

Mediastinal Involvement in Early-Stage Hodgkin's Disease.

Response to Treatment and Pattern of Relapse

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Abstract—*The surface areas of enlarged mediastinal lymph nodes involved by Hodgkin's disease were measured from pre-treatment chest radiographs in 54 patients with stage I and II disease. Employing an arbitrary subdivision of 100 cm², patients were divided into two categories, those with small volume mediastinal lymphoma (≤ 100 cm²) and those with large volume disease (> 100 cm²). Of 19 patients in the latter category, 18 (94.7%) had nodular sclerosing Hodgkin's disease. The mediastinal recurrence rate following radiotherapy was significantly different in the two groups. Thus, of patients with small volume tumour, 5/35 (14%) relapsed compared with 10/19 (53%) of those with large masses.*

Since 1974 combination chemotherapy has been employed electively prior to irradiation for patients with large mediastinal masses. Of 16 assessable patients managed in this way 12 are disease free at 4-60 months (median 24). Radiation therapy as initial management should be avoided in the early stage patient with bulky mediastinal disease and chemotherapy employed initially to secure bulk reduction and facilitate subsequent radical irradiation.

INTRODUCTION

RADIOTHERAPY is regarded as the treatment of choice for stage I and II Hodgkin's disease. However, within these staging categories patients at high risk of relapse can be identified prospectively and treated with combined chemotherapy and radiotherapy. These subgroups include patients with multiple nodal areas involved above the diaphragm [1], those with lymphocyte depleted histology, and patients with large volume mediastinal adenopathy. In the latter group radiotherapy is technically difficult because of the large treatment volume and hence the risk of lung damage. The usually slow rate of progression of nodular sclerosis (the histology generally associated with this presentation) necessitates protraction of treatment with consequent reduction in biological effect [2]. In order to define more precisely the role of radiotherapy in the control of mediastinal Hodgkin's disease a group of patients with radiological evi-

dence of mediastinal node involvement at presentation has been investigated retrospectively in detail.

MATERIALS AND METHODS

Patients

A group of 54 patients with stage I and II Hodgkin's disease treated with radiotherapy alone between 1963 and 1977 and diagnosed as having mediastinal involvement at presentation was selected for study. Only those patients treated after 1970 were pathologically staged but since this study was directed primarily towards local control of mediastinal disease, staging methodology was considered unlikely to influence our findings. A separate group of 16 patients with large volume mediastinal disease treated between 1974 and 1978 by combination chemotherapy followed by radiotherapy was also studied with regard to control of local disease and disease free survival.

Measurements of the mediastinal masses were taken from standard P.A. chest radiographs all performed at the Royal Marsden Hospital using a similar technique, before any

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treatment was given. Because of the irregularity of these masses, a planimeter was used to measure the surface area. An arbitrary upper limit was taken at the lower border of the clavicles and a lower limit at the bottom of the visible mass. A mediastinal mass with a surface area (S) of ≥ 100 cm or a surface area/thoracic diameter (TD) ratio of ≥ 3 was arbitrarily defined as 'small' and those where S was > 100 cm or S/TD > 3 as 'large'.

Patients were treated with ^{60}Co or a 6 or 8 MeV linear accelerator using standard mantle fields. Treatment to infradiaphragmatic nodes was either by a para-aortic strip or an inverted Y. All patients received mid-plane doses of 33–45 Gy to the mediastinum in 3.5–6 weeks treating 5 times weekly. Doses to the supraclavicular fossae ranged from 40 to 45 Gy and doses to the axilla were approximately 5% lower than this. From 1974 patients with large mediastinal masses were treated electively with six courses of chlorambucil, vinblastine, procarbazine and prednisone followed by irradiation [3]. Because of the variation in follow-up times, survival has been calculated using the life table method.

RESULTS

Volume of mediastinal disease and histology

Figure 1 shows mass size in relation to histological sub-type. It is seen that out of 19 large masses as defined above, 18 were associated with nodular sclerosis.

Survival by volume of mediastinal disease

As shown in Fig. 2, there is a significant difference in disease free survival between patients with small and large volume disease. All patients in the latter category treated with radiotherapy alone relapsed (Fig. 3).

Associated lymph node involvement

Ninety-five per cent of patients had associated lower cervical node involvement and 20% axillary node involvement. As previously noted the presence of more than three nodal areas involved above the diaphragm was an adverse prognostic sign. Thus whereas 54% in this category relapsed only 19% of patients with less than three nodal areas involved relapsed.

Pattern of relapse and mediastinal mass size

Figure 4 shows the pattern of relapse ac-

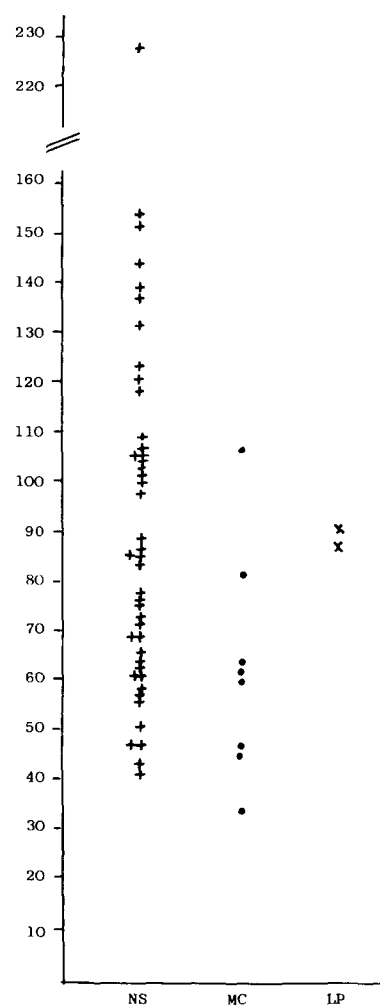


Fig. 1. Mass size in relation to histological sub-type.

cording to mass size. In patients with masses of area less than 100 cm, only 14% (5/35) recurred within the mediastinum compared with 53% (10/19) of those patients with large mediastinal masses. For patients treated by radiotherapy alone, relapses outside the irradiated area were commoner but carried a better prognosis than those within the field as they were often 'rescued' with subsequent chemotherapy. Seven patients relapsed in the lung, three with and four without mediastinal relapse. All initially had large mediastinal masses.

Chemotherapy and large volume mediastinal disease

Patients who were treated electively from 1974 to 1978 with combination chemotherapy before irradiation were studied separately. All patients had large mediastinal masses as defined above. Of 16 assessable patients 12 are alive and disease free at times from 4 to 60 months (median 24 months). Four patients have died. In one patient control was

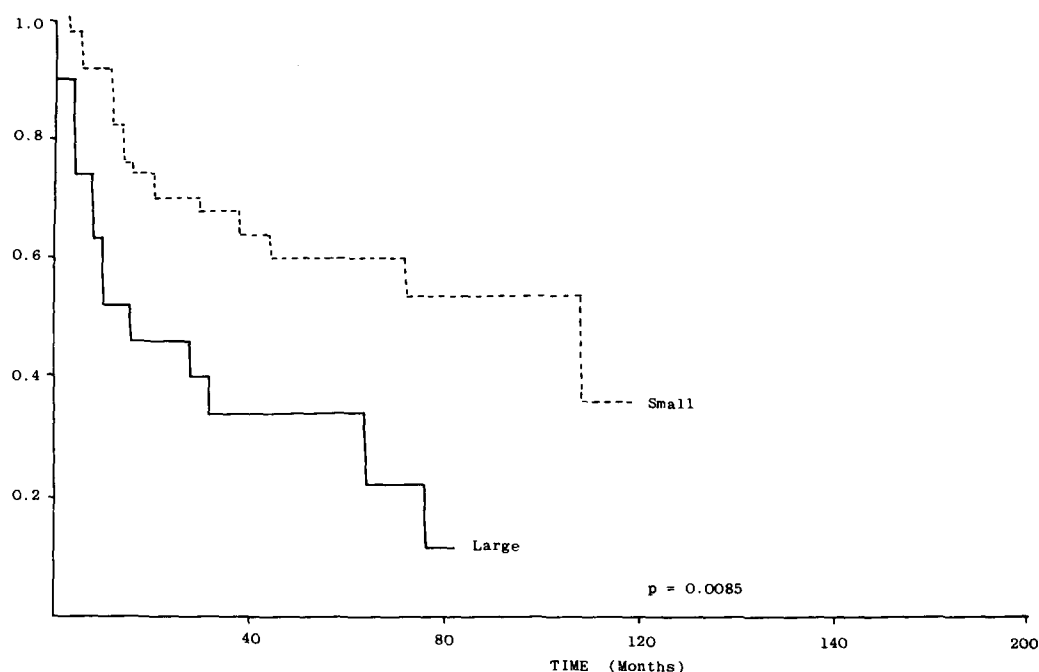


Fig. 2. Probability of disease free survival according to size of mediastinal mass.

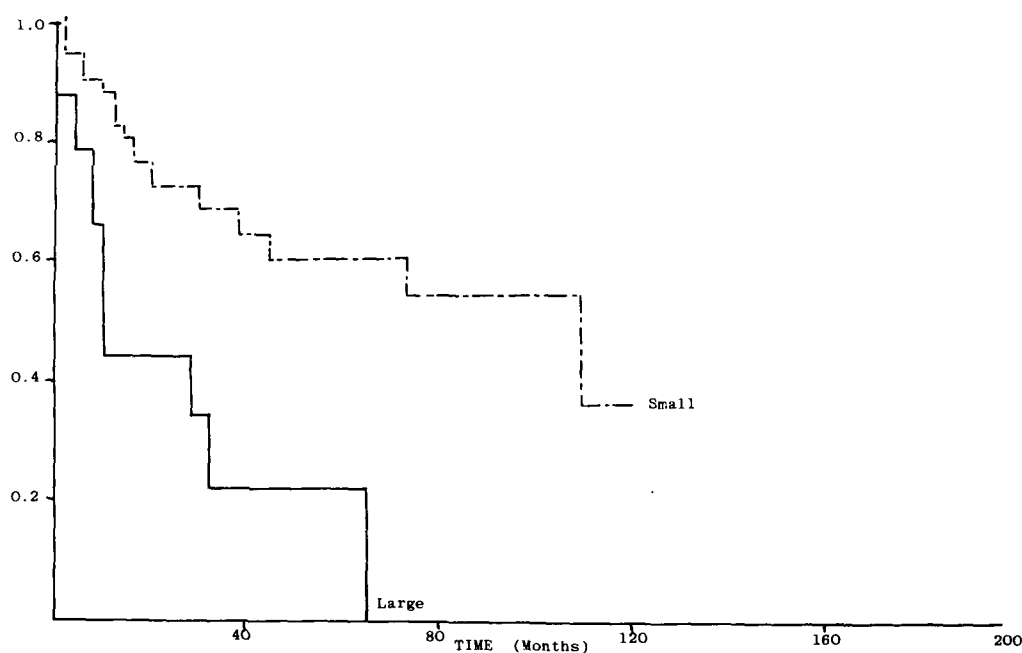


Fig. 3. Probability of disease free survival according to size of mediastinal mass (radiotherapy alone).

achieved for 15 months but his disease then relapsed within the mediastinum and he died 24 months later after further unsuccessful chemotherapy. In the other three patients local control was never achieved and they died at 11, 11 and 14 months, respectively.

DISCUSSION

It is clear that patients with large mediastinal masses treated with radiotherapy alone do badly and that the size of the mass has

prognostic significance. Thar *et al.* [4] who reported on 51 patients with stage I and II Hodgkin's disease record no failure to control disease if the mediastinal mass was less than 6 cm, but relapses in 7/29 patients where the mass was more than 6 cm.

Levi *et al.* [5] reporting on 111 stage I-III A patients, found the commonest relapse pattern to be marginal recurrence within mediastinal nodes or adjacent lung parenchyma. Extranodal lung extension and large mediastinal masses at presentation were pre-

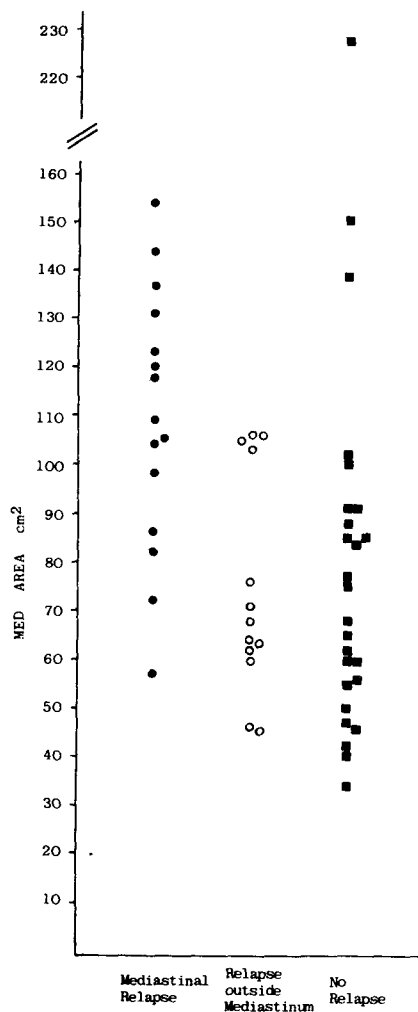


Fig. 4. Pattern of relapse according to mass size.

disposing factors and 86% of these relapses were in patients treated with radiotherapy alone. The size of the mediastinal mass was again of prognostic significance.

Mauch *et al.* [6] have recently reviewed the literature concerning the influence of mediastinal involvement on relapse and survival and have reported their own series of patients with large mediastinal masses. They conclude that if disease measures more than one third of the thoracic diameter, there is a significantly increased incidence of relapse both in the mediastinum and in nodal sites outside the thoracic cavity. They advocate a similar treatment policy to that employed in the present series; that is, chemotherapy as initial treatment followed by irradiation for patients with bulky disease.

Our preliminary results suggest that patients treated by sequential drug-radiation therapy for large volume mediastinal Hodgkin's disease, are doing better than those treated by radiotherapy alone, with a disease free survival at 1 yr of 75% and 2 yr of 63.5%. However, a small proportion of patients with massive disease still presents a serious therapeutic problem as shown by our patients who failed to respond to chemotherapy. A staging system for Hodgkin's disease which takes only site of disease and number of sites involved into consideration is likely to be less predictive of outcome than one which includes bulk as a factor.

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