

TREATMENT OF ADVANCED LUNG CANCER BY EXTERNAL BEAM RADIOTHERAPY AND HIGH DOSE RATE (HDR) BRACHYTHERAPY

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ABSTRACT:

Purpose: Brachytherapy is a highly valued and effective palliative treatment for lung cancer, especially as it reduces intensity of dyspnoea and other symptoms arising from tumours inside the respiratory tract. In some cases, due to the location of the lesion brachytherapy is a treatment of choice. However, its curative role is unclear. A combination treatment of brachytherapy and an external beam irradiation may play a significant role when the mediastinal lymph nodes are involved.

The paper presents the results of treatment of advanced lung cancer patients by external beam irradiation and brachytherapy, and the role of this palliative treatment is discussed.

Material and methods: Between May 1999 and March 2000 at the Greatpoland Cancer Centre fifteen patients with advanced lung cancer were treated by HDR brachytherapy and palliative external beam irradiation using the method of hypofractionation. The patients' age ranged between 39 to 80 years, mean: 54.3 years. The treatment consisted of external beam irradiation (total dose of 20-30 Gy), and a weekly high dose rate (HDR) brachytherapy (three fractions of 7.5 or 10 Gy, at 1 cm from the source). In three cases the treatment was started with external irradiation, whereas in 12 cases the first stage was brachytherapy. During the patients' clinical and endobronchial follow-up of 1, 3 and 6 months, local remission and regression of difficulties in breathing, cough, pain and haemoptysis were assessed.

Results: In all our patients subjective improvement (regression of all symptoms) was found on the first check-up following treatment. In one case complete remission of the tumour lasted for over 6 months, in 9 cases partial remission and in two cases progression were found. Severe complications due to the high total local dose were not observed.

Conclusions: Combined palliative treatment (intraluminal brachytherapy and external beam irradiation) in advanced lung cancer was an efficient method that led to regression of symptoms and improvement of well-being in many patients.

Key words: lung cancer, teletherapy, brachytherapy.

INTRODUCTION

In the palliative treatment for lung cancer brachytherapy is one of the effective methods of controlling dyspnoea caused by obturation. Due to the location of the lesion inside the bronchial tubes, the degree of clinical advancement, and patients' general condition, in some patients brachytherapy is a treatment of choice, which, when carried out on an out-patient basis, takes a short time and leads to a small

number of early complications [1,2,3,4,5,6,7,8].

Indications for palliative brachytherapy include: local relapse following earlier teletherapy, patients with non-small-cell lung cancer accompanied by intense symptoms, mostly dyspnoea caused by obturation of the bronchial tree. The contraindications include: lesion located in the peripheral part of the lung, Pancoast's tumour, superior vein caval syndrome, and massive haemoptysis.

A combination treatment of teletherapy and brachytherapy may be applied using radical doses, and aims at curing the patient (brachytherapy administered to increase the dose within the tumour). It may also be administered for palliative purposes: teletherapy employed to reduce the lymph nodes compressing the bronchi from the outside, or to restore the patency of the bronchi. A combined radiotherapy makes it possible to increase the dose at the vicinity of the tumour over a relatively short period of time. Moreover, the main cause of ineffective teletherapy is due to the lack of local cure, which provides an additional reason why both the above mentioned modalities should be used in combination. [9,10,11,12].

Radical combined therapy has been a subject of many clinical studies since in a number of papers no significant increase in the patients' survival rate as compared with teletherapy used alone has been reported. However, the available data indicate that the incidence of local recoveries is high [2,8,9]. What is also important is that radical therapy may be applied in only a small number of patients as the progress of the disease in most patients is usually highly advanced.

The aim of the present work is a preliminary assessment of the efficiency of a combined palliative therapy for advanced non-small-cell lung cancer.

MATERIAL AND METHODS

Palliative combined teletherapy and brachytherapy was applied in patients who were not qualified for radical radiotherapy on the grounds of the advanced stage of the disease, as well as in those with impaired patency of the respiratory tract and the presence of lymph nodes in the mediastinum. The therapy was conditioned on the degree of efficiency higher than 50 (according to the Karnofsky score) and the presence of the tumour verified by histologically accessible endobronchoscopy.

Between May 1999 and March 2000 15 patients with lung cancer were treated at the Great Poland Cancer Centre using HDR brachytherapy in combination with

palliative teletherapy employing the method of hypofractionation. The patient's age ranged between 39 and 80 years, mean: 54.3 years. In the group of patients under study were 12 men and 3 women, squamous-cell carcinoma being detected histologically in 11 cases and adenocarcinoma in four cases.

(A) Brachytherapy

Following pre-medication one or two endobronchial catheters were placed in the bronchi, verified radiologically. In the treatment 10 Ci of Iridium-192 was applied using an HDR-GAMMAMED 12i unit. To calculate the dose distribution an ABACUS computer programme was employed. Three fractions of 7.5 Gy were administered in 9 patients, and three fractions of 10 Gy were given to 6 patients, at 1 cm from the applicator's axis. A higher fractionated dose was used in patients with the tumour obturating the bronchi by more than 50%. The irradiation (the area within the treatment dose) covered the site of the visible tumour and the fragment of the bronchi 2 cm distally and proximally from the tumour. The treatment was applied at one-week intervals.

(B) Teletherapy

The mediastinum was irradiated from two opposite fields by photons of 9 MV or gamma rays (Co-60) using the method of hypofractionated doses: 5 x 4 Gy/ week or 10 x 3 Gy/week to the total dose of 20 (30) Gy. Due to the availability of the necessary therapeutic equipment, in three patients the treatment was started with teletherapy, whereas in 12 patients it was initiated with HDR brachytherapy. The interval between teletherapy and brachytherapy was on the average 4 weeks. In one case, three months later, a single additional dose of 10 Gy was given caused by the sudden recurrence of intense dyspnoea.

The patients were followed-up clinically, radiologically and bronchoscopically for 1, 2, 3 and 6 months by assessing local remission, regression of dyspnoea, cough and haemoptysis.

RESULTS

The patients tolerated the combination therapy successfully and showed no complications. After the termination of the treatment subjective improvement (regression of dyspnoea, cough, pain and haemoptysis) was found in all patients, including three patients who registered complete remission (CR) and 12 patients who showed partial remission (PR) verified on endobronchoscopic and radiological examination (Table 1). Regression of dyspnoea, cough, haemoptysis, pain and atelectasis was confirmed in 15/15, 10/15, 6/8, 7/10 and 5/7 patients, respectively. Atelectasis partly regressed in two cases. The localization of the tumour did not have any

significant effect on the efficiency of the treatment.

The sequence of the treatment (brachytherapy or teletherapy) did not have any significant effect on the results (Table 2).

During the 6-month follow-up no effect of the dose (within specified limits) and that of the treatment sequence on the regression outcome of complaints was detected. In one case complete remission lasted more than 6 months, and in two cases consecutive examinations revealed progression of the disease (Table 2). During the 6-month follow-up three patients died, two in the second month and one in the third month). One of them died of a cardiovascular disease, and in the case of two others no information was available.

Table 1. Clinical and bronchoscopic assessment according to selected clinical features.

Clinical features	N=	After 4 weeks		After 2 months	After 3 months	After 6 months
		CR	PR			
1/ Patient's age:						
less than 54,3 years	9	2	7	7	6	6
more than 54,3 years	6	1	5	6	4	4
2/ Symptoms:						
- dyspnoea,	15	15		13	10	9
- cough,	15	10	5	11	8	7
- haemoptysis,	8	6	2	6	6	6
- pain,	10	7	3	8	7	7
- atelectasis	7	5	2	6	5	5
3/ Bronchoscopic examination:						
a/ tumour localization:						
- trachea,	2	1	1	2	1	1
- trachea + primary bronchus,	4	0	4	3	1	1
- left primary bronchus,	2	1	1	1	1	1
- right primary bronchus,	5	1	4	5	5	5
- lobar bronchus	2	0	2	2	2	2
b/ diameter of the stenosis:						
< 1/3	2	1	1	2	2	2
1/3 – 2/3	6	2	4	6	5	5
> 2/3	4	0	4	3	3	3
complete	3	0	1	2	0	0
Total:		3/15 20,0%	12/15 80,0%	13/15 86,7%	10/15 66,7%	10/15 66,7%

N – number of patients

CR – complete remission

PR – partial remission

Table 2. Clinical and bronchoscopic assessment according to the method of treatment.

Method of treatment	N=	After 4 weeks		Follow - up		
		CR	PR	2 months	3 months	6 months
1/ tele (20Gy) + 3 x 7,5 Gy	1	0	1	0	0	0
2/ tele (20Gy) + 3 x 10 Gy	2	0	2	2	2	2
3/ 3 x 7,5 Gy + tele (20 Gy)	7	2	5	6	5	5
4/ 3 x 7,5 Gy + tele (30 Gy) + 10 Gy	1	0	1	1	1	1
5/ 3 x 10 Gy + tele (20,30 Gy)	4	1	3	4	2	2

N – number of patients

CR –complete remission

PR –partial remission

tele – teletherapy with higher fractional doses

DISCUSSION

There is a large number of reports on the efficiency of palliative teletherapy for the advanced lung cancer (grade IIIA-B) applied separately. In this group of patients the mean survival time does not exceed 7 to 10 months. These definitely poor results of treatment have provided the rationale for seeking new methods of dose fractionation and ways of combining radiation therapy with chemotherapy, and recently with brachytherapy [9,13,14].

There have been reports of cases of long survival times in patients with locally advanced lung cancer treated radically with a combined therapy of brachytherapy and teletherapy [10,12,15], however the number of such cases is very small. The combination therapy is thought to increase the distant survival rate, although there is a lack of randomized studies to corroborate this hypothesis. Most reports have been concerned with radical combination treatment of the oesophageal lung (stage I and II) [5,7,12,16].

More knowledge has been gained on palliative treatment. The technique of palliative irradiation aims at neutralising the symptoms such as dyspnoea, cough, haemoptysis, and thus at improving the patient's well-being. In most patients brachytherapy applied separately makes it possible to reduce the intensity of the above symptoms [17,18,19,20,21]. There is, however,

a group of patients with advanced oesophageal cancer who may benefit from the combined therapy of brachytherapy and palliative teletherapy. In these patients, dyspnoea is caused not only by the intra-bronchial tumour, but also by the presence of lymph nodes exerting external pressure (compression) on the bronchi. Teletherapy aims at reducing those lymph nodes exerting external pressure on the bronchus, whereas teletherapy helps to restore patency of the bronchus. By combining the above two methods of palliative radiation therapy the dose delivered to the tumour's vicinity can be increased over a relatively short time and the local control improved [10,11,12,14].

The fraction of positive responses to treatment, according to many authors, ranges between 80% and 90% of the patients treated, in most cases ending with complete remission [22,23]. The situation seems to be unclear concerning the dose recommended in brachytherapy. The doses exceeding 10 Gy at 1 cm distance from the catheter's axis lead to the increase in the number of positive responses, however the number of cases with complications, mostly haemoptysis, also increases [25,22,24]. This is the reason why, in the treatment of our patients, we used single doses of 7.5 Gy or 10 Gy, like most of other authors [1,4,5,6,7].

One report provides an analysis of 406 patients who had undergone bra-

chytherapy [24], 324 of which were treated with brachytherapy alone, 65 patients received brachytherapy following teletherapy, and 17 were subjected to an alternate combined treatment. Single doses of 15 Gy, 20 Gy and 10 Gy were administered in 79.6%, 18.5% and 1.9% of all cases, respectively. The most common complication was aggravation of cough in the 2nd and 3rd week after the termination of the treatment. The multifactorial statistical analysis showed that the most important risk factors of acute complications were: increase in the dose to 20 Gy, earlier coagulation with lasers, and second application of brachytherapy. In 65% of cases, control examination revealed complete remission.

[8] made a comparative analysis of retrospective results in a group of patients treated palliatively by brachytherapy alone (3 x 7.5 Gy) and a group of patients additionally treated by teletherapy up to the dose of 37.5 Gy in 15 fractions. The first group registered decrease in dyspnoea (48%), cough (57%) and haemoptysis (97%). However, no difference was found in the outcome of the treatment between the above two groups.

[14] have presented the results of a prospective randomized study of 95 patients with advanced lung cancer. The patients were divided in two groups: the first group was treated by teletherapy alone, and the other underwent combined treatment (teletherapy and brachytherapy). In brachytherapy the dose employed was 7.5 Gy in two fractions, whereas teletherapy used a dose of 30 Gy or 60 Gy. Significantly better effects of treatment (regression of dyspnoea lasting more than three months) were obtained in the group treated by the combination method. However, the patients in this group had the tumour localized in the primary bronchus.

Our results of treatment are similar to those described by other authors [8,9,10,12]. Periodically recurrent regression of dyspnoea was found in all patients. In some cases the improvement occurred within a few hours after the termination of brachytherapy. Regression of dyspnoea was associated with less intense cough, smaller haemoptosis, lower pain in the mediastinum or fewer symptoms of atelectasis.

Six months later subjective and broncoscopic improvement continued in two-thirds of all patients.

The short follow-up in our patients does not make it possible to assess the survival time, however regression of clinical symptoms and improvement in the patients' well-being constitute the best evidence of the efficiency of the treatment in our group of patients.

The complication most commonly occurring within the period of 6 months after the termination of the treatment, as described in the literature, is that of haemoptosis of various intensity and the post-radiation inflammation. Most common late complication is that of bronchial stenosis [26]. Complications are found more frequently after earlier laser coagulation of the tumour inside the bronchus. We have not observed any acute after-treatment complications in our group of patients.

CONCLUSIONS

1. Combined treatment (HDR brachytherapy and hypofractionated teletherapy) of advanced lung cancer may be recommended in cases of intrabronchial tumour associated with mediastinal lymph nodes exerting pressure on the bronchi.
2. In 66.7% of cases treated by the combination therapy regression of dyspnoea and improvement in well-being lasting more than 6 months were obtained.
3. A high local total dose did not affect the frequency of complications.

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