titrated to serum testosterone at 6–8 µg/L, and semen analysed at periodic intervals.

RESULTS

After Clomid therapy 64% of patients had a mean (range) sperm count on semen analysis of $3.8 (1-16) \times 10^6/\text{mL}$; 36% of the patients

remained azoospermic, but enough sperm was retrieved by testicular sperm extraction for successful ICSI.

CONCLUSION

Clomid can be used for treating unobstructive azoospermia. If the number of sperm produced is small it is valuable as a noninvasive method to obtain enough sperm for ICSI. Using a course of Clomid for patients with azoospermia it might be possible to avoid unnecessary invasive procedures for sperm retrieval for ICSI.

P115

Testicular arterial blood flow in normal and azoospermic menS.J. GORDON, S. CAMPBELL*, J. BHARDWA and V.H. NARGUND
*Homerton University Hospital, London, and *Create Health Clinic, UK***INTRODUCTION**

Spermatogenesis depends on adequate arterial blood flow to deliver nutritional and hormonal requirements to the testes. The quantitative determination of blood flow to the testes has recently become more reliably measurable with advances in ultrasound technology. In this study we analysed the Doppler blood flow variables of arteries within and around the testis, comparing men with normal spermatogenesis and azoospermia.

PATIENTS AND METHODS

Spermatogenic function was determined by semen analysis in conjunction with a clinical evaluation and serum hormonal profile.

Fourteen testes were included in the control group with normal spermatogenesis and 24 in patients with azoospermia in the second group. Colour Doppler ultrasonography was used in all subjects to measure arterial velocities at three predefined areas within the scrotum, termed suprastesticular, capsular and intratesticular. Blood flow was compared between the groups and statistical significance assessed using the Mann-Whitney *U*-test.

RESULTS

Patients with unobstructive azoospermia had a significantly lower testicular arterial velocity ($P < 0.01$) and higher impedance to flow than men with normal spermatogenesis. In

particular, the capsular and intratesticular arteries were very significantly different in velocity and waveform values ($P < 0.001$).

CONCLUSIONS

There was a strong correlation between testicular blood flow, as determined by colour Doppler ultrasonography, and spermatogenesis. Arteries running around but closely applied to the testis, termed capsular arteries, are readily recorded and recognizable. Capsular arteries also have the strongest association with spermatogenic function. This may provide a simple noninvasive test to differentiate between unobstructive and obstructive azoospermia.

P116

Early and late morbidity after vasectomy: a comparison of chronic scrotal pain at 1 and 10 years after surgeryR. MANIKANDAN, S.J. SRIRANGAM, E. PEARSON and G.N. COLLINS
*Stepping Hill Hospital, Stockport, Cheshire, UK***INTRODUCTION**

The prevalence and time of onset of chronic scrotal pain after vasectomy is not clearly defined. We therefore sought to evaluate this in two groups of patients at 1 and 10 years after surgery.

PATIENTS AND METHODS

In a retrospective questionnaire-based study two groups were compared; group A included 460 patients who underwent vasectomy 10 years ago (1991–92) and group B another 460 patients who had a vasectomy 1 year ago. Data were collected on immediate

complications, and the incidence and nature of scrotal pain. Pain severity was graded on a visual analogue scale and patients were also asked if they regretted undergoing vasectomy because of the pain.

RESULTS

In all, 182 replies (39.6%) were received in group A and 220 (47.8%) in group B. Early complications included haematoma (in five and two patients, respectively) and wound infection (24 and 17, respectively). In group A, 27 patients (14.8%) were still experiencing scrotal (testicular) pain, with eight (4.3%) describing a pain score of >5 . Three of the 27

regretted having a vasectomy because of pain. In group B, 42 patients (19%) reported persistent scrotal pain, with 13 (5.9%) having a score of >5 . Six of these 42 regretted having a vasectomy because of the pain. In groups A and B, 12% and 5% of patients, respectively, reported not being adequately counselled about the risk of developing chronic pain.

CONCLUSION

Scrotal (testicular) pain after vasectomy is a common long-term complication associated with significant distress. All patients requesting vasectomy must receive appropriate preoperative counselling.

P117

Pre- and intraoperative factors affecting the outcome of vasovasostomy and epididymovasostomy

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The outcome of microsurgical vasovasostomy and epididymovasostomy is variable because it is affected by many factors, some of which are well studied and others not. The objective of this study was to evaluate all the variables related to the patients and procedures, and define the pre- and intraoperative factors that affect the outcome.

PATIENTS AND METHODS

Thirty-six patients (age range 30–54 years) with obstructive azoospermia, treated with vasovasostomy and epididymovasostomy, were reviewed. The level of anastomosis (vasovasostomy, epididymovasostomy or vas-rete testis anastomosis) was based

on level at which sperm are detected in the vasal and epididymal fluid. Statistical analysis was used to evaluate the outcome.

RESULTS

The overall postoperative patency, defined as sperm on semen analysis, of microsurgical vaso-epididymal reconstruction procedures was 60%. The mean (SD) sperm count after surgery was 5.1 (8.7) million/mL and motility 25 (19.8)%. There was no correlation between the patency after surgery or sperm count and any of the variables related to the patients' history and physical examination. There was a significant correlation between the sperm count after surgery and the level of serum

FSH ($P < 0.05$). Also, there was no correlation between the patency or sperm count and the intraoperative findings. However, there was a significant correlation between the patency and the number of sutures used in the anastomosis ($P < 0.05$); the fewer sutures used the better the chance of patency.

CONCLUSION

Detecting sperm in the vasal or epididymal fluid is the key for a successful vaso-epididymal reconstruction. If the level of anastomosis is based on detecting sperm in the vasal and epididymal fluid, the outcome is unaffected by most of the variables related to the patient or to the technique of anastomosis.

P118

The management of epididymo-orchitis in younger men: could (older) urologists do better?

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*Urology Department, Stobhill Hospital, Springburn, and *Genitourinary Medicine Department, Sandyford Clinic, Glasgow, UK***INTRODUCTION**

Sexually transmitted disease (STD) is the commonest cause of acute epididymo-orchitis in men aged < 35 years. Investigations and treatment should be in accordance with this; it may be necessary to contact and treat sexual partners. As testicular torsion is the main differential diagnosis, these patients are often referred to urologists.

METHODS

A questionnaire posted to 240 BAUS members currently working in the UK described a hypothetical case of a 21-year-old man with epididymo-orchitis. Questions were asked

about the most likely pathogens, what investigations and treatment should be initiated, and whether referral to a genitourinary medicine (GUM) clinic would be arranged.

RESULTS

In all, 131 (55%) members replied; 31 of 35 (89%) specialist registrars correctly identified sexually transmitted pathogens as being the most likely cause of infection, against 57 of 85 (67%) consultants ($P < 0.05$), and 123 (94%) would commence empirical antibiotic therapy. Fifty-one different regimens were recorded, only half of which were appropriate; 62 (47%) would routinely refer to a GUM

clinic. Of the others, only 19 of 62 routinely investigated for STD, with 43 (33%) respondents doing neither.

CONCLUSIONS

Despite the existence of UK national guidelines for managing epididymo-orchitis, urologists vary in their approach to it in younger men. Significantly more consultants than their trainees seem not to appreciate the aetiological difference between this condition in the younger and older male population. These results also suggest that many urologists fail to investigate (or refer for investigation) for STD. This may be causing significant preventable morbidity.

P119

A randomized double-blind, cross-over, placebo-controlled trial of sildenafil in neurogenic female sexual dysfunction

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Patients with multiple sclerosis (MS) have a high prevalence of female sexual dysfunction (FSD). There is recent evidence of vaginal and clitoral expression of nitric oxide synthase and phosphodiesterase-5. For men with erectile failure caused by MS, sildenafil greatly improved their sexual function. We evaluated the safety and efficacy of sildenafil for treating FSD secondary to MS.

PATIENTS AND METHODS

Premenopausal women with MS and bothersome symptoms of FSD were recruited;

inclusion criteria included an active sexual relationship, normal oestrogen and androgen levels, and no significant medical or recent psychiatric history. Patients received sildenafil and placebo for each of 12 weeks, with a washout period of 2 weeks between. The starting dose of 50 mg could be changed to 25 or 100 mg after 2 weeks, depending on the response and tolerance. Assessment of response was based on a validated sexual function questionnaire and a quality of life questionnaire at 0, 6, 12, 18 and 24 weeks.

RESULTS

Nineteen women completed both arms of the trial. There was a statistically significant

improvement after sildenafil compared with placebo and baseline in the domains of sensation and lubrication ($P < 0.038$, paired t -test), but no apparent improvement in the capacity to reach orgasm, overall enjoyment, or quality of life.

CONCLUSION

The effects of sildenafil in patients with MS and FSD are to increase their lubrication and sensation, and thus it may have a role in treating certain symptoms of FSD.

Funding: Pfizer UK

P120

What is the relationship of sexual function in men with LUTS?

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There is considerable current interest in the relationship between LUTS and sexual function in men, and in particular whether there is a causative relationship between them. This observational study, performed in a single centre, seeks to explore this area further.

PATIENTS AND METHODS

In all, 1420 men attending a prostate assessment clinic were assessed by the IPSS, the BPH impact index (BPHII), urinary flow rate (Q_{max}), postvoid residual volume (PVR)

and the O'Leary sexual function questionnaire (which assesses erectile, ejaculatory and sexual drive). The results were analysed using Spearman rank correlation and logistic regression techniques.

RESULTS

After excluding those with incomplete data, those who were not sexually active, those with a PSA level of < 20 ng/mL and those who refused to complete the questionnaire, there were 696 evaluable patients. Age, IPSS, BPHII, Q_{max} and PVR all correlated with the overall sexual score, but of these only age, quality of

life and BPHII were independent predictors, while flow rate, IPSS and PVR were not. Analysis by sexual function domain again showed significant inter-relationships, e.g. age was associated with all domains, while IPSS was associated with erectile and ejaculatory dysfunction but not sexual drive.

CONCLUSION

This study confirms that a significant proportion of men with LUTS have sexual dysfunction. The relationship is complex and differs according to the type of sexual dysfunction.