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Stage I Testicular Seminoma Following Orchidectomy—to Treat or Not to Treat

G.K. Zagars

ADJUVANT POSTORCHIDECTOMY radiation has been standard care for stage I seminoma since the early decades of this century [1, 2] and a wealth of experience shows this policy to be effective and safe [3]. In bygone days when there was no curative alternative to radiotherapy, faith in radiographic retroperitoneal staging procedures was never sufficient to risk disease progression by withholding radiotherapy from patients with stage I disease. And, since the morbidity of retroperitoneal lymph node dissection contra-indicated its use in this disease, the true incidence of micrometastatic nodal involvement in stage I was never elucidated. Thus, it was uncertain what proportion of patients actually benefited from adjuvant irradiation. Now, with the additional armamentarium of effective chemotherapy [4, 5], surveillance has emerged as an investigational possibility and several preliminary studies have been reported [6–8]. In this issue of the *European Journal of Cancer* (pp. 1931–1934), the report by von der Maase *et al.* is the first such study, substantial both in the number of patients and in their follow-up, to afford a reliable appraisal of the virtues and limitations of surveillance as a management policy and to provide insights into the pathobiology of this disease.

Whereas pathological findings in the primary tumours have little prognostic significance for patients receiving adjuvant radiotherapy, they assume some importance if treatment is withheld. Von der Maase *et al.* delineate tumour size, histological subtype, tumour necrosis and invasion of the *rete* as significant determinants of metastatic propensity. In multivariate analysis, tumour size was the only feature independently correlated with disease relapse. Patients whose primary tumour was 6 cm or larger (25% of all) had a relapse frequency of 34%, compared with a frequency of 14% in those with smaller tumours. Indirect confirmatory evidence that certain features of the primary tumour are indeed markers of biological aggression comes from studies that show a higher incidence of larger tumours [9], more frequent *rete* and cord invasion [9, 10] and a higher incidence of vascular invasion [9] in stage II than in stage I seminoma. Unpublished data in the University of Texas M.D. Anderson Cancer Center database reveal that the primary tumour was significantly larger in stage II disease (21 patients, size range 2–19 cm, mean size 7.1 cm, median size 6.5 cm) than in stage I disease (137 patients, size range 1–12.5 cm, mean size 4.9 cm, median size 4.4 cm) ($P = 0.001$). This supports the conclusion of von der Maase *et al.* that larger tumours are more likely to have metastasised than smaller ones. However, the authors make no mention of spermatic cord invasion, which we reported to occur more often in stage II than in stage I disease, and to have an adverse effect on the outcome of irradiated patients with stage I disease [10]. It is hoped that this factor, as well as data on pre- and postorchidectomy chorionic gonadotrophin levels will be addressed in forthcoming publications. The practical implications of all this relate to the TNM (tumour, nodes, metastases) staging of this disease. Currently, the staging of seminoma is largely N-based [11]. With increasing use of surveillance for no disease, particularly if patients are selected for this on the basis of putatively favourable T factors, a uniformly accepted T system will need to be developed. Whether tumour size alone, as suggested by von der Maase *et al.*, is adequate, remains uncertain.

Where does surveillance stand as a management option for stage I seminoma? The data provided by von der Maase *et al.* and by others [6–8] establish that surveillance offers a safe alternative to radiotherapy whenever the latter poses significant risks, such as might occur in patients with horseshoe or pelvic kidneys. However, the routine practice of surveillance poses significant problems, some highlighted by von der Maase *et al.* It is now clear that there is a significant incidence of micrometastatic disease in stage I seminoma and that routine radiotherapy substantially eradicates this. Three recent series on a total of 474 patients receiving postorchidectomy radiotherapy reported that only 8 (1.7%) relapsed [10, 12, 13]. This contrasts with the 19% relapse rate under surveillance. Adjuvant radiotherapy affords a better than 10-fold reduction in disease relapse, and concerns that the potential benefits of irradiation in this stage of disease are minimal can be laid to rest. On the other hand, the virtues of any adjuvant treatment cannot be judged solely by disease-free rates. The fact that survival rates are similar for radiation and surveillance (seminoma-specific mortality $< 2\%$) weakens disease-based arguments for adjuvant treatment. Issues of quality of life then assume importance in weighing one approach against the other. Despite decades of observation, there is no convincing evidence that routine postorchidectomy radiation to doses of 25 Gy produces any significant long-term sequelae [3]. Moreover, the initial evaluation and the subsequent follow-up of irradiated patients are simple, cost-effective and free of major stress [3]. In contrast, both the initial work-up and the protocol for surveillance are complex, labour-intensive, stressful and not uniformly amenable to optimal execution. Patients are not always compliant and a significant proportion (in this study, one-third of those who relapsed) are found to have bulky disease at relapse and require chemotherapy. Although disparate quality of life endpoints are difficult to judge, it does appear that patients under surveillance undergo more stress than those receiving irradiation. A prospective quality of life study would best address these issues. The limitations of surveillance are implied by the author's recommendation to observe those with tumours < 6 cm, but to irradiate patients with primary tumours ≥ 6 cm in size, since one third of the latter developed relapse. However, this is not a devastatingly high failure rate and given the high salvage of relapsing disease, one would have expected a more enthusiastic embracement of surveillance. I would rephrase the common argument against adjuvant radiotherapy by asking, "Why be willing to submit 100 patients to the rigours of surveillance to

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benefit 14 and yet be unwilling to do the same for another 100 to benefit 34?"

Despite, and indeed because of, the excellent report by von der Maase *et al.*, I believe that routine postorchidectomy radiation remains the treatment of choice for stage I seminoma. Effective surveillance awaits the discovery of a sensitive and specific serum market for this disease.

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Primary Gastric Non-Hodgkin's Lymphoma: a Therapeutic Challenge

A. Rossi and T.A. Lister

THE STOMACH is the single commonest site of extranodal lymphoma, and this is being diagnosed with increasing frequency. Despite this, and a multitude of papers on the subject, there remain many controversial aspects to be addressed.

WHICH DEFINITION?

Different criteria are followed in the literature. Some, as defined by Dawson [1], are very strict, aiming at being as accurate as possible in establishing the gastric origin of the lymphoma. Whilst pursuing a laudable objective, it is very likely that this underestimates the true incidence, inevitably excluding cases in which there has been 'spread' away from the stomach. Others, recently more widely accepted [2, 3], allow the inclusion of cases in which the stomach is most probably the site of origin, despite limited or extensive dissemination within the abdominal cavity. This approach carries the potential risk of including nodal lymphoma which has spread to the stomach, but almost certainly gives a better picture of the problem.

WHICH HISTOLOGY?

Histological classifications for primary gastric lymphoma have been derived in the past from those in use for nodal counterparts. There is increasing agreement that a separate classification is required reflecting the peculiarity of the gastrointestinal tract. General accord seems to exist on the classification of Isaacson [4], including the MALToma concept as a distinct entity (Table 1). Still a matter of debate is the percentage of primary gastric lymphomas that histologically correspond to those arising in the lymph nodes, as opposed to those of MALT type; according to recent papers less than 50% of primary gastric lymphomas are of MALT origin [5, 6]. The two groups probably behave differently, possibly requiring different therapeutic approaches. Furthermore, it is not yet clear whether high grade MALT lymphoma should be treated differently from low grade.

The acceptance of a single classification will allow comparison

Table 1.

B cell
Lymphomas of mucosa-associated lymphoid tissue (MALT)
— Low grade B cell lymphoma of MALT
— High grade B cell lymphoma of MALT, with or without evidence of a low grade component
— Mediterranean lymphoma (immunoproliferative, small intestinal disease), low grade, mixed or high grade
Malignant lymphoma, centrocytic
Burkitt-like lymphoma
Other types of low or high grade lymphoma corresponding to peripheral lymph node equivalents
T cell
Enteropathy-associated T cell lymphoma (EATL)
Other types not associated with enteropathy

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