Eur J Cancer, Vol. 28A, No. 11, pp. 1851–1852, 1992.
Printed in Great Britain

0964–1947/92 $5.00 + 0.00

Infradiaphragmatic Hodgkin's Disease

M.D. Mason, M. Law, S. Ashley, J. Nichols, M. Brada, M.J. Peckham and A. Horwich

INTRODUCTION

THE RARITY of infradiaphragmatic Hodgkin's disease (IHD) is striking. Despite the fact that the infradiaphragmatic regions harbour a huge proportion of the body's lymphoid tissue, IHD as a presenting feature accounts for no more than around 10% of all patients with Hodgkin's disease [1–6]. Can IHD be considered to be a distinct disease type? The purpose of this short review is to present the Royal Marsden Hospital experience with IHD, to compare our experience with that reported by other centres in the literature and to judge whether the clinical behaviour of IHD does indeed justify viewing it as a separate entity.

Between 1963 and 1987 the Lymphoma Unit at the Royal Marsden Hospital saw 540 patients with clinical stages (CS) I and II supradiaphragmatic Hodgkin's disease. During the same time interval, the unit saw only 53 patients with CS I and II IHD. Evaluating these patients is difficult, not only because of their relative rarity, but also because this time period saw enormous advances in imaging techniques, the introduction and later evaluation of staging laparotomy, and great changes in treatment philosophy particularly with the introduction of effective combination chemotherapy [7]. Perhaps we can do no more than to define the questions to be answered over the coming decades.

EPIDEMIOLOGY

The age-specific incidence curve of Hodgkin's disease shows a striking bimodal peak [8]. It has been suggested previously [1] that patients with IHD tend to be older than average. However, the median age of our patients at presentation was 37 years, which is almost identical to the mean age of CS I and II patients in the EORTC database [6]. While the patient numbers in the present series are too small for definitive conclusions to be drawn, our experience is compatible with the view that patients with IHD might be represented by the same typical age-specific incidence curve as seen in supradiaphragmatic Hodgkin's disease.

On the other hand, the male preponderance in patients with IHD asserted in the literature [1–4,6, 9] does appear to be substantiated by the present series in which 45 patients were male and only 8 female. Why this should be so is mysterious.

HISTOLOGY

It is intriguing that lymphocyte predominant histology appears to be more common than expected in IHD [6]. In the present series 17 out of 53 patients had lymphocyte predominant disease, and of those patients with CS I disease, the typical picture (seen in 7 out of 11 patients) was of inguinal lymphadenopathy and lymphocyte predominance. Lymphocyte depletion is correspondingly uncommon, and was seen in only one patient in the present series. Whether it is IHD that is remarkable, or whether it is mediastinal Hodgkin's disease with its preponderance of nodular sclerosis that accounts for a difference in histological subtypes across the diaphragm is unclear. In the present series, histology on 14 patients was classified as nodular sclerosing, and 17 mixed cellularity.

THE ROLE OF STAGING LAPAROTOMY

21 of the patients in this series underwent a staging laparotomy as part of their planned management. 5 of these patients had previously been clinically evaluated as having stage I disease and it was noteworthy that none of these patients had their staging altered as a result of laparotomy. By contrast, 11 out of 16 (69%) patients who were CS II prior to laparotomy had a greater extent of disease demonstrated as a result of their surgery. Of these patients 7 (44%) had demonstratable splenic involvement.

It is hard, therefore, to recommend the routine use of staging laparotomy in CS I patients on the basis of this small series, and this would accord with the experience in other centres as reviewed by Krikorian *et al.* [1]. It is difficult to know whether there is a role for staging laparotomy in CS II patients, but given the extent to which these patients are upstaged by surgical staging, there may be some justification for more aggressive therapy from the outset, without the use of staging laparotomy.

DISTRIBUTION OF DISEASE

It was striking that 91% of our patients had disease in the inguino-femoral region as part of their original sites of disease and that this was the mode of presentation in the majority of these patients. Disease in the pelvis and para-aortic region was seen in 43 and 59% of patients, respectively, while splenic disease was demonstrated in 27%, a figure which is likely to be an underestimate because not all patients underwent pathological staging. All patients with splenic involvement also had para-aortic disease, and one might predict that in patients clinically staged alone, the presence of para-aortic disease would imply a substantial likelihood of splenic involvement.

CLINICAL STAGE AT PRESENTATION

In terms of the stage of disease assessed purely clinically (ignoring the results of subsequent pathological staging), the distribution in this series appeared to be broadly similar to that seen in series of supradiaphragmatic disease. As elsewhere, CS Ib is an uncommon presentation accounting for only 1 patient in this series. 10 patients had clinical stage Ia, 26 patients had CS IIa, and 16 patients CS IIb. All of the patients with CS I disease presented with peripheral lymphadenopathy in the groin, and as mentioned earlier, most of these patients had lymphocyte predominant histology.

Correspondence to M.D. Mason.
The authors are at the Lymphoma Unit, The Royal Marsden Hospital, Sutton, Surrey, U.K.
Received 22 Apr. 1992; accepted 30 Apr. 1992.

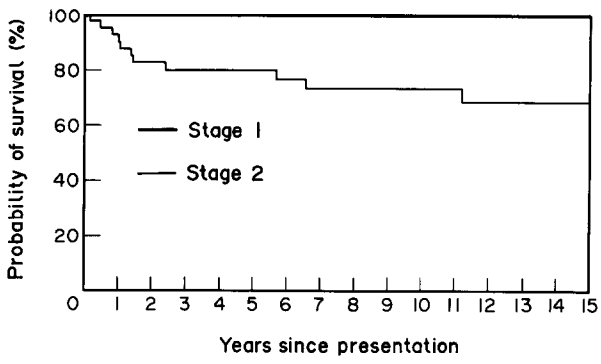

Fig. 1. Infradiaphragmatic Hodgkin's disease. Time to death from Hodgkin's disease by clinical stage.

ASSESSMENT OF THE RESULTS OF TREATMENT FOR IHD

In the present series 32 patients were treated with radiotherapy alone, 8 patients with chemotherapy alone and 13 with combined modality therapy, i.e. radiotherapy plus chemotherapy. All patients with CS I disease were treated initially with radiotherapy. This comprised involved field radiation to the ipsilateral groin in 1 patient, but in all remaining patients inverted Y radiotherapy was performed.

The crude relapse rate after radiotherapy for CS I patients was 27% (3 out of 11). By contrast, in clinical stage II patients 43% (9 out of 21) relapsed when treated with radiotherapy alone as initial treatment. This contrasted with a relapse rate of only 23% (3 out of 13) when radiotherapy was combined with chemotherapy for CS II patients. As with supradiaphragmatic disease, the crucial question is whether it is possible to salvage such radiotherapy failures. The acturial survival of patients with IHD is shown in Fig. 1, broken down according to CS I or CS II patients. In CS I patients the cause-specific survival at 15 years was 100%, and it is difficult, therefore, to fault a policy of clinical staging followed by inverted Y radiotherapy for this group of patients. The actuarial survival figures for CS II disease appear to be broadly similar to those seen in series of supradiaphragmatic Hodgkin's disease: as in supradiaphragmatic disease it seems reasonable to hope that salvage chemotherapy would not compromise the overall survival of these patients. However, other series have also cast doubt on the adequacy of radiotherapy alone in CS II patients [1]. The crude relapse rate in the small group of 8 patients treated with chemotherapy alone was 75% (6 out of 8), but 4 of the patients in this group never entered complete remission and it is likely that this figure is an artefact of patient selection within a small group.

CONCLUSIONS

Our data lend weight to the contention that infradiaphragmatic Hodgkin's disease as an entity is distinct in certain respects to supradiaphragmatic disease. So far we have no explanation for its rarity, or the apparent predominance of males among those affected. It is difficult to draw specific treatment recommendation from such a small group of patients and in the future it will be necessary to combine data from other centres in order to attempt to make firm recommendations. For the present it appears that a policy of clinical staging and inverted Y radiotherapy is reasonable for CS I disease, while for CS II disease, most radiotherapists would feel that a relapse rate of 43% was excessive. We would suggest that such a patient, particularly if they had para-aortic node involvement, be considered for combined modality therapy from the outset.

1. Kirkorian JG, Portlock CS, Mauch P. Hodgkin's disease presenting below the diaphragm: a review. *J Clin Oncol* 1986, **4**, 1551–1562.
2. Cuomini L, Magrini S, Mungai V, Biti GP, Ponticelli P. Stage I and II Hodgkin's disease presenting in infradiaphragmatic nodes. *Tumori* 1982, **68**, 519–525.
3. Doreen MS,Wrigley PFM, Jones AE, *et al.* The management of localized, infradiaphragmatic Hodgkin's disease: experience of a rare clinical presentation at St. Bartholomew's Hospital (Abstract) 1984, Second International Conference on Malignant Lymphoma.
4. Krikorian JC, Portlock CS, Rosenburg SA, Kaplan HS. Hodgkin's disease stages I and II occuring below the diaphragm. *Cancer* 1979, **43**, 1866–1871.
5. Sutcliffe SB, Gospodarowicz MK, Bergsagel DE, *et al.* Prognostic groups for management of localized Hodgkin's disease. *J Clin Oncol* 1985, **3**, 393–401.
6. Henry-Amar M, Aeppli DM, Anderson J, *et al.* Workshop statistical report. In *Treatment Strategy in Hodgkin's Disease.* Colloque Inserm/John Libbey Eurotext, Vol. 196, 1990, 169–428.
7. DeVita VT, Serpick AA, Camrone PP. Combination chemotherapy in the treatment of advanced Hodgkin's disease. *Ann Intern Med* 1970, **73**, 881–895.
8. Mueller NE. In Selby P, McElwain T, eds. *Hodgkin's Disease.* Oxford, Blackwell Scientific Publications, 1987, 68–93.
9. Barrett A, Gregor A, McElwain TJ, *et al.* Infradiaphragmatic presentation of Hodgkin's disease. *Clin Radiol* 1981, **32**, 221–224.