

Endolymphatic Radiotherapy in Malignant Lymphomas Its Potential "Prophylactic" Value in Cases with Negative Lymphograms

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Summary

From 1961 to 1969 426 patients (208 with Hodgkin's disease and 218 with non-Hodgkin's lymphoma) underwent endolymphatic radiotherapy with Lipiodol ^{131}I at the National Cancer Institute of Milano. For this study, only those patients with stage I, II or III disease (with or without systemic symptoms), who were not previously treated, and who had a complete follow-up were reviewed. It appears that while in the cases where there is lymphographic evidence of involved lymph nodes, endolymphatic radiotherapy is not of value, in the cases with apparently negative lymphography, endolymphatic radiotherapy can reduce the incidence of relapse in the inguino-retroperitoneal nodes to a statistically significant degree.

From 1961 to 1969, 426 patients (208 with Hodgkin's disease and 218 with non-Hodgkin's lymphoma) underwent endolymphatic radiotherapy (E.R.T.) with Lipiodol ^{131}I at the National Cancer Institute of Milano (1-7).

The purpose of this report is to evaluate the loco-regional effect of E.R.T. on the inguino-iliac-paraaortic lymph node chains (Fig. 1, 2).

For this study, only those patients with stage I, II or III disease (with or without systemic symptoms), who were not previously treated, and who had a follow-up of at least 2.6 years for Hodgkin's disease and 2.0 years for non-Hodgkin's lymphoma, were reviewed. One hundred and seventy (106 with Hodgkin's disease and 64 with non-Hodgkin's lymphoma) of the 426 patients fulfilled these criteria.

These patients were monitored at 2 month intervals with careful clinical and radiological examinations, to evaluate both the general course of the disease as well as its evolution in the inguino-retroperitoneal nodes which had been treated with E.R.T. For this report, only relapsing disease (recurrence or extension) in these lymph nodes was considered as significant, regardless of the possible evolution of disease at other sites or the survival of the patient.

The results obtained in this group of patients were compared with another group of patients whose only significant difference was that they underwent a diagnostic lymphogram rather than E.R.T. Of 511 such patients (238 with Hodgkin's disease and 273 with non-Hodgkin's lymphoma) there were 155 (77 and respectively 78) who met the same criteria regarding stage of disease, lack of prior therapy and length of follow-up.

The two groups of patients were sufficiently homogeneous so as to permit comparison among the different case series. However, it should be noted that whether or not E.R.T. was used, was not determined in a random fashion, but rather was chosen for selected patients. Various other treatment modalities were also employed in both groups, depending upon the stage of disease or simply according to the involvement of the retroperitoneal nodes, such as chemotherapy (CT), external beam radiotherapy (RT) or both. The different combinations of therapy in the two groups of patients are outlined in Table 1.

In this period of time, RT was given with TCT, treating only the involved regions (not with upper or lower mantle fields). CT usually employed a single agent. Treatment was the same in the two groups of patients under investigation

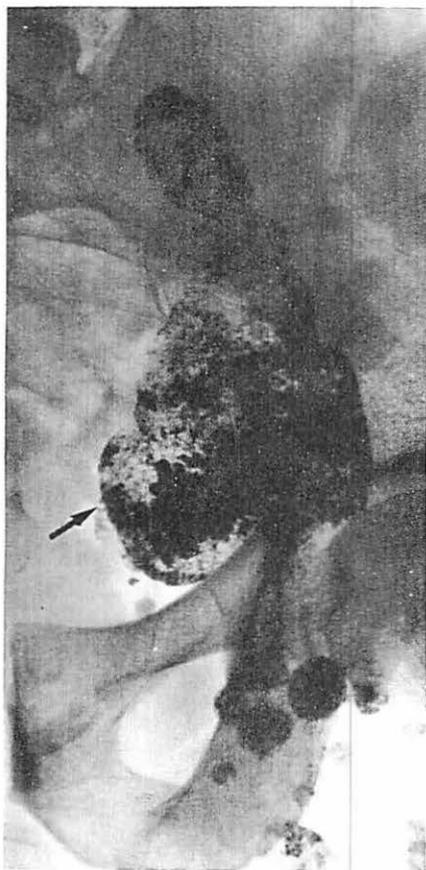


Fig. 1a M.S. male, 32a. non-HD Lymphoma Diffuse Lymphocytic Poorly Differentiated Stage III A Initial radiographic evaluation after ERT (25 mCi for each foot).



Fig. 1b Same case. Follow up film after 21 days.

Table 1 Types of treatment in the group on study and in the control group

Therapy	Hodgkin's disease	non-Hodgkin's lymphomas
I^{131}	20/106	12/64
I^{131} + RT	14/106	7/64
I^{131} + CT	31/106	29/64
I^{131} + RT + CT	41/106	16/64
Total group on study	106	64
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F	20/77	18/78
F + RT	10/77	9/78
F + CT	20/77	28/78
F+RT+CT	27/77	23/78
Total control group	77	78

F = Diagnostic lymphography
 I^{131} = Therapeutic lymphography
 RT = Radiotherapy
 CT = Chemotherapy



Fig. 2a D.S. male, 29a. non-HD Lymphoma Nodular Histiocytic Well Differentiated stage II B. Initial evaluation after ERT (same doses).



Fig. 2b Same case. Follow up film after 35 days.

The technique for E.R.T. was the same of diagnostic lymphography: doses injected were ranging from 40-50 mCi of ^{131}I for each patient. Physical properties of Lipiodol ^{131}I , body distribution, side effects and complications are extensively treated in the R.R.C.R. Monograph n. 37 (4).

Results

In Table 2 are the results of those patients whose inguino-iliac-para aortic lymph nodes were treated only with ^{131}I , in comparison with its control group who received no subdiaphragmatic therapy. There is no evidence of any difference in the relapse rate in this region in the two groups.

Table 3 shows the results of those patients whose nodes were treated with ^{131}I as well as external beam radiotherapy (RT) in comparison with its control group who received subdiaphragmatic RT. Once again, E.R.T. does not appear to alter the relapse rate.

In Table 4 are tabulated the results of those patients treated with E.R.T and CT, in comparison with its control group who received CT alone. In these patients with negative lymphograms there appears to be some beneficial effect of E.R.T. on the relapse rate, while their time of appearance is similar.

Table 2A Hodgkin's disease

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131}	20	+ 1 - 19	0 1	2.5
F	20	+ 0 - 20	0 0	

Table 2B Lymphocytic and Histiocytic Lymphomas

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131}	12	+ 2 - 10	1 0	0.6
F	18	+ 0 - 18	0 0	

Lymphography + = pathological lymphography

Lymphography - = negative lymphography

Table 3A Hodgkin's disease

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + RT	14	+ 9 - 5	2 0	0.10
F + RT	10	+ 6 - 4	2 0	1.10

Table 3B Lymphocytic and Histiocytic Lymphomas

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + RT	7	+ 4 -	0 0	
F + RT	9	+ 6 - 3	1 0	0.6

In Table 5 are the patients treated with I^{131} I, RT and CT in the inguino-retroperitoneal nodes, in comparison with its control group who received subdiaphragmatic RT and general CT. In those patients with negative lymphograms there is noted a beneficial effect of E.R.T., with no instance of relapse in treated nodes as compared to its control groups which manifested relapse in these sites.

In Table 6 are reported the results of all patients who received E.R.T. compared to those who did not, regardless of the various other types of additional therapy employed (i.e. none, RT, CT or RT + CT). In those patients with a positive lymphogram no significant difference is noted in the relapse rate in those nodes. However, in these with negative lymphograms a significant decrease in the relapse rate is noted in patients receiving E.R.T. (from 22% to 9% in Hodgkin's disease and 25% to 6% in non-Hodgkin's lymphomas). No significant difference in the relapse-free interval was noted.

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Table 4A Hodgkin's disease

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + CT	31	+ 10	6	1.6
		- 21	4	1.8
F + CT	20	+ 3	1	2.6
		- 17	8	1.7

Table 4B Lymphocytic and Histiocytic Lymphomas

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + CT	29	+ 12	10	1.0
		- 17	2	0.5
F + CT	28	+ 12	12	0.9
		- 16	8	0.5

Table 5A Hodgkin's disease

Therapy	No. cases	Lymphography	Unfavourable Cases No.	Time of appearance (median in years)
I^{131} RT + CT	41	+ 31	12	1.9
		- 10	0	
F + RT + CT	27	+ 18	9	0.1
		- 9	3	1.8

Table 5B Lymphocytic and Histiocytic Lymphomas

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} RT + CT	16	+ 14	3	1.4
		- 2	0	
F + RT + CT	23	+ 16	4	1.0
		- 7	3	1.6

Discussion

It must once again be noted that this is a retrospective study and that the patients were not randomly assigned to the group receiving E.R.T. A potential bias due to selection of patients could be present and therefore might prejudice the results. With that potential limitations, the following observations can be made.

From the data presented, it would appear that E.R.T. has no usefulness in patients with positive lymphogram, since there was no difference in relapse rates in the inguino-retroperitoneal nodes between the two groups of patients. Of interest, however, are the data obtained from the cases with negative lymphograms. Table 7 tabulates all cases with negative lymphograms, comparing the group which received E.R.T. with the control group which did not, unresponsive of the varying additional therapeutic modalities employed (i.e., none, RT, CT or RT + CT). The relapse rate in the opacified abdominal nodes in the group receiving E.R.T. was 8%, compared to a relapse rate of 23% in its control group ($P < 0.005$).

When the lymphogram was negative, there was no difference between the relapse rates in cases treated only with E.R.T., and in those whose inguino-retroperitoneal nodes were untreated.

Table 6A Hodgkin's disease

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + RT and/or CT	106	+ 51 - 55	20 5	1.8 1.1
F + RT and/or CT	77	+ 27 - 50	12 11	1.2 1.8

Table 6B Lymphocytic and Histiocytic Lymphomas

Therapy	No. cases	Lymphography	Unfavourable cases No.	Time of appearance (median in years)
I^{131} + RT and/or CT	64	+ 32 - 32	14 2	1.0 0.5
F + RT and/or CT	78	+ 34 - 44	17 11	0.1 0.1

Table 7 Hodgkin's disease and non-Hodgkin's lymphomas

Evaluation of Cases with Negative Lymphography

Therapy	No. cases	Unfavourable cases No.	%	Time of appearance (median in years)
I^{131} + RT and/or CT	87	7	8	1.5
F + RT and/or CT	94	22	23	1.3

This may be explained if the radiologic diagnosis in cases with normal lymphography was always correct and furthermore, if the disease had always been favourably controlled in the supradiaphragmatic involved sites. However, another possibility is that the opacified nodes were so minimally involved with tumor as to be radiologically undetectable but nevertheless controlled by the E.R.T.

There was a moderate benefit in cases with negative lymphography who were treated with chemotherapy, with or without R.T (Table 4-5). In this group, the utilization of C.T. was usually prompted by the presence of extensive disease above the diaphragm, or of systemic symptoms, or both.

In these cases a "prophylactic effect" of I^{131} on the inguino-iliac-para-aortic lymph nodes, which were radiologically not involved, can be seen.

In conclusion, from a series of cases followed for a sufficient period of time, it appears that while in the cases where there is lymphographic evidence of involved lymph nodes, E.R.T. is not of value, in the cases with apparently negative lymphography, E.R.T. can reduce the incidence of relapse in the inguino-retroperitoneal nodes to a statistically significant degree.

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Bilateral Chylothorax — Complication in Malignancy

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Summary

Bilateral chylothorax is a rare condition caused by traumas and disorders with perforation or destruction of main lymphatics in the thorax leading to lymph leakage. Two patients with bilateral chylothorax are presented one of whom was successfully operated on. Etiology, diagnostics and therapy of this condition are discussed.

Leakage of lymph to the pleura, chylothorax, is a very uncommon form of pleural effusion but merits attention on account of the diagnostic and therapeutic peculiarities. The condition is generally elicited by trauma, injuries in the lower part of the thorax usually leading to right-sided chylothorax, injuries in the upper part to left-sided (1). Another fairly common cause is tumour, the effusion arising from obstruction and/or erosion of the thoracic duct (2). Occasional cases have been reported of ruptured cysts or lymphangioma in the thoracic duct, as well as specific infections such as tuberculosis and filariasis (3). As a rule the effusion is unilateral. Only a few cases have been published with bilateral chylothorax.

Several surveys have been made of case reports. Reviewing the literature up to the mid-1950s, *Nix et al.* (4) found 479 cases of chylothorax but only 155 satisfied their criteria; of these, 32 were combined with chyloperitoneum. In the period 1945-65 *Kuntz* (5) found 300 cases, 19 of them bilateral. Six of them had been caused by occlusion of the thoracic duct as a result of neurinoma (1 case), polyserositis tuberculosa (1 case), pleural endothelioma (1 case), lymphogranulomatosis (2 cases) and reticulum-cell sarcoma (1 case); the last of these also had chyloperitoneum. The material of *Nix et al.* (4) included 8 cases of unspecified malignancy with uni- or bi-lateral chylothorax.