
PALLIATIVE TREATMENT OF ADVANCED LUNG CANCER WITH RADIOTHERAPY AND THAI HERBAL MEDICINE AS SUPPORTIVE REMEDY

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ABSTRACT

OBJECTIVE: To evaluate the supportive effect of Thai herbal medicine, Vilac Plus (G716/45) on standard palliative radiotherapy in advanced stage IIIB-IV lung cancer compare with historic control from the literature reports.

PATIENTS AND METHODS: Thirteen patients in advanced lung cancer stage IIIB-IV with poor performance status were treated by palliative radiotherapy in adjuvant with the Thai herbal tonic solution (Vilac Plus G716/45)

RESULTS: Thirteen patients (8 male, 5 female) in advanced stages lung cancer with poor performance status, stage IIIB 11 cases, stage IV 2 cases. Median age 66 years (range 44.4-83 years). The pathological diagnosis were 5 cases of squamous cell carcinoma, 2 cases of adenocarcinoma, 1 case of bronchioalveolar carcinoma, 1 case of mixed squamous and adenocarcinoma and 4 cases of clinically advanced lung cancer as evidenced by computed tomography chest scan/chest X-ray. The results of treatment 4-6 weeks after radiotherapy revealed 76.92% (10/13 cases) of clinically improvement and 23.08% (3/13 cases) of clinically stable. Overall response rate was 46.15% (6/13 cases) of partial response and 53.85% (7/13 cases) had shown stable diseases. Patterns of failure were found to be locally progressing 46.15% (6/13 cases) at the primary site, 30.77% (4/13 cases) at the locoregional, 23.08% (3/13 cases) at the locoregional with distant metastases. Median follow-up time is 18 months (range 7-50 months). Clinical benefit rate, evaluated at ≤ 15 months was 72.72%. However the median survival period analysis required longer follow-up and more detail assessment.

CONCLUSION: The results of this study are promising in the aspect of good quality of life and preferable because of the cost effectiveness to be used as an adjuvant for radiotherapy.

Key words: advanced lung cancer, palliative radiotherapy, Thai herbal medicine

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INTRODUCTION

Advanced non small cell lung cancer has been recognized to have very poor prognosis in spite of multimodality treatment. In advanced lung cancer, palliative radiotherapy alone or in combination with the appropriated combination of chemotherapeutic agents are the available method of treatment with not fully satisfactory results especially in solid tumors. The disadvantages of chemotherapeutic agents are not only, several side effects, poorly response of the tumors, both the primary and secondary but also the cost of the drugs are very expensive. The other modality may be using oral epidermal growth factor receptor (EGFR) inhibitors which have demonstrated antitumor activity in advanced non small cell lung cancer without the serious side effects. Both of these agents are very expensive, therefore can not be accessible by the low socioeconomic group of patients. Based on this rationale, the Thai herbal medicine as another choice for supportive to the standard palliative radiotherapy are used in this study. The Thai herbal medicine (Vilac Plus) has been proven to have no acute oral toxicity in animal study.¹ No traces of prednisolone and dexametasone were detected.² An In Vitro study, the Vilac Plus presents an important antioxidant capacity.³ The recipe of the ingredients of the Thai herbal tonic solution consisting of three edible herbs, the whole part of mushroom namely *Ganoderma Lucidum*, *Houttuynia Cordata* Thunb (leaves) and the roots of *Boesenbergia Rotunda* Holtt (Kra chai), all of them were found to be an effective anti-tumor promoting agents.^{4,5} The procedure of this project has been approved by the Committee of Khon Kaen University Human Ethics (HE 480745).

OBJECTIVE

To evaluate the supportive effect of Thai herbal medicine, Vilac Plus on standard palliative radiotherapy compare with historic control from the literature reports in stage IIIB-IV lung cancer.

PATIENTS AND METHODS

This study is performed at the radiotherapy division, department of radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002. During the period of March 2003 to June 2005, thirteen patients in advanced lung cancer stage IIIB-IV according to TNM staging⁶⁻⁹ with poor performance status were treated by palliative radiotherapy in adjuvant with the Thai herbal tonic solution (Vilac Plus) daily dose of 15-30 cc. orally tid, p.c. as a supportive remedy. Inclusion criteria are: (1) advanced stages of lung cancer; (2) lung cancer with superior vena cava obstruction; (3) metastatic lung cancer; (4) poor performance status; (5) minimal reponse of the tumor to standard radiotherapy 30-40 Gy in 3-4 weeks; (6) the informed consent had been signed by the patients. Exclusion criterior are: (1) advanced stage lung cancer treated with chemotherapy; (2) The patients refused to have this treatment modality. After 4-6 weeks of completion of this treatment, 1 case of stage IV NSCLC was withdrawn to undergo chemotherapy and 1 case of superior sulcus tumor to be treated by surgery. The evaluation and analysis of the results had been performed in the aspect of clinical improvement, complete response, partial response, stable diseases, progressive response, median follow-up time and clinical benefit were evaluated ≤ 15 months after the completion of this sehematic treatment. The procedure of this project has been approved by the Committee of Khon Kaen University Human Ethics (HE 480745).

All cases, selected for this clinical trial were staged by the revised and new staging of the international TNM system for lung cancer.⁶⁻⁹

RADIOTHERAPY TECHNIQUE

The radiotherapy technique used for the patients used in this project has been two parallel opposing fields, AP-PA, with telecobalt or linear accelerator (6MV). The patients were treated in the supine position with two lateral opposing fields at the

tumor with a margination of about 2-3 cms around the opague density of the tumor seen in chest X-ray film.

Regional lymph nodes irradiation were performed in cases with lymph node involvement. The prescribed dose ranges were between 20-60 Gy in 15-30 fractions, five fractions per week, depending on the performance status of the patients and the tumor volume. The dose to spinal cord was limited to 40-45 Gy.

RESULTS

The 13 patients (8 male, 5 female) in advanced stages lung cancer, stage IIIB 11 cases, stage IV 2 cases with poor performance status were treated by palliative radiotherapy in adjuvant with the Thai herbal tonic solution (Vilac Plus). In this group of patients, the median age was 66 years (range 44.4 - 83 years). The pathological diagnosis were 5 cases of squamous

cell carcinoma, 2 cases of adenocarcinoma, 1 case of bronchioalveolar carcinoma, 1 case of mixed squamous and adenocarcinoma and 4 cases of clinically advanced lung cancer as evidenced by computed tomography chest scan/chest X-ray as shown in table 1. The results, evaluated at 4-6 weeks after radiotherapy revealed 76.92% (10/13 cases) having clinically improvement and 23.08% (3/13 cases) were clinically stable as shown in table 2. Overall response rate of partial response was 46.15% (6/13 cases) and 53.85% (7/13 cases) had shown to have stable diseases. Patterns of failure were found to be locally 46.15% (6/13 cases) at the primary site, 30.77% (4/13 cases) at the locoregional nodes and 23.08% (3/13 cases) at the locoregional and metastases, as shown in table 3-4. The median follow-up time is 18 months (range 7-50 months). Clinical benefit rate evaluated at 15 months was 72.72%. However the median survival analysis required longer follow-up and more detail assessment.

Table 1 Patient characteristics

Patient characteristics	cases
Gender	
Female	5
Male	8
Age in years	
Median (range)	66 (44.4-83)
Stage of disease	
III B	11
IV	2
Median follow-up time (range) in months	18(7-50)
Pathology	
SCC	5
Adenocarcinoma	2
Mixed Adeno CA. + SCC.	1
Bronchoalveolar CA	1
Clinically advanced lung cancer (CT-Chest, CXR), no histological diagnosis available	4

Table 2 Subjective response rate.

The subjective response rate after 4-6 weeks of radiotherapy.

Subjective response	cases	%
Clinically improvement	10/13	76.92
Clinically stable	3/13	23.08

Table 3 Objective response rate.

The objective response rate after 4-6 weeks of radiotherapy.

Objective response rate	cases	%
Partial response	6/13	46.15
Stable diseases	7/13	53.85

Table 4 Patterns of failure.

The patterns failure rate after 4-6 weeks radiotherapy.

Patterns of failure	cases	%
Local	6/13	46.15
Locoregional	4/13	30.77
Locoregional +metastases	3/13	23.08

CASES REPORT

CASE 1

An elderly Thai man 60 years old with chief complaints of chronic cough, hemoptysis, dyspnea, chest pain and neck mass with poor performance status and underlying hepatitis B surface antigen positive. Physical examination revealed clubbing finger, palpable left supraclavicular lymph nodes 3 cm x 2.5 cm and decreased breath sound on left lower lung field. Bronchoscopy revealed extrinsic pressure and mucosal infiltration about 1 cm of left mass proximity to carina. The cytology was revealed to be suspicious

of malignancy with atypical squamous epithelial cell. Therefore the repeated bronchoscopy was done for definite diagnosis. The bronchoscopic findings revealed tumor involved at the left lower lung with extension to carina and left main bronchus. The endobroncheal biopsy revealed necrotic tissue with clusters of moderate differentiated squamous cell carcinoma. The chest film PA revealed a larged left lower lung cavitary mass with irregular inner border and left lower lung atelectasis as shown in figure 1A. The thoraco-lumbar spines AP and lateral films revealed no definite bony destruction. The final diagnosis was advanced bronchogenic carcinoma at least stage \leq 3B, T3N3Mx, with poor performance (Eastern Co-operative Oncology Group 3).

Treatments:

1. Palliative radiotherapy by linear accelerator (6MV) 2,160 cGy in 2 weeks was given at the primary tumor and 4,500 cGy in 3 weeks at right supraclavicular region.
2. Antibiotic therapy was given for treatment of obstructive pneumonia and the Thai herbal tonic 15 cc tid, p.c before radiotherapy treatment. Delayed time of the radiation treatment about 4 months was due to a long waiting list because of inadequate radiotherapy machine and radiotechnologist, palliative cases have to give the priority for the curable cases and have to be put in a long waiting list.
3. Herbal Tonic (Vilac Plus) 15 cc tid, p.c. was given orally concurrent with radiation therapy.

The result of treatment in this case revealed nearly complete response of the tumor as shown in figures 1A-1G with good quality of life and the patient resume to his normal routine living style.

The last visit was 05/02/07 and median follow-up time was 16 months after diagnosis whereby median survival in the literatures was 10-15 months.¹⁰⁻²⁸

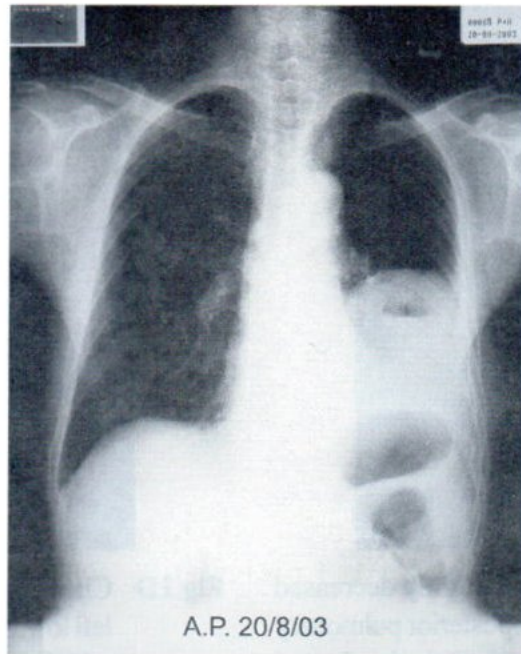


Fig.1A Chest film PA revealed the larged left lower posterior pulmonary cavitary mass with irregular inner border and atelectasis of left lower lung before radiotherapy treatment.

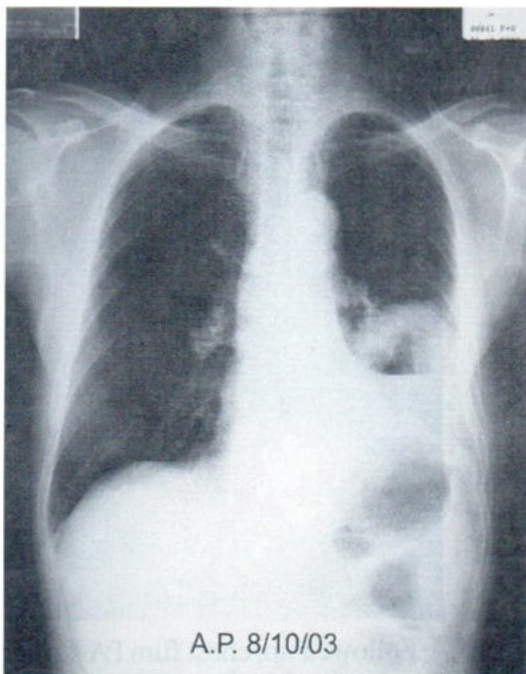


Fig.1 B1

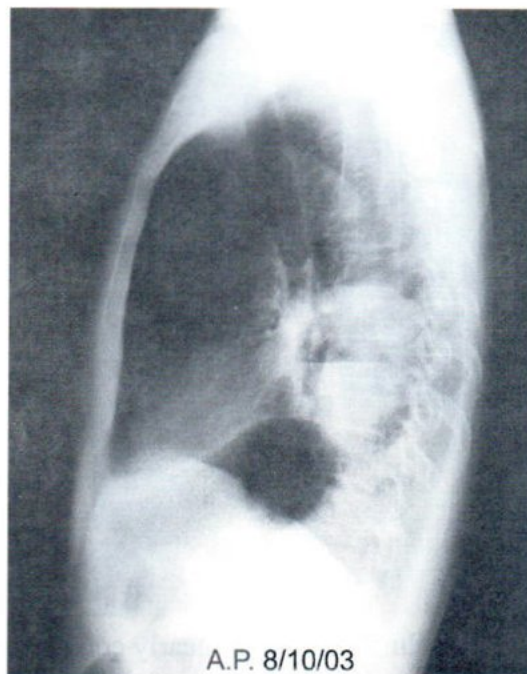


Fig.1 B2

Fig.1 B1-B2 Chest film PA and lateral before treatment revealed a larged left lower posterior pulmonary cavitary mass with irregular inner border and atelectasis of left lower lung, after antibiotic and Thai herbal tonic before radiotherapy treatment due to delayed waiting list for radiotherapy.

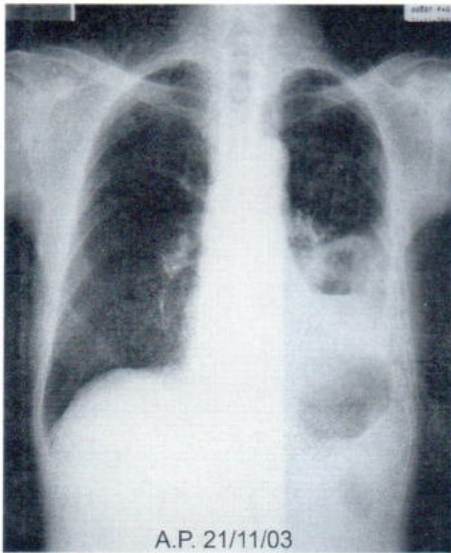


Fig.1C Chest film PA revealed slightly decreased in size of the left lower posterior pulmonary cavitory mass with irregular inner border and atelectasis of left lower lung after antibiotic combined with Thai herbal tonic, immediately after radiotherapy with a tumor dose of 2,160 cGy in 2.5 weeks.



Fig.1D Chest film PA revealed decreased in size of left lower posterior pulmonary cavitory mass with irregular inner border and atelectasis of left lower lung after radiotherapy combined with Thai herbal tonic, 2 months after radiotherapy with a dose of 2,160 cGy in 2.5 weeks.

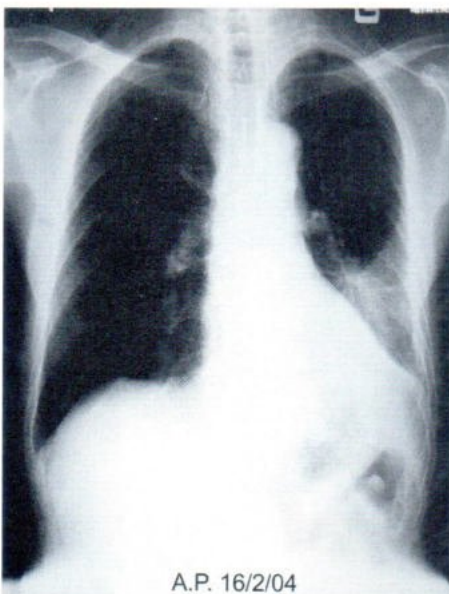


Fig.1E Chest film PA revealed nearly complete regression of the left lower posterior pulmonary tumor mass with atelectasis of left lower lung after radiotherapy combined with Thai herbal tonic, 3 months after radiotherapy 2,160 cGy in 2.5 weeks.

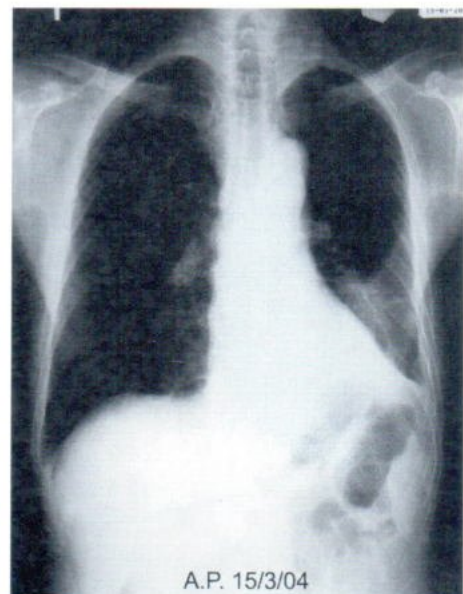


Fig.1F Followed up, chest film PA 4 months after radiotherapy revealed nearly complete regression of the left lower posterior pulmonary tumor mass and atelectasis of left lower lung.

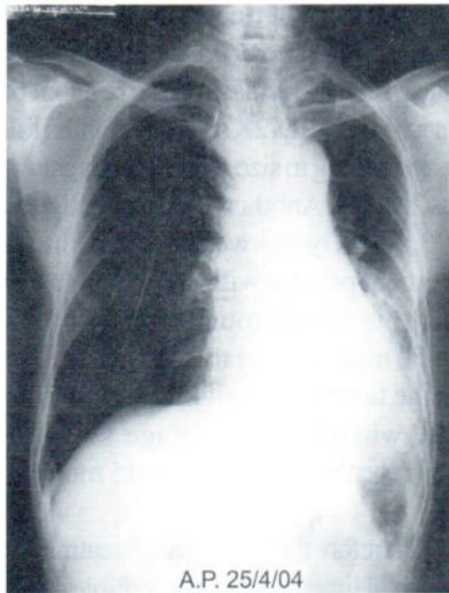
**Fig.1 G1****Fig.1 G2**

Fig.1 G1-G2 Chest film PA and lateral view 5 months followed up revealed nearly complete regression of the left lower posterior pulmonary tumor mass and atelectasis of left lower lung.

CASE 2

A Thai man 42 years old presented with a past history of heavy smoking for 20 years with a chief complaint of cough, dyspnea and chest pain. Physical examination revealed pale conjunctiva, clubbing of fingers, weakness of all extremities. P.A. film of the chest showed a large tumor mass, size 6x8 cms. at the Rt. upper lobe as shown in fig.2A. Percutaneous needle biopsy at the tumor mass in the right upper lobe, was done with a pathological report of having an adenocarcinoma, poorly differentiated as shown in fig. 2C and 2D.

The final diagnosis of the patient was having non-small cell lung cancer (adenocarcinoma, poorly differentiated at least stage IIIB(T₃N₂-3Mx) with poor performance status. (Eastern Co-operative Oncology Group 2-3). It was noted that no brain metastasis was detected as seen by computed tomographic brain scan. P.A. chest after treatment by radiotherapy, with a dose of 3,000 cGy in 3 weeks, followed up in 3 months, fig.2B, revealed the tumour

size to be unchanged, but with partial atelectasis of right upper lobe.

Followed up tomography of the chest 1 week after treated by radiotherapy showed obstructive atelectasis of right upper lobe with para-aortic nodes and malignant pleural involvement.

Treatments

1. Palliative radiotherapy by linear accelerator (6MV) 4,000 cGy in 4 weeks was given at right upper lung and 3000 cGy in 3 weeks at right supraclavicular region.

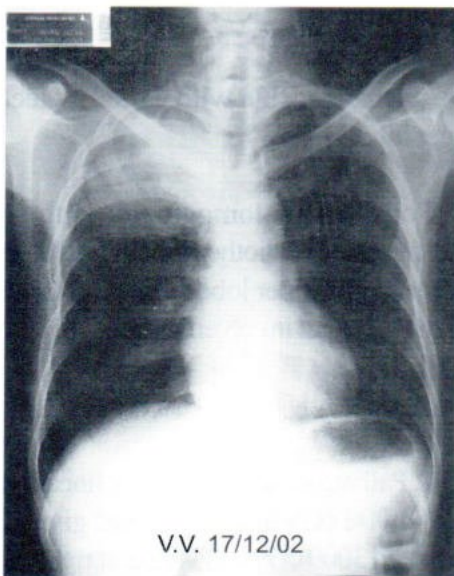
Second course of palliative radiotherapy with linear accelerator (6MV) 2,000 cGy in 2 weeks was given at right upper lung field, 6 months after palliative radiotherapy due to recurrent (1st course) of the tumor.

Third course of palliative radiotherapy with linear accelerator 6,600 cGy in 6.5 weeks was given at the right upper lung, 9 months after initial radiotherapy due to a second recurrent of the tumour. P.A. chest film revealed the lung mass in the right upper lobe grow bigger and also the increasing of the serum CEA level to be 84.96 ng/dl (normal range was 0-2.5 ng/dl). After palliative radiotherapy, the patient enjoyed good quality of life and the film chest showed the disease to be stable 50 months after radiotherapy combined with herbal medicine. The serum CEA level was declined to 4.96 ng/dl (normal range 0-2.5ng/dl)

Herbal Tonic (Vilac Plus)15 cc tid, p.c. was given orally after radiation therapy 3,000 cGy in 3 weeks, as a supportive adjuvant to radiation therapy.

The result of treatment in this case reveal partial response of the primary tumour at the right upper lobe which is decreasing in size about 6 months as shown in figures 2D-2K. After 8 months follow-up, there was increasing in size of the tumor again as shown in figures 2M-2N. Another course of palliative radiotherapy (3,000 cGy in 3 weeks+Vilac Plus 15 cc tid, pc), the patient present with good quality of life and resumed to his normal routine living style. The last visit was 50 months after treatment. P.A. film chest revealed the tumor at the right upper lobe remain to be stable, whereby the average survival in the literatures revealed, was only 10-15 months.¹⁰⁻²⁸

Therefore this modality of treatment revealed longer survival time than the competible cases treated by the conventional methods in the literatures, treated by palliative radiotherapy without Vilac Plus.



Case 2
Fig.2A Film chest PA revealed a large tumour mass in the right upper lung before treatment.

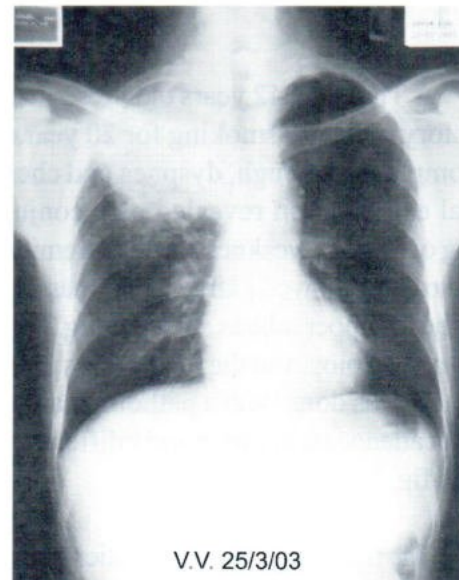


Fig.2B Film chest PA revealed stable of tumour size after radiotherapy 3,000 cGy in 3 weeks



Fig 2C Microscopic picture (100x) revealed a sheet of tissue composed of mainly fibrous tissue and embedded atypical cells in adenocarcinoma, poorly differentiated.

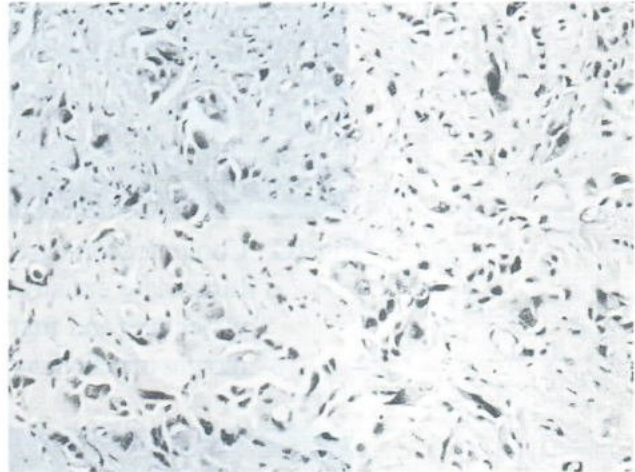


Fig.2D Microscopic picture(400x) Tumor cells were pleomorphic. Some of them arranged in gland-like structure. Mucin production was seen, both intracellular and extracellular in microscopic picture of adenocarcinoma, poorly differentiated.

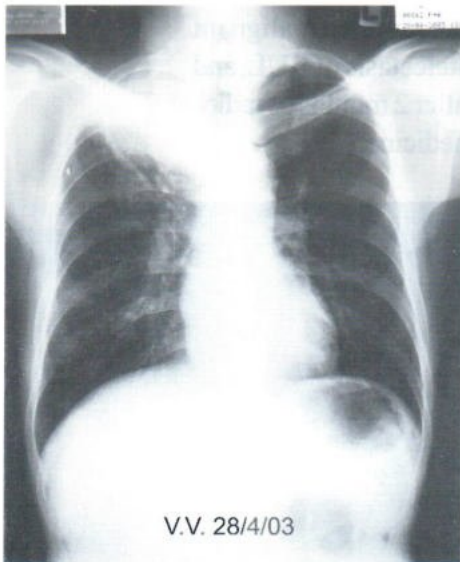


Fig.2E Film chest PA revealed partial regression of tumour size after radiotherapy 4,000 cGy in 4 weeks.



Fig.2F Film chest PA revealed partial regression of tumour after 1 month of radiotherapy combined with herbal medicine.

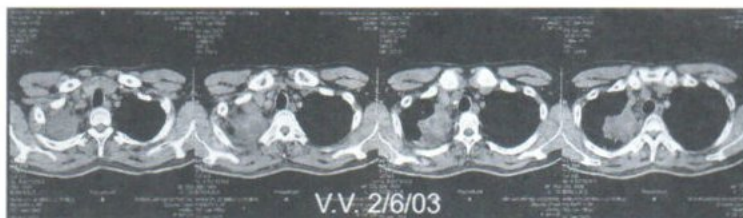


Fig.2G Computed tomography chest scan revealed malignant lung mass causing obstructive atelectasis of right upper lung and malignant pleural involvement after 2 months of radiotherapy combined with herbal medicine.

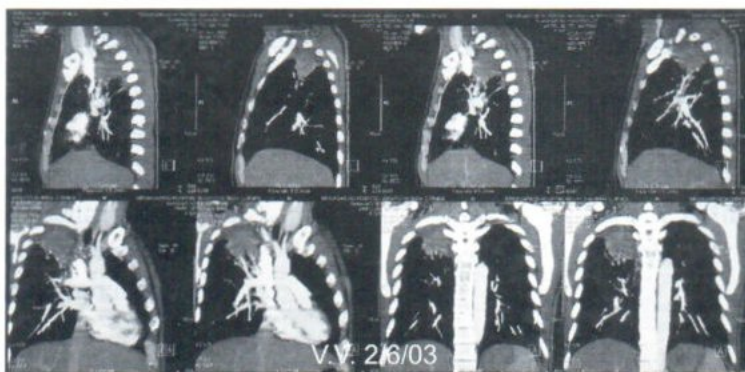


Fig.2H Computed tomography chest scan revealed malignant lung mass causing obstructive atelectasis of RUL, and malignant pleural involvement after 2 months of radiotherapy combined with herbal medicine.

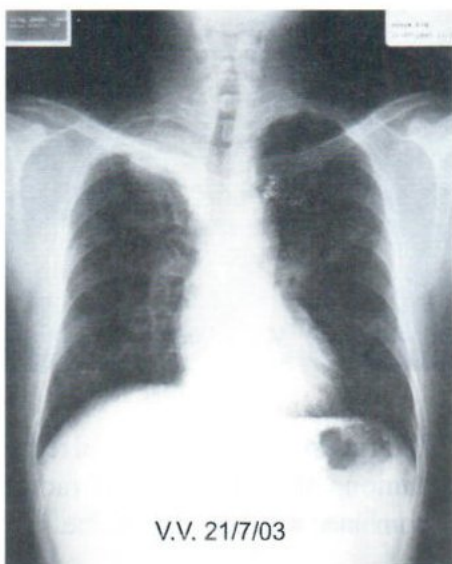


Fig.2I Film chest PA revealed partial regression of tumour size after 3 months radiotherapy combined with herbal medicine.

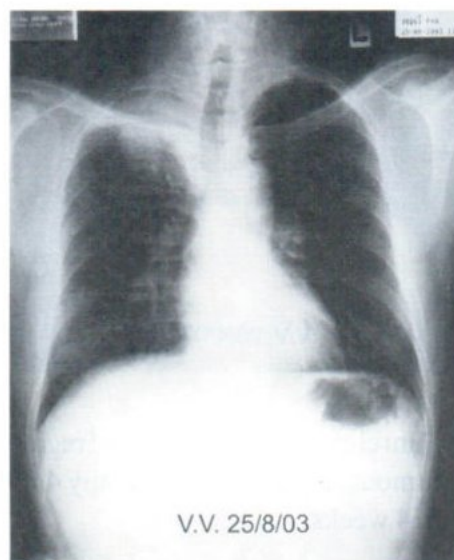


Fig.2J Film chest PA revealed partial regression of tumour size after 4 months of radiotherapy combined with herbal medicine.

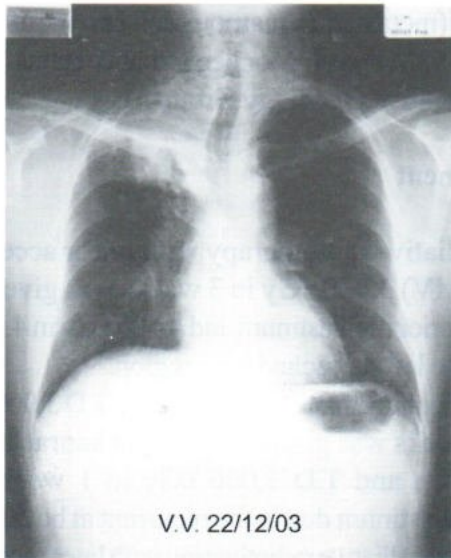


Fig.2K Film chest PA revealed partial regression of tumour size after 8 months of radiotherapy combined with herbal medicine.

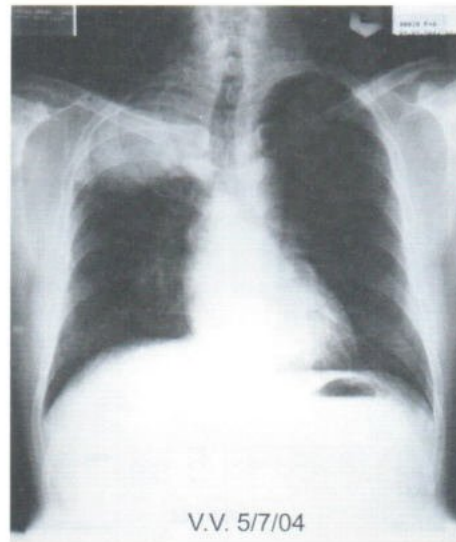


Fig.2L Film chest PA revealed decreased in size of tumour after 13 months of radiotherapy combined with herbal medicine.

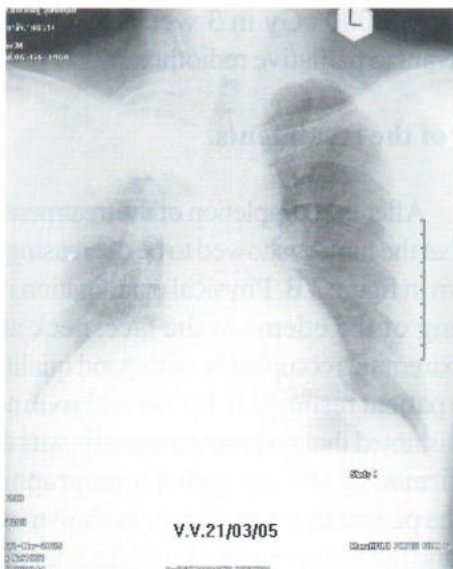


Fig.2M Film chest PA revealed slightly decreased in size of the tumour after 27 months of radiotherapy combined with herbal medicine.



Fig.2N Film chest PA revealed stable of the tumour size after 45 months of radiotherapy combined with herbal medicine.

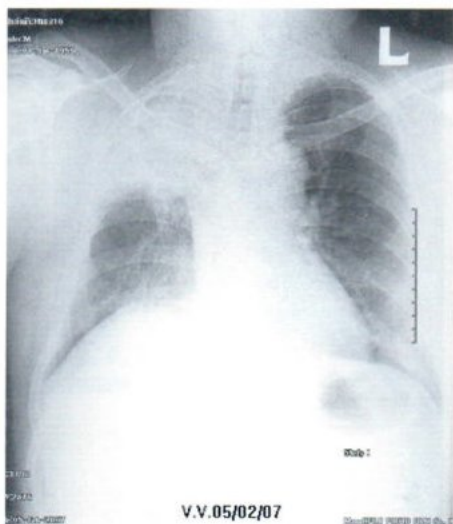


Fig.2 O Film chest PA revealed stable of the tumour size after 50 months of radiotherapy combined with herbal medicine .

CASE 3

A Thai man, 56 years old came to the hospital having a past history of heavy smoking with the chief complaints of severe edema of face, neck, both upper extremities and dyspnea. Physical examination revealed superior vena cava syndrome with masses in the left supraclavicular region. The film chest PA showed widening of superior mediastinal masses with multiple nodules in both lung fields. Lymph node biopsy was done and the pathological report revealed to be metastatic squamous cell carcinoma. Computed tomography of the chest revealed anterior mediastinal masses with homogeneous enhancement with multiple pulmonary nodules in both lungs. The follow-up film chest PA showed widening of superior mediastinal shadows with multiple nodules in both lung fields as shown in figure 3A. The final diagnosis of the patient was superior vena cava syndrome, non small cell lung

cancer (metastatic squamous cell carcinoma), stage IV (T4N3M1) with poor performance status (Eastern Co-operative Oncology Group 3).

Treatment

1. Palliative radiotherapy with linear accelerator. (6 MV) 3,000 cGy in 3 weeks was given to the superior mediastinum and 4,500 cGy in 4.5 weeks to the left supraclavicular region.
2. A second palliative radiotherapy T.D 3,000 cGy in 2 weeks was given to the right supraclavicular region and T.D 1,000 cGy in 1 week to the mediastinum due to the recurrent at both regions.
3. Third palliative radiotherapy with linear accelerator 3,000 cGy in 2 weeks was given to the left supraclavicular region and the left hilar lymph node due to recurrent of the tumor.
4. Herbal Tonic (Vilac Plus) 15 cc tid, pc. was given orally after the third course of palliative radiation therapy 3,000 cGy in 3 weeks as a supportive adjuvant to palliative radiotherapy.

Result of the treatments.

After the completion of the treatments, it was found that the tumors showed to be decreasing in sizes as shown in figure 3 B. Physical examination revealed subsiding of the edema of the face, neck and both upper extremities completely with good quality of life and the patient resumed to his normal routine living style. It is noted that no brain metastasis was detected as confirmed by the computed tomographic brain scan. The patient live with cancer as shown in figures 3C-3F and the last visit was 47 months after diagnosis and treatment, whereby survival in the medical records for the comparable cases were only 10-15 months.¹⁰⁻²⁸

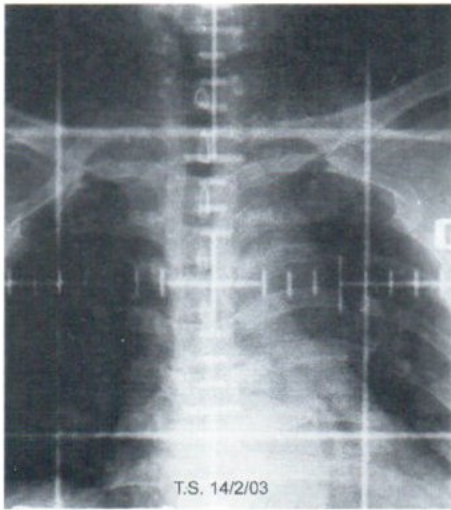


Fig.3A Chest film PA showed anterior mediastinal and left supraclavicular masses with multiple nodules both lungs before treatment.

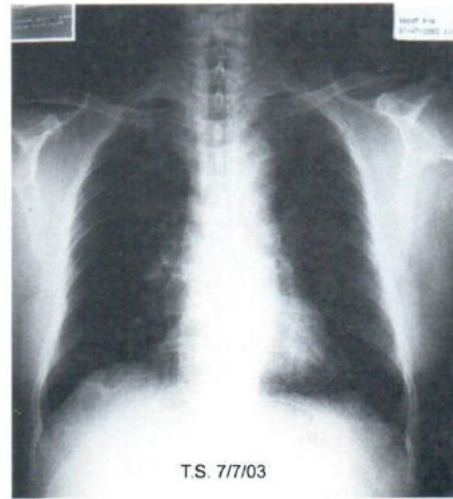


Fig.3B Chest film PA revealed nearly complete regression of the masses at left supraclavicular and mediastinum after treatment 4 months.



Fig.3C Chest film PA revealed nearly complete regression of the masses at left supraclavicular and mediastinum after treatment 18 months.

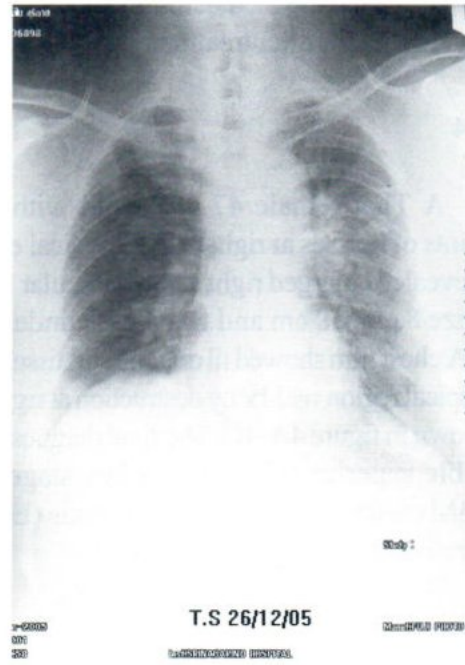


Fig.3D Chest film PA revealed stable of the tumour at mediastinum and both lungs after treatment 34 months.

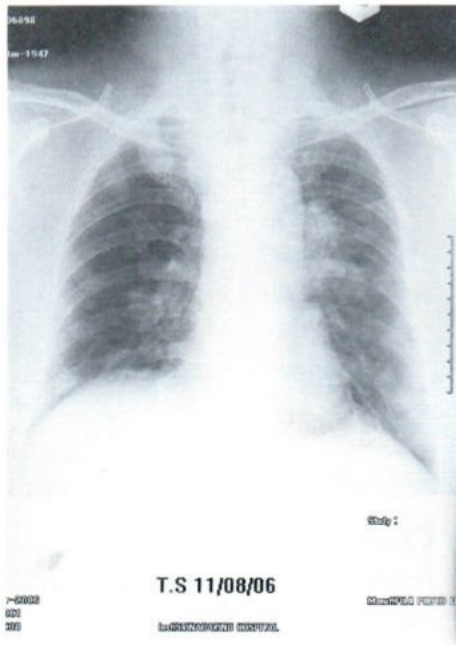


Fig.3E Chest film PA revealed progression of the tumors at the mediastinum and both lungs 42 months after treatment .

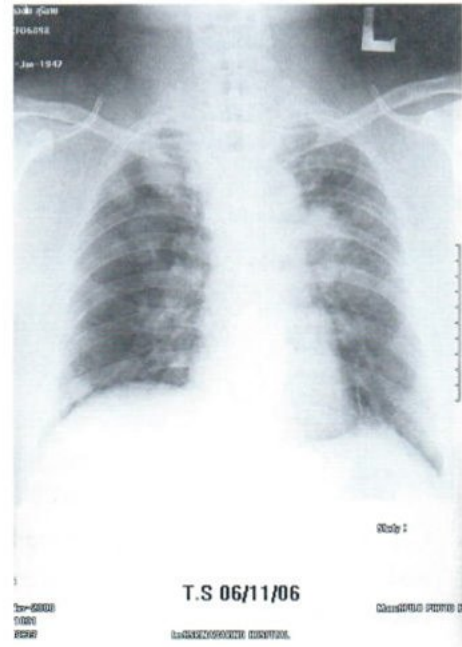


Fig.3F Chest film PA revealed progression of the tumors at the mediastinum and both lungs 44 months after treatment .

CASE 4

A Thai female 47 years old with chief complaints of masses at right neck. Physical examination revealed enlarged right supraclavicular lymph nodes size 8 cm x 8 cm and fixed with underlying tissue. PA chest film showed ill defined soft tissue mass in right apical region with bony destruction at right first rib as shown in figure 4A-4C. The final diagnosis was inoperable superior sulcus tumor,late stage \geq III B,T3N3Mx with poor performance status (Eastern Co-operative Oncology Group2-3).

Treatment

1. Palliative radiotherapy with cobalt-60 unit 6,600 cGy in 6.5 weeks was given to the primary tumor

and the right supraclavicular region with additional doses to the right supraclavicular region, 600 cGy in 3 days.

2. The Thai herbal tonic (Vilac Plus) 15 cc tid, pc. was given orally concurrently with the palliative radiation therapy.

The result of treatment in this case revealed decreased in size of the tumor as shown in Figure 4D with good quality of life. **The patient live with cancer and the last visit was 24 months afer diagnosis whereby median in medical literatures was 10-15 months.¹⁰⁻²⁸ Therefore this case revealed longer survival than statistical records in the medical literatures.**

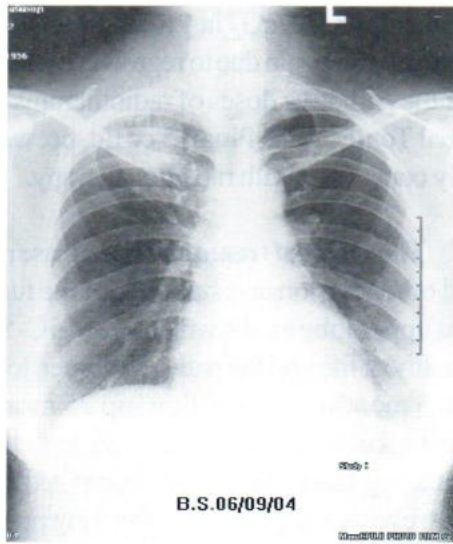


Fig.4A Chest film PA showed ill defined soft tissue mass in the apical and supraclavicular region with bony destruction at first rib, right side.

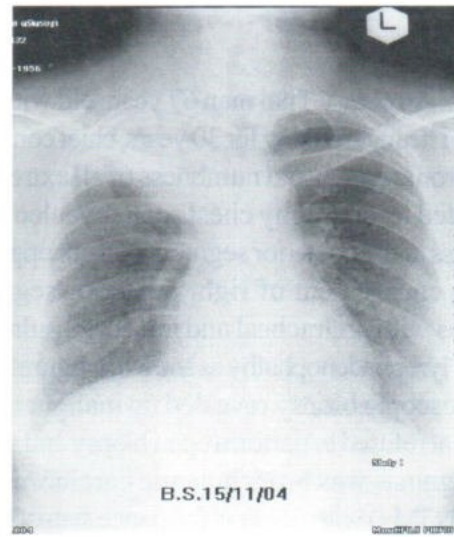


Fig.4B Chest film PA, 2.5 months later revealed increasing in size of the mass in the apical and supraclavicular region with bony destruction at the first rib, right side.

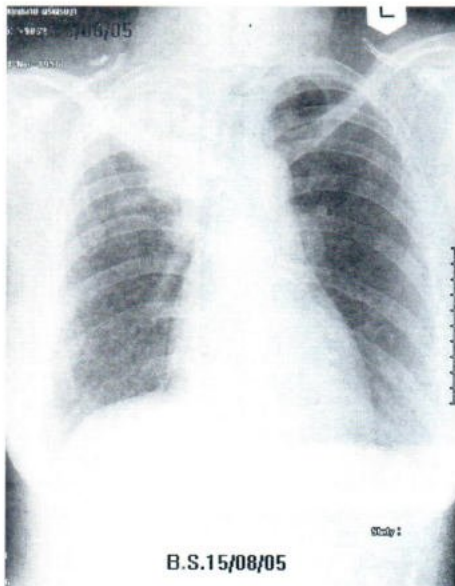


Fig.4C Chest film PA revealed ill defined soft tissue mass in the apical and supraclavicular with bony destruction of the first rib, right side.

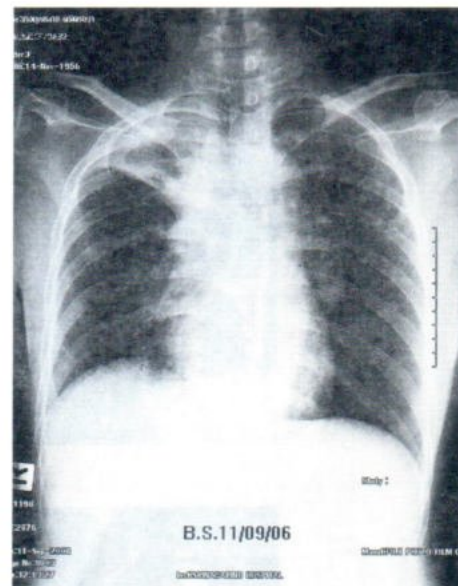


Fig.4D Chest film PA revealed decreased in size of the tumour 1 year after treatment.

CASE 5

An elderly Thai man 67 years old with a past history of heavy smoking for 30 years, chief complaints were chronic cough and numbness of all extremities. Computed tomography chest scan revealed large lung mass at the posterior segment of right upper lobe causing encasement of right posterior segmental bronchus with pretracheal and left aorto-pulmonary window lymphadenopathy as shown in figure 5A-5B. Bronchoscopic biopsy revealed no malignancy and the patient refused to perform open biopsy and surgery. The diagnosis was bronchogenic carcinoma stage IIIB(T3N3Mx) with poor performance status(Eastern Co-operative Oncology Group2-3).

Treatment

1. Palliative radiotherapy by linear accelerator (6MV) 3,780 cGy in 4.5 weeks was given to the primary tumor and regional lymph nodes and 13 months after initial treatment, a second palliative

radiotherapy 3,420 cGy in 4 weeks was given to the primary tumor again due to regrowth of the tumour after the palliative doses of radiotherapy.

2. Herbal Tonic (Vilac Plus)15 cc tid, pc. was given orally concurrent with radiation therapy.

The result of treatment in this case revealed a period of regression and stability of the tumour at the right upper lobe as shown in figure 5C-5H with good quality of life and the patient resumed to normal life for 25 months. After follow-up 25 months the patient complaints of productive cough and chest film PA revealed regrowth of tumor. The computed tomography chest revealed large right upper lung pulmonary mass 8cm x5 cm causing narrowing of right main bronchus with no associated lymphadenopathy. **The patient live with cancer and the last visit was 29 months after diagnosis whereby the median survival in the literature records was 10-15 months.¹⁰⁻²⁸ Therefore this modality revealed longer survival time than the median survival in the literatures.¹⁰⁻²⁸**



Figure 5A

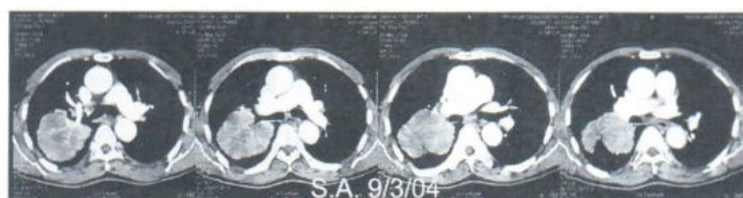


Figure 5B

Fig.5A-5B Computed tomography chest scan revealed large lung mass at posterior segment of right upper lobe causes encasement of right posterior segmental bronchus with pretracheal and left aorto-pulmonary window lymphadenopathy.

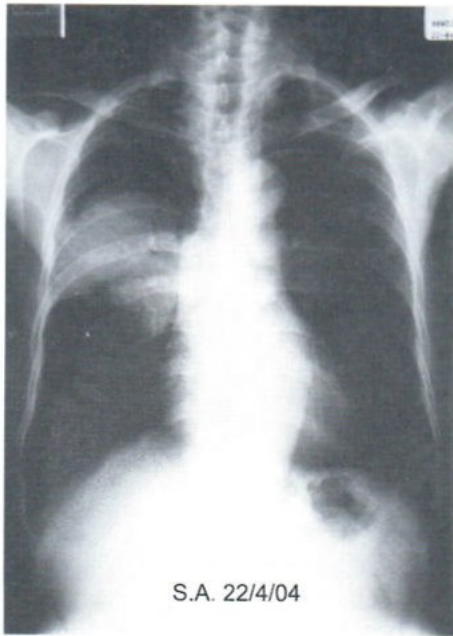


Fig. 5C Chest film PA revealed stable of the tumour at right upper lobe.

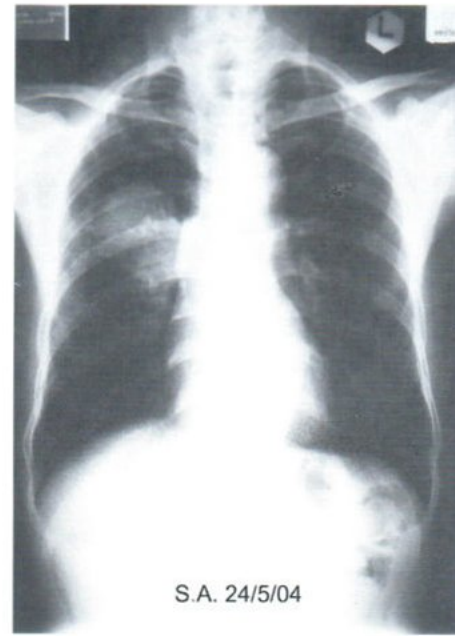


Fig. 5D Chest film PA revealed stable of the tumour at right upper lobe.

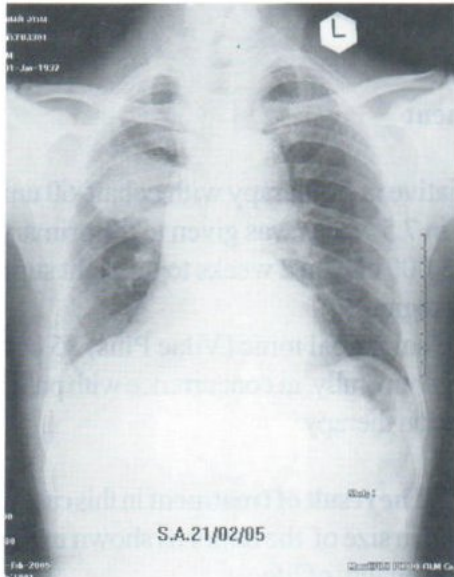


Fig. 5E Chest film PA revealed quiescence of tumour at right upper lobe.

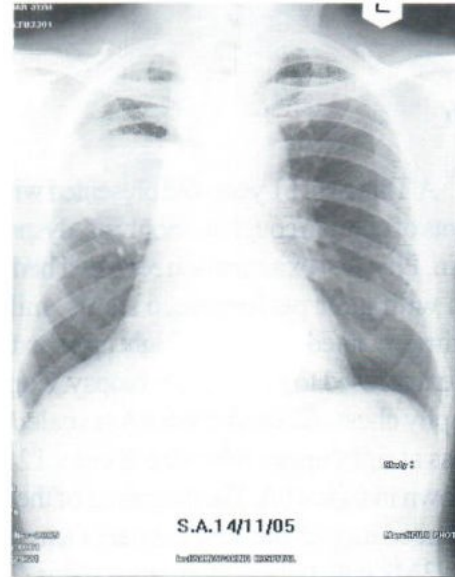


Fig. 5F Chest film PA revealed quiescence of tumour at right upper lobe.

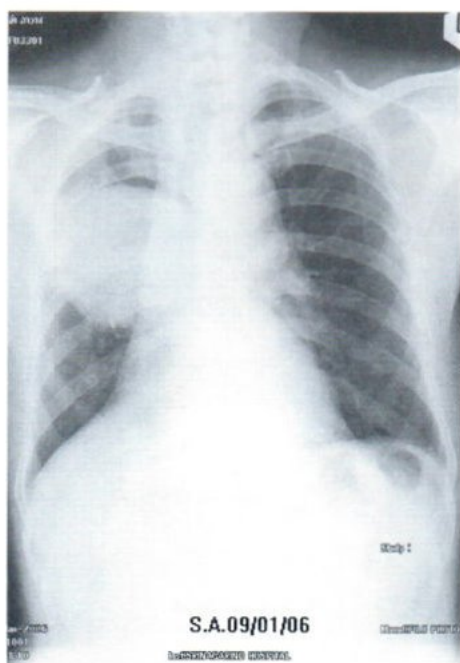


Fig.5G Chest film PA revealed quiescence of tumour at right upper lobe.

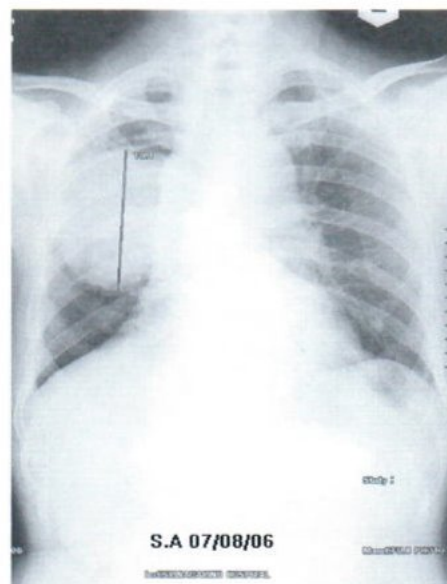


Fig.5H Chest film PA revealed the tumour at right upper lobe start to grow bigger.

CASE 6

A Thai man 51 years old presented with chief complaints of chronic cough, hemoptysis, dyspnea and chest pain. Physical examination revealed bed ridden old man with poor performance status, mild pale conjunctivae, marked swelling of right upper extremity. The patient refused to have tumor biopsy. Computed tomography chest scan and chest PA revealed larged lung mass at right upper lobe size 8 cm x 12 cm x 8 cm as shown in figure 6A. The diagnosis of the patient was advanced inoperable lung cancer at least stage \geq III B, T3N3Mx with poor performance status. (Eastern Co-operative Oncology Group 3).

Treatment

1. Palliative radiotherapy with cobalt-60 unit 6,000 cGy in 7.5 weeks was given to the primary tumor and 3,000 cGy in 2 weeks to the right supraclavicular region.
2. The Thai herbal tonic (Vilac Plus) 15 cc tid, p.c. was given orally, in concurrence with palliative radiation therapy.

The result of treatment in this case revealed decreased in size of the tumor as shown in Figure 6B with good quality of life.

The patient live with cancer as shown in figures 6B-6G and the last visit was **12 months afer diagnosis whereby survival in the previous literatures was 10-15 months.**¹⁰⁻²⁸

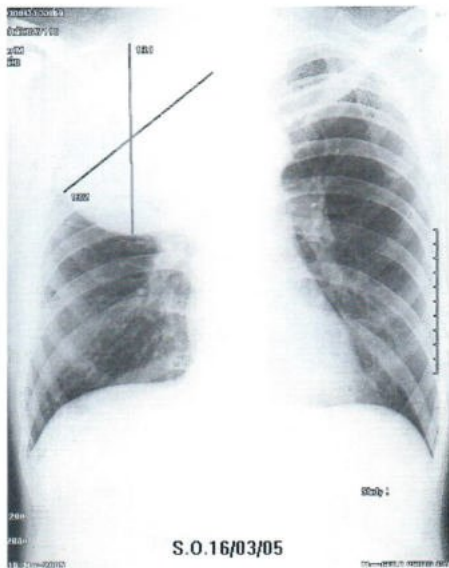


Fig.6A Chest PA revealed larged lung mass at right upper lobe size 8 cm x 12 cm. at right upper lobe.

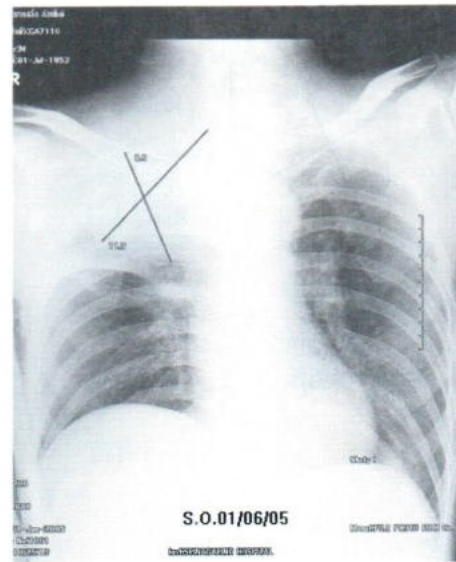


Fig.6B Chest PA revealed decreased in size of the tumor at right upper lobe

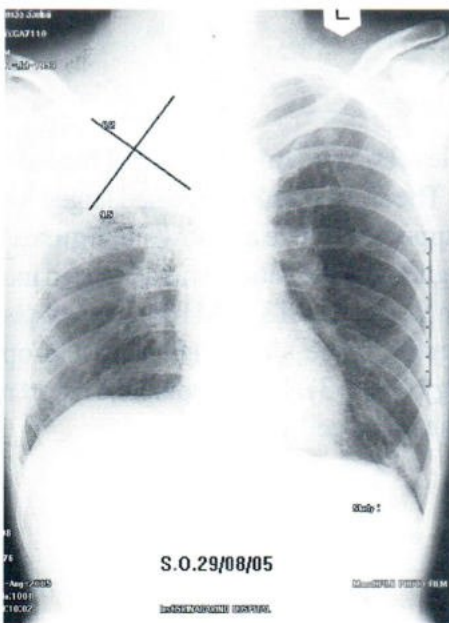


Fig.6C Chest film PA revealed stable of the tumour at right upper lobe.

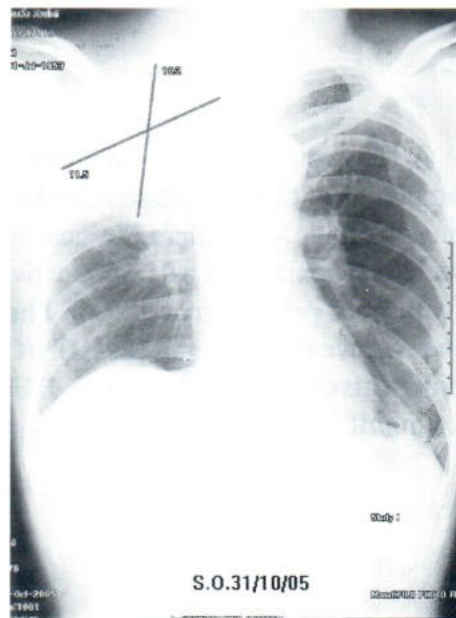


Fig.6D Chest film PA revealed stable of the tumour at right upper lobe.

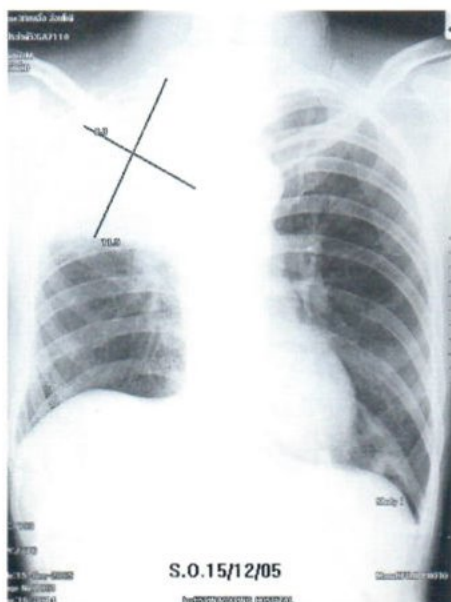


Fig.6E Chest film PA revealed stable of the tumor at right upper lobe.

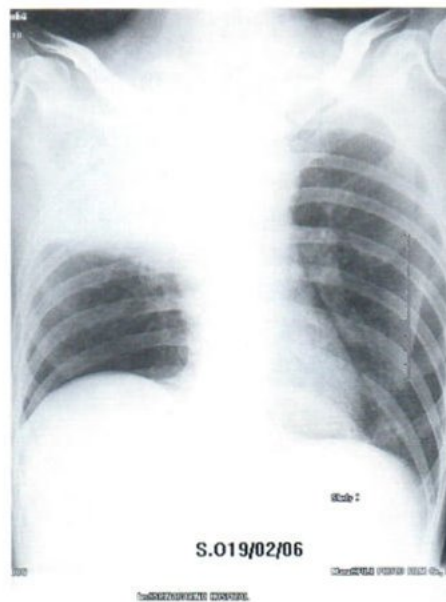


Fig.6F Chest film PA revealed tumor at right upper lobe started to grow bigger.

CASE 7

A Thai woman 69 years old presented with chief complaints of chronic cough, chest pain and underlying of chronic renal failure. Physical examination revealed cachexia, mild pale conjunctivae, bed ridden with poor performance status. **The renal function test revealed rising in the BUN/Cr level according to his chronic renal failure, BUN level was 55.6 mg/dl (normal range = 5.8-19.1 mg/dl),**

Cr = Creatinine

and Cr level was 4.6 mg/dl (normal range = 0.5-1.5 mg/dl). The chest film PA revealed larged lung mass at left upper lobe, size as shown in **figures 7A-7B**. The diagnosis of the patient was advanced inoperable lung cancer stage IV,T3N3M1 (bone metastasis) with poor performance status. (Eastern Co-operative Oncology Group 3). The pathological report revealed to be squamous cell carcinoma.

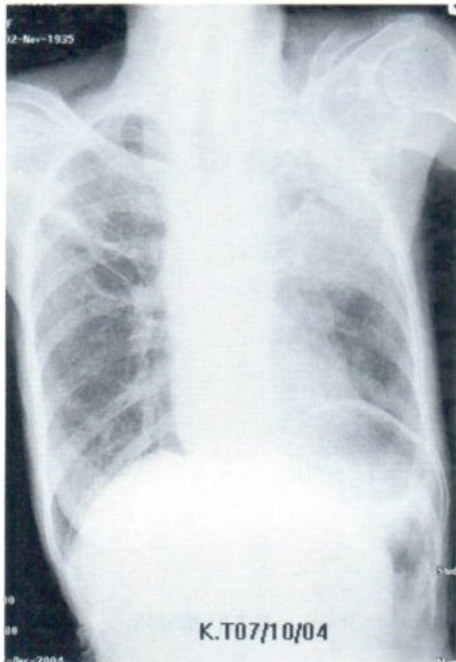


Fig. 7A

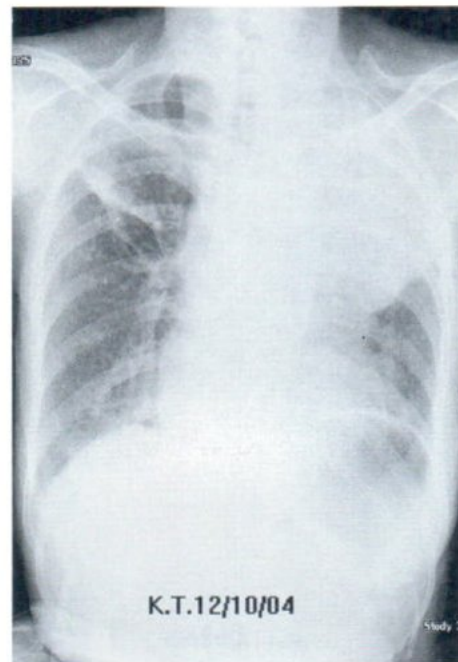


Fig.7B

Fig. 7A-7B The chest film PA revealed larged lung mass at left upper lobe.

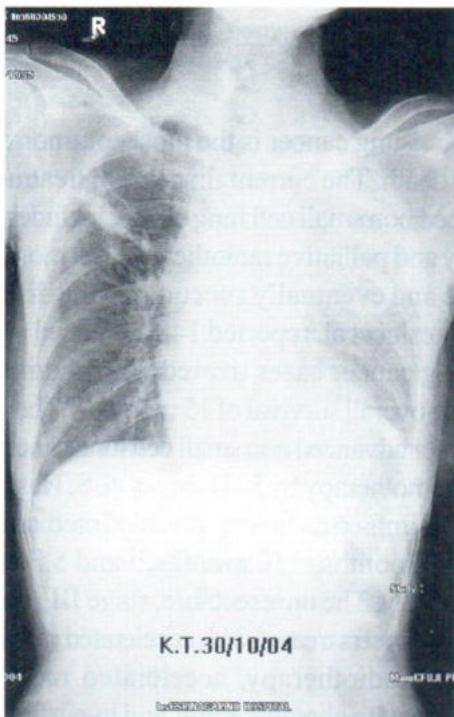


Fig. 7C

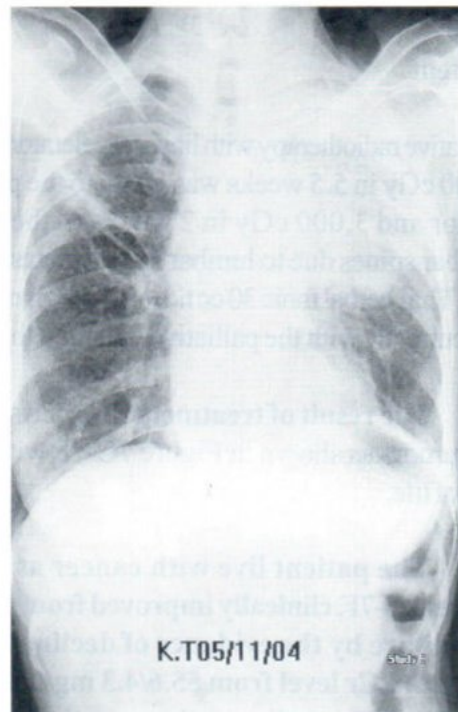


Fig. 7D

Fig. 7C-7D The chest film PA revealed stable of the tumor mass at left upper lobe.

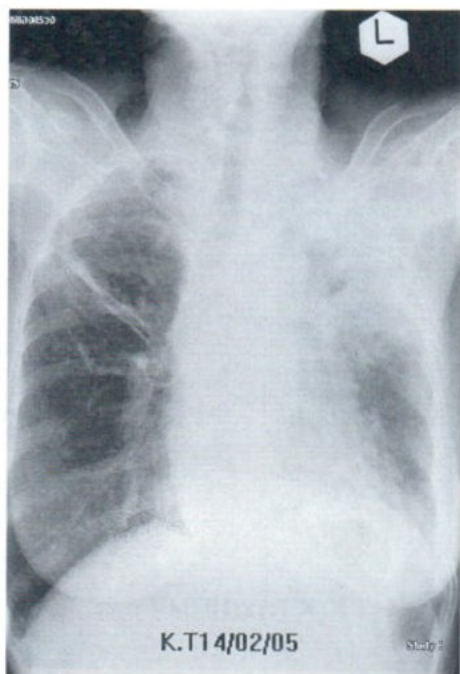


Fig. 7E

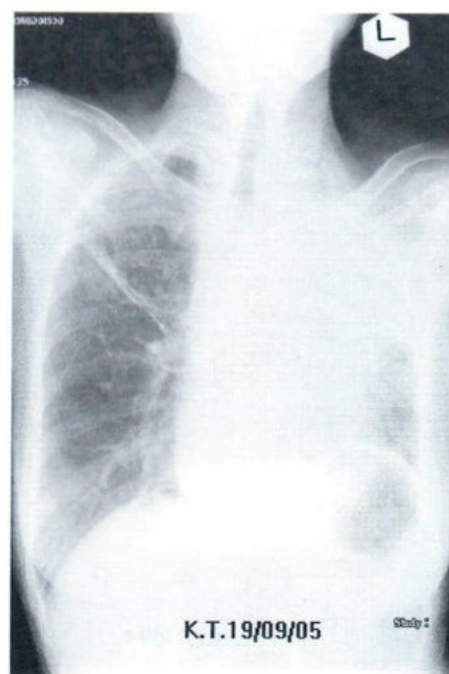


Fig. 7F

Fig. 7E-7F The chest film PA revealed stable of the tumour mass at left upper lobe.

Treatment

1. Palliative radiotherapy with linear accelerator (6MV) 4,800 cGy in 5.5 weeks was given to the primary tumor and 3,000 cGy in 2 weeks to the whole lumbar spines due to lumbar spines metastases.
2. The Thai herbal tonic 30 cc tid, p.c. was given orally concurrently with the palliative radiation therapy.

The result of treatment revealed stability of the tumors as shown in Figure 7C-7F with good quality of life.

The patient live with cancer as shown in figures 7C-7F, clinically improved from chronic renal failure by the evidence of declined in the serum BUN/Cr level from 55.6/4.3 mg/dl to 18.6/1.5 mg/dl. The median follow-up time was 13 months afer diagnosis whereby survival in the previous medical records was 10-15 months.¹⁰⁻²⁸

DISCUSSION

Lung cancer is the most common cause of cancer death. The current first-line of treatment with advanced non small cell lung cancer includes chemotherapy and palliative radiotherapy, but most patients relapse and eventually succumb to the disease.¹⁰⁻²⁸ M. Lyikesici et al. reported 140 advanced non small cell lung cancer cases treated with chemotherapy showing overall survival of 15 months.¹⁰ The previous reports for advanced non small cell lung cancer treated with chemotherapy by R. Huber et al, S. Hasturk et al, and M. Zimmermann et al, revealed median survival to be 4.2 months,¹¹ 10 months,¹² and 5.3 months¹³ respectively. The unresectable, stage III, non-small cell lung cancers treated with accelerated radiotherapy, standard radiotherapy, accelerated radiotherapy combined with chemotherapy and hyperfractionated radiotherapy combined with chemotherapy was reported by Wake B. et al revealed median survivals of 14.4, 13.8, 15 and 14.5 months respectively.¹⁴ A

report of advanced non small cell lung cancer by Hansen O et al, the patients treated by 3D conformal radiotherapy revealed a median survival of 15.8 months, and 5 year survival were 17%.¹⁵ Saunders M et. al and Sause W et. al, reported of randomized trial stage III non-small cell lung cancer treated with standard radiotherapy and hyperfractionated radiotherapy revealed a median survival of 13 months for standard radiotherapy, where as 16.5 months for hyperfractionated radiotherapy¹⁶ and 11.4 months for standard radiotherapy, 12.5 months for hyperfractionated radiotherapy respectively.¹⁷ The stage III non-small cell lung cancer was reported by Jeremic et al. that the treatment underwent by using hyperfractionated radiotherapy and hyperfractionated radiotherapy combined with chemotherapy revealed a median survivals of 8 months by hyperfractionated radiotherapy and 13-18 months by hyperfractionated radiotherapy combined with chemotherapy respectively.¹⁸ Ball et.al. reported of stage III non-small cell lung cancer treated with radiotherapy revealed a median survival of 13.8 months.¹⁹ Kawahara M et. al. reported a prospective nonrandomized phase II trial using concurrent chemotherapy and split course radiotherapy on 61 inoperable cases of locally advanced non-small cell lung cancer revealed a median duration of responses of 276 days, and a median survival time of 450 days. The survival analysis in this study appeared to be 1, 2, and 3 year survivals ranging from 60%, 37%, and 28%, respectively. The report of the 13 cases of non small cell lung cancer stage IIIA presented the median survival of 358 days and 1, 2, and 3 year survivals were 50%, 50%, and 42%, respectively. In non-small cell lung cancer stage IIIB (48%), medial survival was 450 days and 1, 2, and 3 year survivals were 63%, 33%, and 25%, respectively.²⁰ We carried on our study of palliative treatment in late stages of cancer using palliative radiotherapy and Thai herbal medicine as supportive remedy. Palliative radiotherapy in advanced lung cancer using Thai herbal tonic solution (Vilac Plus) registered by Thai FDA as an supportive remedy showing varying degree of synergistic palliative values. Prolonged survival follow-up in 1 case with superior vena cava obstruction revealed 47 months whereby

the reports of median survival in superior vena cava obstruction from others reported in the literatures were 12-15 months.¹⁰⁻²⁸ The superior vena cava syndrome is usually associated with advanced malignancy and has a dismal prognosis.²⁶⁻²⁸ It has been reported that in the patients received continuous irradiation (6,000 rads in 30 treatments in 6 weeks) and split course therapy (2 courses of 2,500 rads in 10 treatments with a 3 week break between courses), revealed the median survival of 1.2 months in patients not completing treatment course and 12 months for the patients who received the completed treatment.²⁶⁻²⁸ The other reports of superior vena cava obstruction who had received standard therapy by irradiation alone, chemotherapy alone, and combined modality revealed a median survival of 62 weeks. It is noted that not only longer follow-up time are shown in our study but also good quality of life without serious side effect had been achieved by our patients. The longer follow-up time in 1 case of metastatic squamous cell carcinoma with superior vena cava syndrome was 47 months after the initial diagnosis while a case of stage III B non small cell lung cancer, adenocarcinoma poorly differentiated was 50 months.

The enhancing effect of Vilac Plus in prolonging the survival of these patients can be explained under the principle of antioxidant potential of Vilac Plus® where the analytical report by the KRL Test (SPIRAL -Patent) laboratories, France, Durand, (Written personal communications).³ The assessment of antioxidant potency of Vilac Plus® had been performed in vitro assay of the product using Trolox® (vitamin E analogue) and Gallic acid as reference standards. The blood samples of the volunteer were being used as the specimen. The analysis was performed by the KRL Test. This tonic product may contribute a complementary supportive effect through its powerful antioxidant effect,³ that the analysis report revealed the impressive results of antiradical potency. This Vilac Plus® presents in vitro as an important antioxidant capacity, which increases with the dose of the product up to a concentration of 50 mL per liter of the reaction medium.

At a concentration of 50 ml/l, the Vilac Plus® increases the resistance of the control blood to free radical aggression up to 277.22%. This 3.8 time increased in the blood resistance induced by the product represents an antiradical effectiveness that is equivalent to 557.45 micromoles of Trolox® (Vitamin E analogue) or 320.92 micromoles of Gallic Acid per liter of the reaction medium.³ Thereby, a 50 ml drink of Vilac Plus® has an antioxidant activity which is equivalent to 557 micromoles of Trolox® or 321 micromoles of Gallic Acid. The assessment of antioxidant capacity had been performed by Kirial Laboratories.³

The mechanism of the antioxidants or antiradical effect to support and enhancing cancer therapy effect are well recognized by all oncologists both in prevention, inhibition or even blocking the proliferation of cancer cells particularly in lung cancer. The hypothesis of the synthetic ascorbic acid as well as all organic vegetable products produce both preventive and therapeutic adjuvant for lung cancer.²⁹⁻³¹ The trials had been performed either on the smoker and non-smoker groups patients. The mechanism of the antioxidants on enhancing the therapeutic effect of cancer contributing to potentiate radiotherapy effect in biochemical aspect of the antioxidants²⁹⁻³¹ can be explained in 3 mechanisms.

- (1) The antioxidant molecules facilitating the pathway of concentration of retinoic acid and beta-carotene by acting on the carcinogenesis factors of the lung such as 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone in smoke-exposed lung cancer patients.
- (2) In consequence with these inhibit the extracellular signal for lung cancer cell proliferation and antigen production.
- (3) Finally blocking the regulation of protein synthesis of lung cancer, then either the distant metastasis or progression will eventually decrease in incidence.

The consequences of the 3 mechanisms will be evidenced in the reduction of the tumor size and number of lesions and eventually reduction the chance

of distant metastasis of the tumor, where in this study, not only prolonged survival time but also low incidence rate of brain metastasis were noted. Therefore, the more powerful antioxidant affects, the better enhancing effect on the regression of tumor lesions. The potentiations of the therapeutic effect can be expected, in addition to those 3 mechanisms of the antioxidants agent, the benefit for lung cancer therapy as being alternative approaches strategy against lung carcinogenesis through maintaining normal tissue level of retinoic acid, inhibiting the activation of mitogen activated protein kinase pathway nor cell proliferation and proliferation of p53.²⁹

Those 3 mechanisms presenting the systematic effects may also be considered in immunological balance effect on top not only in biochemical considerations. The clinical trails of Vilac Plus® in the study as an supportive adjuvant to radiation therapy on lung cancers have shown this potentiative and synergistic effect due to powerful antioxidant properties with the longer survival time, better quality of life and with the reduction of chance of distance metastasis are noted. The cost effectiveness is another considerable issue for this protocol of the study compared to chemotherapeutic agents and oral epidermal growth factor receptor (EGFR) inhibitors of lung cancer treatments.

The notably enthusiastic results of this study can be drawn the terms of:

1. Good quality of life being observed in all cases
2. Prolonged survival follows up time in most of the cases compared with the previous reports in other modality of treatments. Some of them live normally with diseases.
3. The distant metastasis particularly to the brain was notably reduced in rate. The overall performance of the patients had been improved. Therefore, the considerations and analysis of results may be based on the hypothesis of the well being caused by holistic immuno-modulation, enhancing by available macro and micronutrient in the subcellular

level in the body, in addition to the classical radiological effects and antioxidants effects on the cancer therapy.

It is also noticeable that at the initial doses of Vilac Plus being administered, the patients developed a fever for a few days similarly to the symptom of the children getting a shot of triple antigen for immunization. This bring us to consider the process which had been used to prepare this product by the fermentation of the ingredients using the bacteria namely *Lactobacillus casei* spp. (Registered in Gene Bank number AF 320255), *Lactobacillus plantarum* spp. (Registered in Gene Bank number AF 320256).

Hence, the enhancing effect on this treatment modality that is noteworthy to consider that this lysate product of Vilac Plus may contribute in the provokation of the body immunity by providing the production of acquired immunity in the body of the patients. This activity was the cause of fever in the patient as we had observed. Therefore the enhanced transfers factor can facilitate the immunity to differentiate between the cancer cells from the host cells.

The more precise target killing of cancer cell by any modality of treatments can be achieved. This evidence represented by reduction of tumor mass or reduces the chance of distant metastasis. This hypothesis will be possible only if the micronutrients had been provided to be the factor available into subcellular level of the system for synthesis of the acquired immune system. Immunity involvement should be concerned as another contributing factor on this modality of treatment. It may be worth our while to further investigate deep in detail in the immunological enhancing effect of this supportive remedy in the future.

CONCLUSION

The results of this study are promising in the aspect of good quality of life and preferable because of the cost effectiveness to be the adjuvant for radiotherapy. The value can be expressed as follows:

1. Clinically improvement was 76.92%
2. Longer median follow-up time was 18 months (range 7-50 months).
3. Clinical benefit rate > 15 months was 72.72 %.
4. Prolonged median follow-up time of 47 months after initial diagnosis revealed in 1 case of stage IV (T4N3M1) with poor performance status, metastatic squamous cell carcinoma with superior vena cava obstruction.
5. Prolonged median follow-up time of 50 months revealed in 1 case of stage IIIB(T3N2-3Mx) with poor performance status, non small cell lung cancer adenocarcinoma poorly differentiated.
6. **Declined of the BUN/Cr level from 55.6/4.3 mg/dl to 18.6/1.5 mg/dl** in 1 case of stage IV, T3N3M1 (bone metastasis) with underlying chronic renal failure, poor performance status, squamous cell carcinoma was noted.

Cr = Creatinine

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