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Comments and Critique

The Management of Seminoma

THERE HAVE been major advances in the development of management principles for non-seminomatous germ cell tumours (NSGCT) of the testis in the last 10 years. For understandable reasons, parallels have been drawn and attempts made to translate these principles to seminoma. It should come as no surprise that this has not always worked well for what is, typically, a different disease with distinct epidemiology, biology, pathology and clinical behaviour.

The management of stage I disease is a case in point. Stage I NSGCT is an almost ideal model for a surveillance policy following orchidectomy. It is associated with reliable tumour markers to facilitate early relapse detection, and the vast majority of recurrences occur in the first year, thus limiting the period during which intensive surveillance is required. It is relatively radioresistant and often disseminates via the blood stream, thus the practice of irradiating the para-aortic nodes failed to cure a significant proportion of cases. None of this is true of seminoma. It is not surprising, therefore, that surveillance has not caught on for stage I seminoma, despite some enthusiasm which followed its introduction in NSGCT [1, 2]. The only possible rationale for surveillance in seminoma is that the alternative (which, at present, is radiotherapy to the para-aortic nodes) means treating about 5 out of 6 cases unnecessarily. Substituting a short period of unnecessary treatment with a prolonged period of unnecessary investigation (surveillance) does not represent progress if the treatment is not hazardous. The evidence currently supports the view that 30 Gy in 15 fractions over 3 weeks to a 'dog-leg' field is effective and associated with a low level of late side-effects [3]. The current UK Medical Research Council randomised trial is comparing this with a smaller para-aortic strip field technique. Routine prophylactic mediastinal irradiation in stage II seminoma is no longer practised in most centres, and chemotherapy is generally employed in all cases of bulky (> 5 cm) stage II disease.

Cases of more advanced seminoma are rare in comparison with NSGCT and so experience of chemotherapy is less. However, it is becoming apparent that seminoma is more sensitive to chemotherapy than NSGCT, as well as being more radiosensitive. Recent reports of single-agent carboplatin highlight this suggestion [4, 5]. The 3-year failure-free survival was 74% in the UK study, and (after a median follow-up of 18 months) 64% in the Germany study. Given the clinical behaviour of seminoma, both reports must be regarded as early. Randomised trials are currently comparing carboplatin with cisplatin in combination as initial treatment for advanced seminoma. The fact that the vast majority of carboplatin failures in the studies quoted above were successfully rescued with cisplatin-based combination chemotherapy implies that carboplatin may turn out to be less effective as first treatment. Until the results of the trials are available, carboplatin must be regarded as experimental in advanced seminoma. Recommended standard treatments include bleomycin/etoposide/cisplatin [6] and cisplatin and etoposide without bleomycin 'EP' [7].

Attempts to draw parallels with NSGCT in the management of residual masses following chemotherapy in seminoma have also exemplified important differences between the two tumours. Standard practice in NSGCT is elective lymph node dissection for residual retroperitoneal masses. About 20% contain carcinoma and 40% contain differentiated teratoma. The patients are young and tolerate the procedure very well. In seminoma, the situation is quite different. Pronounced fibrotic changes make surgery much more difficult and complications more frequent, especially in the older patient population. The overall risk of having residual tumour appears to be about 12% only [8]. Although routine radiotherapy has been recommended for these residual masses [9], many patients would receive quite extensive unnecessary treatment and in others who have been treated with radiotherapy to the site in question previously, it would be inappropriate. Thus, others [10] prefer careful observation for 2 years, with frequent repeat CT scans, reserving radiotherapy or salvage chemotherapy for the minority who progress.

Our understanding of the efficacy of chemotherapy in seminoma is increasing slowly. On the other hand, we are rapidly learning how to minimise both short- and long-term toxicity from experience in NSGCT. As this trend continues, the consequences of giving chemotherapy to groups, many of whom can not benefit, are less important. Thus, Oliver *et al.* [11] have argued that the time is approaching when chemotherapy may be realistically tested in stage I seminoma. Chemotherapy will have to be extremely effective and with very minor short- and long-term side-effects to supplant radiotherapy in this setting. They have been using carboplatin as a single agent for two courses. The published experience in advanced disease so far gives cause for concern that this may not be good enough.

The ultimate aim should be to show that a management policy is so effective that, once treated, patients can be discharged from follow-up immediately. Not only can one then avoid the patient anxiety generated by regular follow-up, but the more successful a treatment becomes, the less cost-effective it is to try to detect the ever smaller number of cases who will relapse.

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1. Thomas GM, Sturgeon JF, Alison R, *et al.* A study of post-orchidectomy surveillance in stage I testicular seminoma. *J Urol* 1989, **142**, 313–316.

2. Duchesne G, Horwich A, Dearnaley DP, *et al.* Orchidectomy alone for stage I seminoma of the testis. *Cancer* 1990, **65**, 1115–1118.
3. Fossa SD, Aass N, Kaalhus O. Radiotherapy for testicular seminoma stage I: treatment results and long term post-irradiation morbidity in 365 patients. *Int J Radiat Oncol Biol Phys* 1989, **16**, 383–388.
4. Schmoll HJ, Bokemeyer C, Harstrick A, *et al.* Single agent carboplatin (CBDCA) for advanced seminoma: a phase II study (abstr). *Proc Am Soc Clin Oncol* 1991, **10**, 181.
5. Horwich A, Dearnaley D, Mason M, A'Hearn R. Single agent carboplatin for advanced seminoma. *Proc Am Soc Clin Oncol* 1991, **10**, 172 (abstract).
6. Williams SD, Roth BJ, Chemotherapy of testis cancer: a review. *Int J Radiat Oncol Biol Phys* 1991, **22**, 213–217.
7. Dirix LY, Van Oosterom AT. Chemotherapy in metastatic seminoma. In Horwich A, ed. *Testicular Cancer: Investigation and Management*. London, Chapman and Hall Medical, 1991.
8. Thomas G. Management of metastatic seminoma: Role of radiotherapy. In Horwich A, ed. *Testicular Cancer: Investigation and Management*. London, Chapman and Hall Medical, 1991.
9. Fossa SD, Borge L, Aass N, Johannesen NB, Stenwig AE, Kaalhus O. The treatment of advanced metastatic seminoma: Experience in 55 cases. *J Clin Oncol* 1987, **5**, 1071–1077.
10. Schultz SM, Einhorn LH, Conces DJ Jr, Williams SD, Loehrer PJ. Management of postchemotherapy residual mass in patients with advanced seminoma: Indiana University experience. *J Clin Oncol* 1989, **10**, 1497–1503.
11. Oliver RTD, Lore S, Ong J. Alternatives to radiotherapy in the management of seminoma. *Br J Urol* 1990, **65**, 61–67.

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Screening for Colorectal Cancer

AFTER CARCINOMA of the bronchus, colorectal cancer kills more people than any other malignancy in the developed Western world. Currently, more than 24 000 new cases and 17 000 deaths from the disease are being reported in England and Wales annually [1]. Prognosis is largely determined by the extent of spread of the disease at presentation, corrected 5-year survival figures of 30–40% reflecting that the majority of patients still present with lymph node or distant metastases [2]. Slight improvements in survival have been matched by an increasing incidence of the disease in Great Britain so that death rates have changed little for 40 years. Public health measures to reduce disease incidence require a greater understanding of aetiological (probably largely dietary) factors as well as a willingness by the population to accept changes in lifestyle. They are unlikely to have any impact for decades. While recent reports of perioperative radiotherapy and chemotherapy are encouraging for Dukes' B and C tumours, currently the most promising potential method for improving disease prognosis would seem to be screening for asymptomatic early stage disease.

The basis for screening relates to the biology and natural history of the disease. There is widely accepted evidence that most colorectal cancers slowly develop in stepwise fashion from normal mucosa through enlarging adenomatous polyps to localised surgically curable malignancy, eventually culminating in disseminated incurable disease [3, 4].

The process of screening aims to preferentially detect large adenomas and early cancers by the investigation of certain asymptomatic individuals selected from a large population by a positive screening test, their treatment leading to both a reduction in mortality from colorectal cancer as well as a decrease in its incidence.

The incidence of colorectal cancer increases exponentially with age, those over 50 years old making up only 37% of the population yet accounting for 95% of cases and more than 96% of deaths [1]. To be cost-effective, screening needs to be applied to this older age group (average risk) unless other risk factors for colorectal cancer apply. Of particular interest among high-risk groups are those with genetically determined cancer. The recognition of phenotypic markers (hypertrophy of the retinal pigment epithelium and mandibular osteoma) for familial adenomatous polyposis (FAP) as well as the recent availability of linked DNA markers has allowed for greatly improved prediction of level of risk for family members. However, this condition represents only 1% of all colorectal cancer cases. A recent endoscopic study of 640 relatives of 34 patients with sporadic colorectal neoplasia suggests that 19% of all colorectal neoplasias might be genetically determined [5]. It may be that appropriate genetic markers, determined from a simple blood test, will be able to stratify a population at average risk into those with a particularly high risk who could be offered screening and those at lower risk where risk outweighs benefit. The principle of stratifying broad risk groups is illustrated by a longitudinal study of 1618 patients with rectosigmoid adenomas followed for a mean of 14 years—those with tubular adenomas < 1 cm (43% of the series) were found to be at no increased risk of subsequent colon cancer in contrast to those with larger, more villous polyps [6].

A screening test should be inexpensive, rapid and simple and is not intended to be diagnostic, those with positive tests requiring further evaluation. The use of symptom questionnaires is ineffective because colorectal symptoms are common and poorly predictive and because the presence of symptoms may signify more advanced disease. Digital rectal examination will detect no more than 10% of cancers while rigid sigmoidoscopy will adequately visualise only the distal 16 cm [7] allowing detection of, at most, 40% of all colorectal cancers. The method is further disadvantaged by the fact that it is unpleasant and inconvenient. However, an uncontrolled study of 26 000 subjects undergoing rigid sigmoidoscopy found 58 cancers, 81% of which had no evidence of lymph node or distant metastasis, with 90% 15-year survival [8]. Furthermore, a recent case–control study of the efficacy of screening sigmoidoscopy in the setting of regular health checks has shown a significant 70% reduction in death from rectosigmoid (but not colon) cancer [9]. Following a simple enema, fibreoptic flexible sigmoidoscopy (FOS) allows

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