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THE IMAGE OF INNOVATION

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THE ASEAN JOURNAL OF RADIOLOGY

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CONTENTS

# DIAGNOSTIC YIELD IN COMPUTED TOMOGRAPHY OF THE BRAIN IN CLINICAL ABSENCE OF NEUROLOGICAL DEFICIT PATIENTS

**Luckana GIRAPONGSA, M.D.**[1]

## ABSTRACT

**Objective:** 1. to assess diagnostic yield in computed tomography of the brain in variable complaints and clinical absence of neurological deficit patients.
2. to determine correlation between age, sex, underlying disease and the abnormal computed tomographic finding.

**Materials and methods:** During July 2005-September 2006, 115 patients with variable complaints but clinical absence neurological deficit were examined by general medicine, neurologist and neurosurgeon (53 women, 62 men, mean age 53.03, range 11-95 years) at the general medicine department. The clinical records were reviewed for clinical information.

Three observers assessed the plain and contrast study of the computed tomography of the brain for abnormal findings. The outcomes described as negative finding, minor positive findings (abnormal finding without changed of treatment) and major positive findings (abnormal finding with changed of treatment).

**Results:** The positive study (major and minor positive) in the computed tomography of the brain in clinically no neurodeficit patients is 59.1%. There was 35.7% with major positive, or distinctive abnormal findings with altering of the management.

The ages and underlying diseases have strong correlation with abnormal CT findings but there is no correlation with sex.

**Conclusion:** Diagnostic yield in hospital-based patients with variable complaints but without clinically neurological deficit was about 60% but enough for decision of treatments, the yield remained only 35.7%. In advanced ages and underlying disease patients had the evidence base for more opportunity in having abnormal computed tomography but no difference between sex. The strictly following guideline for each complaint will help in increasing the yield.

**Key words:** diagnostic yield, clinical absence neurological deficit.

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## INTRODUCTION

The computed tomography scan (CT scan) of the brain is one of the most worldwide and useful diagnostic equipment using for diagnosis including pre and post treatment evaluation in many human diseases. Because of the hazard of the exposure to radiation the exposed radiation, the risk for contrast study reaction and high cost, there are many attempts for developing absolute indications, avoiding unnecessary CT scan of the brain.

The overviewed indications for CT scan of the brain are

1. Intracranial
   - Acute stroke: for rule out hemorrhage
   - Transient ischemic attack
   - Acute subarachnoid hemorrhage especially headache with focal neurological sign, nausea/vomiting or Glasgow coma score below 14
   - Acute head injury in or Glasgow coma score below 9
   - Space occupying lesion as tumor
   - Suspected hydrocephalus
   - Chronic headache with epilepsy, changes of personality.
   - Intracranial infection: to rule out raised intracranial pressure prior to lumbar puncture.
   - Detection or evaluation of calcification as oligodendroglioma.
   - Others as mental status change, acute neurological deficit
2. Extracranial
   - Middle or inner ear symptoms including vertigo.
   - Sinus diseases.
   - Congenital anomalies
   - Orbital lesions, including eye trauma.
   - Fracture of the temporal bone, skull and face.
   - Evaluation of the skull base including primary or secondary bone lesion.
   - Craniomaxillofacial surgery.

Every neurological deficit patients with variable complaints have absolute indication for imaging study as CT scan or MRI. In clinical absence of the neurological deficits patient, only some complaints such as trauma have true indication. There is a doubt for other complaints for diagnostic yield. Hirano et al presented that yields of CT scan of the brain in absence of neurological deficit is low (6% for true positive and 8.5 % with leading to treatment change) and concluded better criteria defined to guide decision about which patients need CT scans.[1] There are few evidence-base studies for diagnostic yield of the computed tomography of the brain in the clinical absence of neurological deficit.

There are possible factors as advanced ages, preexisting disease or even sex may relate to abnormal CT findings as brain atrophy or small vessels diseases.

This study aims to assess diagnostic yield in computed tomography of the brain in patients with variable complaints but without clinical neurological deficit and to determine the correlation of age, sex and underlying diseases to the abnormal computed tomographic finding.

## MATERIALS AND METHODS

A retrospective study of all patients identified on the general medicine department at Prachuab kirikhun hospital who presented with multiple complaints but clinically absence of neurological deficit and who underwent computed tomography scan of the brain during the 14-months period from July 2005 to September 2006, were undertaken.

The medical records were reviewed for clinical information and the clinical absence of the neurological deficit were proven by general medicine chinicians, neurologists or neurosurgeons. The lists of

the complaints for each patient were collected. Exclusion criteria are patients with history of head injury, known malignancy and previous intracranial surgery.

All patients received one or more investigations with CT scan of the brain. The CT scan was performed by axial 5 mm at the posterior fossa and 10 mm slice thickness of the rest using GE CT SYTEC 2000. The contrast study was given if it indicated.

Results were analyzed using SPSS version 11.5. Confidence intervals of 95% and p-value of $< 0.05$ were considered statistically significant. The Spearman's rank correlation coefficients at $p<0.005$ was used to determine the association between age, sex, underlying disease and abnormal CT findings. Logistic regression determines the relation between each clinical presentation and abnormal CT finding.

## RESULTS

115 patients who have multiple complaints and clinical absence of neurological deficit were included. The age ranged from 11 years to 95 years and the mean age was 53.03+/-21.86 years. There are 53.9% male (n = 62) and 46.1% female (n =53).

Each patient presented with one obvious complaint listed below;

**Table 1** Number of patients with varying age as shown in table 1 .

| Age range (years) | No. of patient |
|---|---|
| Under 30 | 20 |
| 31-40 | 20 |
| 41-50 | 14 |
| 51-60 | 11 |
| 61-70 | 15 |
| OVER 71 | 35 |

| ***Complaints*** | ***Number of patients*** |
|---|---|
| *Chronic headache* | *30 (26.1%)* |
| *Convulsion* | *27 (23.5%)* |
| *Alteration of conscious* | *19 (16.5%)* |
| *Vertigo* | *18 (15.7%)* |
| *Numbness* | *6 (5.2%)* |
| *Fever* | *5 (4.3%)* |
| *Syncope* | *5 (4.3%)* |
| *Fatigue* | *3 (2.6%)* |
| *Other* | *2 (1.7%)* |

All the CT scans of the brain with clinical absence of neurological deficit patients were reviewed. There are three patterns of interpretation as

1. negative finding means normal finding.
2. minor positive finding means abnormal finding without change of the treatment.
3. major positive finding means abnormal finding lead to change of the treatment.

Overall diagnostic yields for variable complaints with clinical absence of neurological deficit is about 59.1% (n = 68). The minor positive findings is about 23.4% (n = 27) and the major positive findings is about 35.7% (n=41), about 40.9 % (n=47) is negative findings.

There are strong correlation between abnormal CT findings and ages, underlying diseases but there is no correlation with sex, using Spearman's rank correlation coefficients at $p<0.005$ and logistic regression.

| ***Topic*** | ***p- value*** |
|---|---|
| *Age* | *0.009* |
| *Sex* | *0.441* |
| *Underlying diseases* | *0.022* |

There is no correlation between abnormal findings and each complaint such as alteration of conscious, vertigo, headache, syncope or etc, by using Spearman's rank correlation coefficients at $p<0.005$ and logistic regression.

**Table 2** Diagnostic yields classified to each complaint as shown in table 2

| Complaints | CT findings | | |
|---|---|---|---|
| | Negative | Minor positive | Major positive |
| Chronic headache | 15 (50%) | 2 (6.7%) | 13 (43.3%) |
| Convulsion | 11 (40.7%) | 9 (33.3%) | 7 (25.9%) |
| Alteration of conscious | 5 (26.3%) | 5 (26.3%) | 9 (47.4%) |
| Vertigo | 7 (40.7%) | 6 (33.3%) | 7 (25.9%) |
| Numbness | 2 (33.3%) | 1 (16.7%) | 3 (50%) |
| Fever | 3 (60%) | 0 | 2 (40%) |
| Syncope | 7 (80%) | 0 | 1 (20%) |
| Fatigue | 0 | 3 (100%) | 0 |
| Other | 0 | 1 (50%) | 1 (50%) |

| ***Complaints*** | ***correlation significance*** |
|---|---|
| *Chronic headache* | *-0.57* |
| *Convulsion* | *-0.58* |
| *Alteration of conscious* | *0.109* |
| *Vertigo* | *-0.03* |
| *Weakness* | *0.13* |
| *Numbness* | *0.058* |
| *Fever* | *0.011* |
| *Syncope* | *-0.136* |
| *Other* | *0.135* |

## DISCUSSION

Due to the risk of radiation exposure, contrast induced reactions and expenses, the CT scan of the brain must be performed only in the necessary cases. In the clinical absence of neurological deficit patients, excepted in trauma, there were few studies of finding diagnostic yield for CT scan of the brain. Hirano et al presented that diagnostic yields of CT scan of the brain in absence of neurological deficit is low (6% for true positive and 8.5 % with leading to treatment change).[1] In this study, the diagnostic yields of CT scan of the brain was about 59.1% and major positive findings with leading to alter management about 35.7%. The different in the results may be due to more strictly following guideline in each complaint than the previous study. In convulsion, nearly all of the positive findings are firstly generalized seizure, complicated seizure[2] and having underlying disease as AIDS which prone to opportunistic infection and need to imaging. Some of the negative studies are alcoholic withdrawal syndrome. If there were better strictly guideline to be followed with exclusion of the alcoholic withdrawal syndrome patients, the diagnostic yield would be higher.

Another reason of low diagnostic yield may be due to the difficulties in finding out of the accuracy of clinical assessment especially in older patients. For example, in chronic headache and alteration of conscious, the evidence-based red flags for headache are paralysis, papilledema and reduced conscious level.[3] In most positive studies in both chronic headache and alteration of conscious the patient have an advanced ages and pre-existing diseases prone to evaluation actually conscious level such as alcoholism, cirrhosis with impending hepatic encephalopathy. It may be resulting in underestimate exactly conscious level to normal level in clinical records.

There are strong correlation between advanced age, pre-existing disease and abnormal CT finding. If patient have more advanced age or pre-existing disease, he will have chances to be detected the abnormal CT both major and minor positive findings.

Takeda et al presented atrophy of the brain started to occur in the 40s in men and the 50s in women. Both CSF space volume and BAI; brain atrophy index (% CSF space volume / cranial cavity volume) increased exponentially with age after the 30s in both sexes.[4] It means even in the normal CT scan of the brain, older patients will show abnormal finding as brain atrophy which interpreting as minor abnormal finding.

Gur RC et al presented gender differences in age effect of brain atrophy by men who are susceptible to ageing effect than women.[5] Takeda et al also sup ported that BAI will doubled in 19.4 years in men and 17.4 years in women.[6] Even more in the same mean range of age in both sexes, in this study, there is no correlation with sexes and the abnormal CT finding. The inadequate sample size may possibly be the answer.

M wasey et al presented diagnostic yield in vertigo with clinical neurological deficit to be low and not cost effective to be done in emergency cases of dizziness.[7] In this study, there were high diagnostic yields because nearly entire of the patients with positive study have old ages with risks of factors as DM, HT. The major positive study is cerebral infarction.

In fever, the diagnostic yield is about 40 %. It may be related to the positive patients who are immuno-compromised as AIDs and prone to have opportunistic infection with demonstrable neurological symptoms. But on the other hand, the major positive study in our study is cerebellar AVM which clinically presented with fever and less severe headache. There is no definite positive cerebellar sign. But due to too small sample size, this cannot be concluded for this indication.

**BAI** = Brain Atrophy Index

In the literature reviews there were evidence varying from 10-78.6 % positive diagnostic yield in syncope[8] which is about 20 % of positive findings in this study. The only one with positive study has pre-existing diseases as DM, HT. This should be suggested to the clinician for requesting CT scan of the brain in syncope patients especially in no pre-existing disease after performing the other investigations.

The rest of the complaints as numbness, fatigue or others cannot be evaluated due to too small sample size. There are no relation between each complaints and abnormal finding from CT scan of the brain, may be also due to too small sample size. In further study, it should delineate diagnostic yield of the CT scan of the brain for each complaints with absence of neurological deficit in greater sample size.

## CONCLUSION

The overall diagnostic yields in the computed tomography of the brain in variable complaints and clinical absence of neurological deficit patients are not low when strictly following the guideline. In advanced ages and pre-existing disease, patients prone to have abnormal CT findings even there is no absolute indication. But different sexes have no correlation in opportunity for detecting abnormal CT finding.

## ACKNOWLEDGEMENT

The author feel indebted to the radiographic and general medicine department of the Prachuab Kirikhan hospital for data collection, Dr. Supunnee Praditsathawong for research reviewing and Mrs. Kulnita sungkua for statistic analysis.

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# LEFT-SIDED DIAPHRAGMATIC HERNIA SIMULATING A LEFT PLEURAL EFFUSION: A CASE REPORT

**Nitaya THONGSIBKAO,[1] Supaporn KITVANITPASERT[1]**

## ABSTRACT

This is a case report of delayed presentation of Congenital Diaphragmatic Hernia, simulating a left pleural effusion on the routine chest X-ray. Subsequent Computerized tomography (CT) proved that was the diaphragmatic hernia, containing the large bowel and omentum.

**Keywords:** Diaphragmatic hernia, pleural effusion, Computerized tomography(CT).

## INTRODUCTION

Congenital Diaphragmatic Hernia usually presents as the respiratory distress in neonatal period. The incidence is about 1: 3000 live births. There is some delayed presentation, such as dyspnea, chest pain, abdominal pain, nausea, vomiting, etc, which may be discovered from 1 month of life up to adulthood.[1-5] This case report described the clinical and unusual findings on the chest films. The diagnosis was proved by the Computerized tomography, subsequently. Chest radiographs, Computerized tomography of the thorax, upper GI study and barium enema were illustrated.

## CASE REPORT

A 26 years old Thai male patient presented with dyspnea for 1 week. He has no history of trauma or underlying disease. Clinical examination revealed a healthy young man with decreased breath sounds and dullness on percussion at the left lower hemithorax.

Chest film showed soft tissue density in the left lower hemithorax with meniscus sign (Figure 1A ) and left lateral decubitus film revealed that density, moved along dependent part. (Figure 1B). His previous medical record showed normal chest x-ray 5 years ago. The initial impression was the left pleural effusion, but no fluid was found from the thoracocentesis. So the CT scan of the thorax was performed, on reviewing the CT scan, it showed contents from the abdominal cavity, such as omentum and large bowel loops. The omental fat was depositing along dependent part of left hemithorax. (Figure 2 A-D)

Herniated distal transverse colon, splenic flexor and proximal descending colon were confirmed diagnosis by the barium enema study (Figure 3). Upper GI series revealed no part of stomach herniated into the chest. (Figure 4)

Although the treatment of choice is surgical repair of the diaphragm, but the patient refused.

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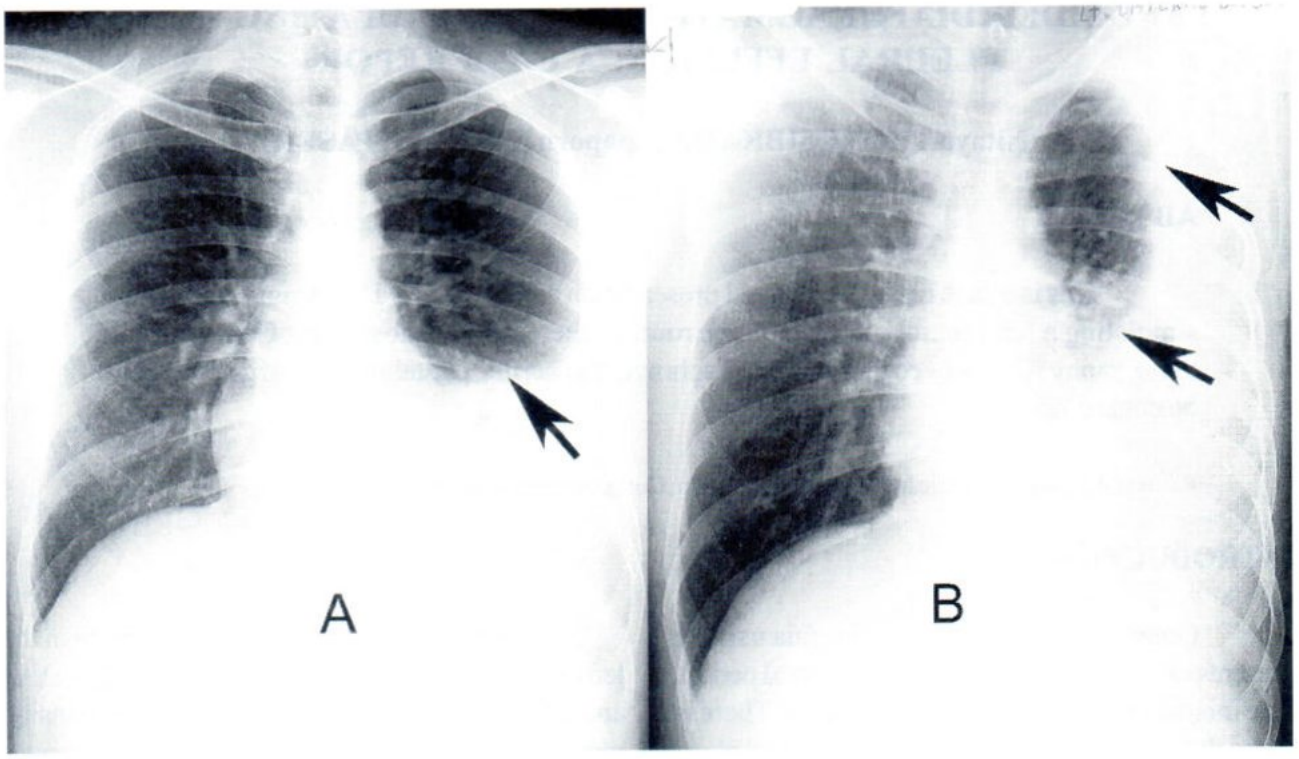


**Fig.1-A, B** Chest film PA (A) showed soft tissue density in the left lower hemithorax with meniscus sign (black arrow) and on left lateral decubitus film (B) also confirmed that the soft tissue density was movable along dependent part, likely to be free fluid (black arrow) in the pleural cavity.

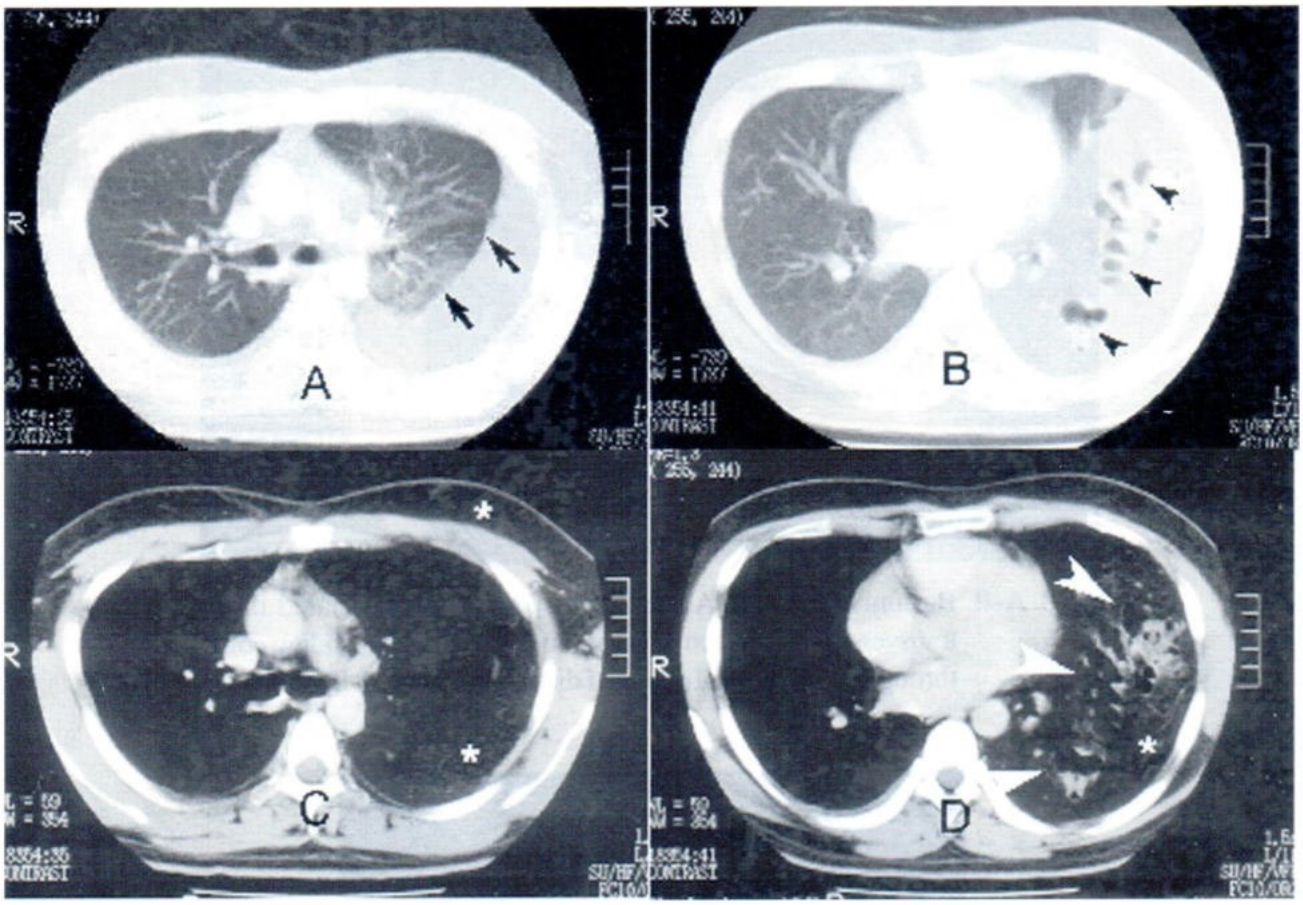


**Fig.2 (A- D)** Thoracic CT scans :

**Fig.2 A, 2C** At the carinal level, there was fat density lesion occupying along the posterolateral portion of the left hemithorax, produced "meniscus's sign" (black arrow), resembling of pleural fluid curve. Note the density of fat was as the same as subcutaneous fat (*). This is corresponding with omental fat.

**Fig.2B, 2D** At the four chambers view level, there were large bowel loops (arrow head) surrounding with omentum fat (*) in the left hemithorax.

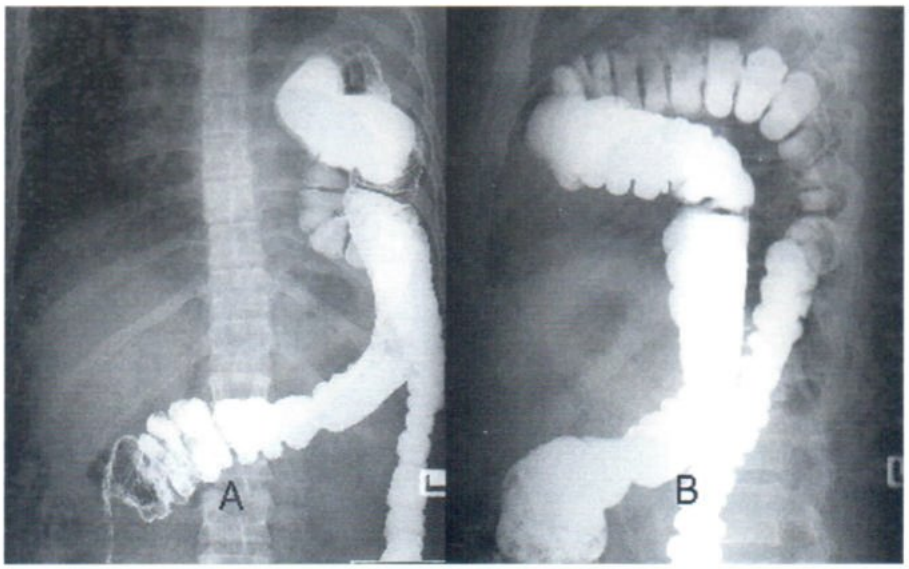


**Fig.3 A-B** Barium enema AP (A) and lateral (B) showed herniated distal transverse colon , splenic flexure and proximal descending colon through posterolateral defect of diaphragm into left hemithorax.

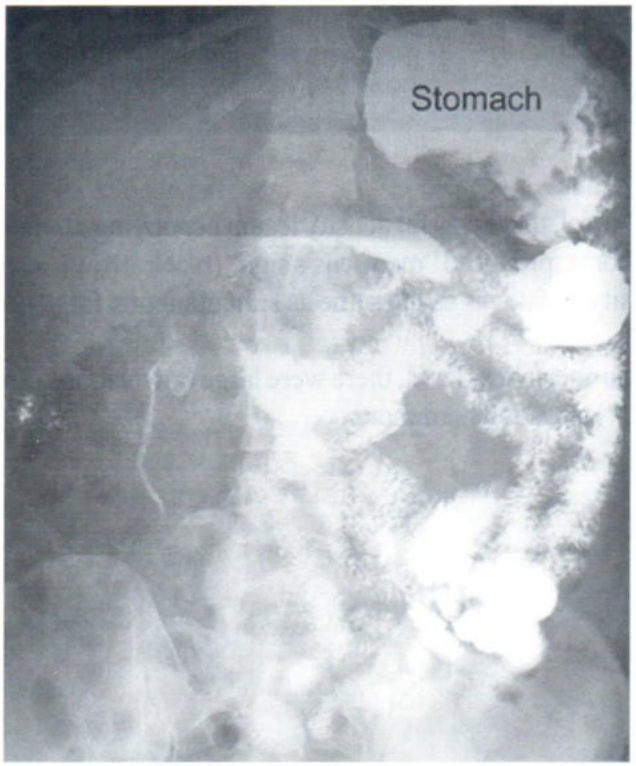


**Fig. 4** Upper GI study reveals that there is no part of stomach, herniated into left hemithorax.

## DISCUSSION

Dorsolateral congenital diaphragmatic hernia or Bochdalek hernia(B-D hernia) is the most common of congenital hernia that is a defect of the posterolateral aspect of diaphragm, and resulting to herniation of the intraabdominal organ into the left hemithorax. In most case there is no peritoneal sac.[2-4] Clinical presentation is usually during neonatal period as respiratory distress. The delayed presentation may be from 1 month up to adult hood, although it is uncommon in adult life. The incidence of delayed presentation is 5-25%.[5-8] The oldest patient which was report in the literature is 46 years.[9] It is known that a previous normal chest film does not rule out the presence of hernia.[3,6-7,10-11] The chest symptoms in adult life are varied from mild respiratory symptom to the death from the compromised cardiovascular and respiratory systems, due to mass effect from herniated organ. The abdominal symptoms may be vague such as dyspepsia, nausea and vomiting to severe strangulation or perforation of bowel.[3-4, 12-14] The hernia has also been reported as simulating a pleural effusion.[9,15-16]

The explanation offered for the delayed presentation is that the liver and spleen protect the bowel to herniate through small diaphragmatic defect. However, when the defect is increasing in size with somatic growth and herniation may be provoked by mechanical factors that increased intra-abdominal pressure such as coughing, sneezing, intestinal obstruction, obesity, pregnancy, etc.[3, 17-18]

Plain films, barium meals, barium enema, Computed tomography and Magnetic resonance imaging (MRI) establish the diagnosis.[9, 18-20] It may be diagnosis only with unusual course of the nasogastric tube, if there is herniation of the stomach into the thoracic cavity.[6,13] Barium meal or barium enema will be useful to demonstrate the herniated gastro-intestines. CT scan provides an accurate and non-invasive method for the diagnosis of suspected diaphragmatic herniation. Coronal MRI is valuable in demonstration the relationship of the herniation to the diaphragm. Because of the life threatening complications such as cardiopulmonary arrest due to mediastinal compression by herniated viscera, failure to thrive, incarceration or strangulation of bowel or acute bleeding, some authors recommend surgery immediately upon firm diagnosis.[2-3,6,21]

The herniated organ in the chest cavity in this case was the large bowel together with omentum. The movable and layer of omental fat in the dependent part of the chest films made the misdiagnosis as the pleural effusion. The correct diagnosis was made by CT scan, which was clearly demonstrated the herniated abdominal organs into the left hemithorax.

In conclusion, the delayed presentation of congenital diaphragmatic hernia and the variable symptoms make difficulty in diagnosis, so a careful examination and a strong index of suspicion are useful to reach the correct diagnosis.

## ACKNOWLEDGEMENT

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# PERCUTANEOUS CT-GUIDED RADIOFREQUENCY ABLATION OF PRIMARY LUNG CANCER: A CASE REPORT

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P. PAKCHANANUN, MD,[2] K. TANISARO, MD,[3]
S. HAIRUNPIJIT, RT[1]

## ABSTRACT

Successful application of percutaneous CT-guided radiofrequency ablation (RFA) of a peripheral bronchogenic carcinoma in a 62 years old female patient was reported. RFA was the favored treatment option in this patient, who was not a candidate for surgery and presuming inoperative stage. A 14 G Leveen Needle Electrode (Radio Therapeutics, Corporate, USA) with an array diameter of 4.0 cm. connected to a 200 watt Generator (RF 3000, Radio Therapeutics Corporate, USA) was inserted into a 3.5 cm. squamous cell carcinoma of the lateral basal segment of the right lower lobe. RFA resulted in almost completely tumor necrosis replacing by thin-wall cavitation on post-ablation CT-imaging. After treatment of post procedural pneumothorax and post-ablation pneumonia the patient had a better life quality, with gaining in weight for at least 6 months of followed up period. Further clinical experience and prospective studies for a longer period are necessary to determine the long term efficacy of RFA in the treatment of lung tumors.

## INTRODUCTION

Primary bronchogenic carcinoma is among the most common occurring malignancies in the world and is the leading cause of cancer death. Standard surgical resection and lymph node dissection remain the foundation for the treatment of early stage of NSCLC and isolated pulmonary metastases.[1,2] Conventional treatment strategies for treatment of patients with malignant lung tumors in advanced stages include surgery, chemotherapy, and radiation. Unfortunately many patients found are not suitable for operation due to advanced-stages of disease or having co-morbidities that preclude surgery. Conventional treatment with radiation and/or systemic chemotherapy may not significantly improve the survival in these patients.[3,4]

Percutaneous RFA under CT guidance is a minimally invasive, effective, and safe method for the treatment of some malignant and benign conditions in the lungs.[3,5,6] Radiofrequency ablation (RFA) has been used for a decade for the treatment of primary and secondary liver tumor.[7] RFA is a method of tumor destruction that works by generating radiofrequency waves that are converted into heat, thus producing coagulation necrosis of the lesion.[8] Early results are promising and indicate that substantial tumor reduction and eradication is possible.[9] The advantages of percutaneous RFA over invasive surgery include its potential for reduction of morbidity and mortality, decreasing cost, and ability to be performed on an outpatient basis.[10] Recently, RFA is

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feasible and can be performed safely in the setting of an open thoracotomy. Complete tumor cell necrosis was noted in the small tumors.[11] Improvements in technology have made it possible to treat larger lesions by RFA and this has led to a wider clinical applications.[1] Although RFA has been used for unresectable liver lesions with success,[12] to our knowledge very little experience of bronchogenic carcinoma treated by CT-guided percutaneous RFA has been reported. The surrounding lung parenchyma provides an "insulating effect" and thereby represents an optimal environment for RFA of lung tumors.[3] As a minimally invasive technique, RFA may be a complement to standard treatment methods in the palliative care situation, and hence alleviate the patient symptoms and improving life quality.

## CASE REPORT

A 62 years old female with a presumptive diagnosis of lung cancer on imaging was referred to the Chest Disease Institute. The patient had no underlying disease. Initial CT scan revealed a 3.5 cm.x 3.5 cm. bronchogenic carcinoma in the lateral basal segment of the right lower lobe, without hilar/mediastinal lymph node enlargement. However there were two small nodules less than 1 cm. in the RML that assumeed to be metastatic nodules with minimal right pleural effusion. No endoluminal tumor was detected at bronchoscopy. FNAB was performed and confirmed a diagnosis of RLL non-small cell lung cancer. First, the assuming tumor staging was stage IV due to non -provable two small RML nodules with also minimal right pleural effusion. The patient refused surgery and her disease staging relatively was not suitable for surgery. The decision was made to treat the tumor with RFA followed by chemo and radiotherapy. After informed consent was obtained, CT-guided percutaneous RFA was performed under conscious sedation and analgesia, using 7 mg midazolam hydrochloride (Dormicum) and 90 mg pethidine chlorhydrate injected intravenously. Vital signs and cardiac status were monitored by pulse oxymetry and electrocardiography throughout the procedure. Spiral CT scans (Picker 5000, Philips, Eindhoven, The Netherland) with 5-mm. contiguous slice were performed to plan the intervention. The depth from the skin to the edge of the lesion was calculated from a relevant CT image. Local anaesthesia was obtained using 10 ml of 0.5% bupivacaine solution. A 15-gauge Leveen Needle Electode tines forming as umbrella-shaped array diameter of 4.0 cm and a shaft working length of 15 cm. was inserted and deployed under CT guidance into the bronchogenic carcinoma in three target points (fig. 1a). After connection of the electrode with a Radiofrequency Generator (RF 3000, Radio Therapeutics Corporate, USA), RFA was started at an energy level of 80 watts. The deployed energy was increased by 10 watts up to 180 watts until tissue-impedance rose and further current flow into the tumor volume. In this patient the impedance peak was 900 ohms after an interval of 15 min. To obtain complete necrosis, after a delay period to allow re-hydration and cooling adjacent to the array wires, second and third RFA cycles were started into the other two target points, respectively.

The electrode was then removed. CT scan immediately after the procedure revealed ground glass opacities representing presumably small areas of haemorrhage into the surrounding lung parenchyma as well as pleural effusion and thickening. The occurring pneumothorax during the procedure was aspirated after the third cycle completely without the need for ICD tube drainage (figure 1b). After experiencing mild pain overnight at the puncture site, the patient had pain free. She also suffered from nausea and vomiting due to analgesic drug adverse reaction for a day. Following RFA her temperature was elevated for three days possibly due to the effected of tumor lysis. She refused the complementary chemo and radiotherapy and was discharged from the hospital seven days after the procedure, pain free without analgesia. One month after RFA the patient developed pneumonia and was admitted into the hospital in her province. After completing treatment of infection, the tumor was almost completely lysis after two months later, which showed on CT imaging replacing the tumor with thin-wall

cavities. There was no tumor mass that could be taken for tissue analysis by FNAB (figure 2). The patient's condition was clinically favorable with good appetite and gaining weight. On 3-months followed up by CT imaging, a recurrence is suggested at the anterior wall of the cavity as thickening of soft tissue shadow. FNAB was performed and cytologically proved to be a recurrence (figure 3). A second treatment was given by RFA. She still had a good quality of life at the 6 months follow up.

**FNAB** = Fenestration Aspiration Biopsy **RFA** = Radio Frequency Ablation

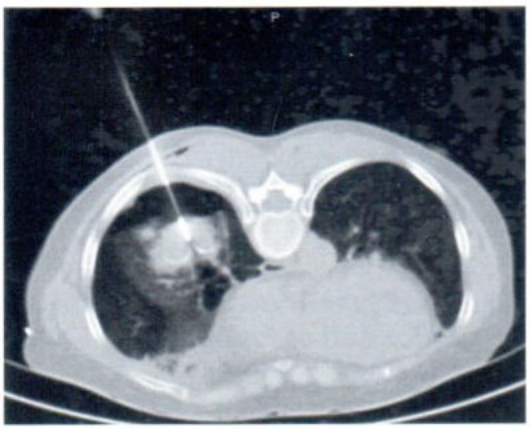
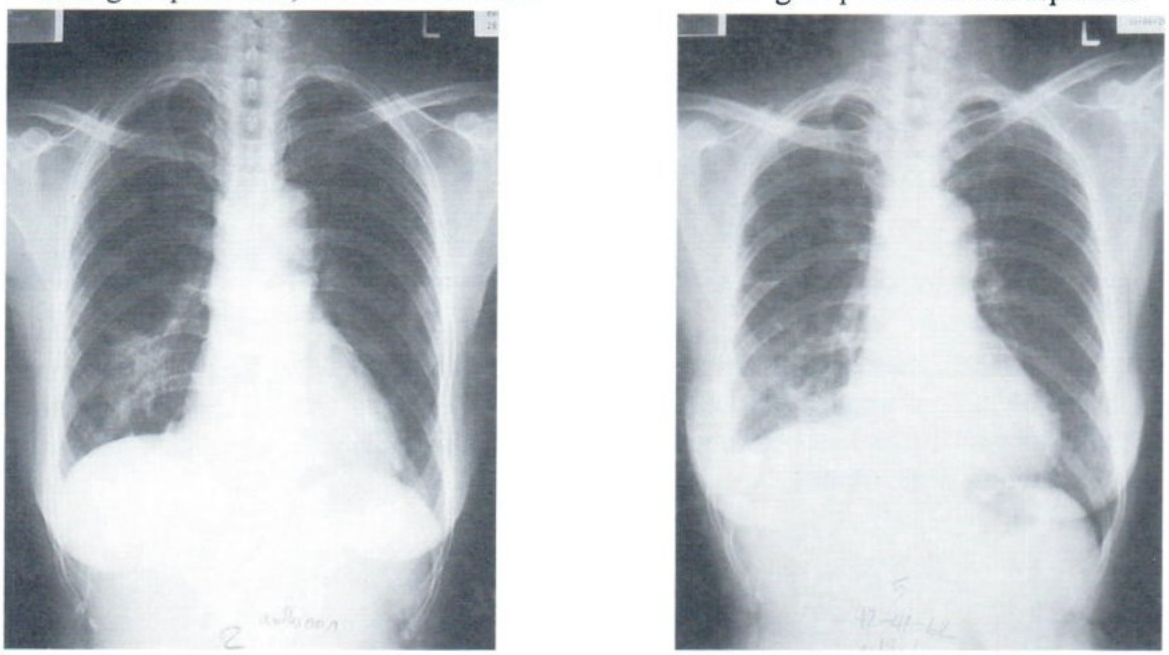


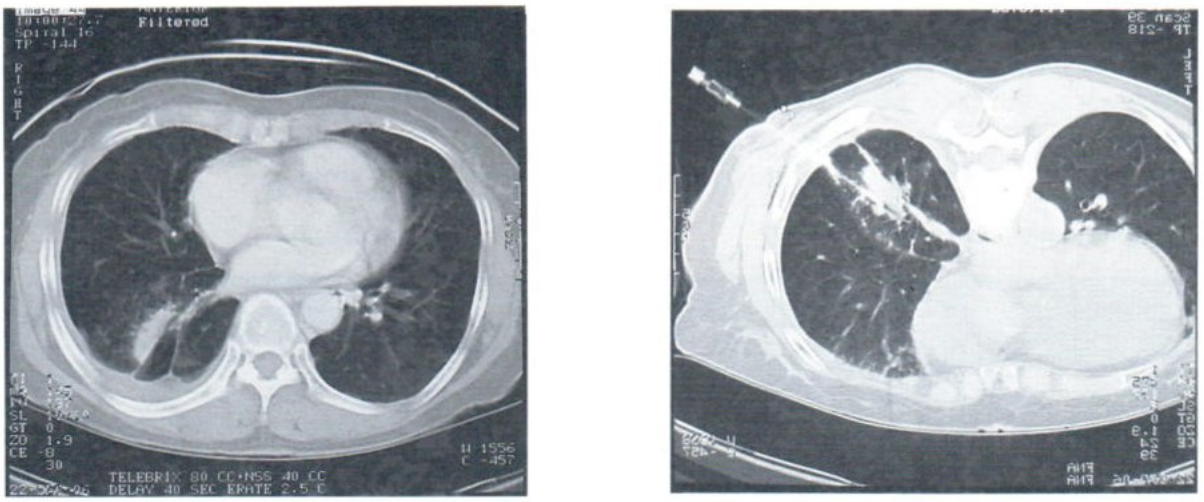
**Fig. 1a** CT scan during RFA demonstrates LeVeen needle electrode with umbrella-shaped electrode tines placed into a 3.5 cm tumor mass at the lateral basal segment of RLL. Pleural effusion, thickening and pneumothorax during the procedure, were demonstrated.

**Fig. 1b** Control CT scan immediately after RFA reveals ground glass opacities representing hemorrhage into the surrounding lung parenchyma as well as minimal pleural effusion and thickening. The occurring pneumothorax during the procedure was aspirated.



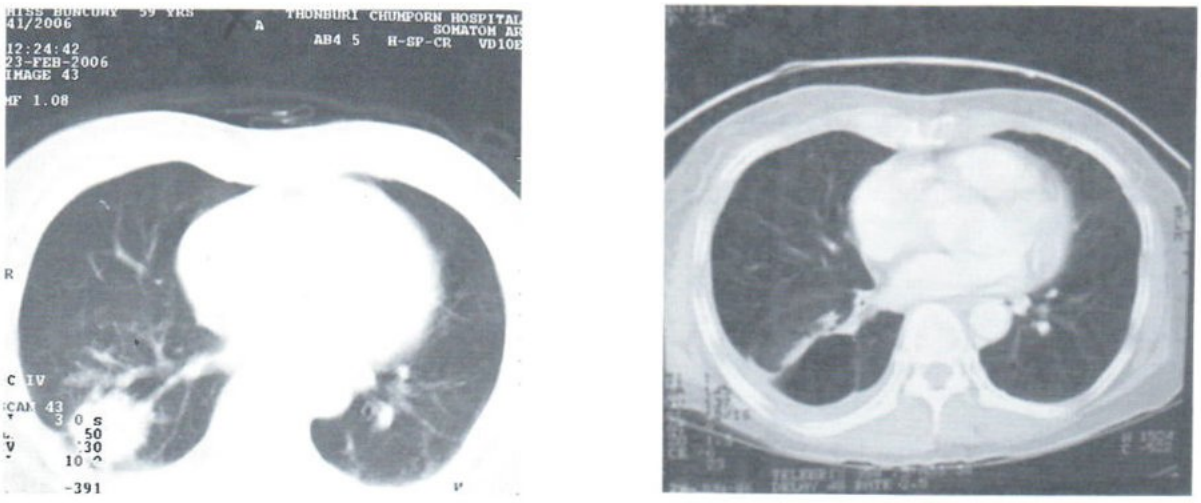
a b

**Fig.2 a,b** Comparison of prior and post radiofrequency ablation on plain chest films (a,b)




a b

**Fig.3 a,b** CT scan after 3 month post ablation shows decreased in size of thin wall cavity with pleural thickening. There was a progressive tissue thickening at the anterior wall of the cavity (a). FNAB was performed (b) and tissue analysis proved to be a recurrent tumor.




c d

**Fig.3 c,d** CT scans (c,d). The treated mass were demonstrated as a thin wall cavity (d) replacing the tumor mass at the lateral basal segment of RLL (c) after 2 month followed up. Only soft tissue thickening at the anterior wall that had not been obtained for tissue analysis. Same degree of pleural effusion and thickening is demonstrated.

## DISCUSSION

Primary lung cancer is the most common and frequent malignancy worldwide. Often, it occurs in patients who are not candidates for surgery due to co-morbid conditions (heart disease, emphysema) or having late stages of the disease.[7] In such patients, the usual treatment options are radiation or chemotherapy, or a combination of the two. Radio-frequency ablation is being considered as a new option, either alone or as an adjuvant to chemotherapy, radiation therapy, and limited pulmonary resection.[13, 14]

Since 1990, RFA is an alternative method for the treatment of liver tumors (primary and metastatic) under US or CT guidance.[7] RFA is a promising minimally invasive technique and has proved to be an effective and safe procedure for the treatment of benign and malignant tumor in several organs. There is increasing interest in its uses in the treatment of malignant lung lesions, such as bronchogenic carcinoma and occasionally lung metastases.[14] RFA can be performed under conscious sedation and local anaesthesia and offers the possibility of treating patients who are not suitable for surgery or other treatment modalities due to age, co-morbidity, or extent of disease.[5] RFA of malignant lung lesions may have a lesser morbidity than radiation therapy by preserving surrounding healthy lung tissue. The risks of thoracotomy and resection may outweigh the potential benefits of surgery.

Potential complications using RFA in the treatment of lung tumors are bleeding, infection, pleural effusion and pneumothorax.[15]

Dupuy et al.[14] first reported three patients with unresectable lung tumors treated with RF ablation. Jonathan et al.[10] described the CT appearance of thoracic neoplasm after treatment with radiofrequency ablation. RFA was the favored treatment option in our patient due to advanced staging and the affected part was rishes in blood vessels. After treatment pneumonia occurred with favored resulting. Oral prophylactic antibiotic drug which was not given in this patient was recommended to prevent post-ablation pneumonia. Pneumothorax during the procedure was monitored and completely got rid of, by aspiration during and after the procedure. No pneumothorax was shown in post-ablation CT scan, so the intercostal chest drainage tube was not necessary. Interestingly solid mass had disappeared replacing with thin-wall cavitation on 2-months follow up. CT scan showed the lesion to be suggestive of almost complete tumor necrosis. The patient's temperature was elevated for three days after RFA and decreased without antibiotic drug, likely to have been due to tumor lysis and this occurrence should not be misinterpreted as infection, that the blood count may be helpful.

In our experience, the role of CT imaging, not only provide us with accuracy in the localization planning before the procedure to be undertaken, but also helping us to assess the successfulness of the tumor lysis as the zones of consolidation surrounding the treated tumor in shape of ground glass opacities immediately after the procedure.[9] On follow up CT scan post-ablation, cavitation within the treated tumor was a common finding that often contracted over time.[10] In this case we found thin-wall cavitation representing almost representing the entire tumor necrosis, that was also decreased in size over time, on follow up. The recurrence found at the anterior wall that was lack of ground glass opacification on immediately post-ablation CT scan and thicker on 2-month follow up CT scan, was treated by a second RFA and a satisfactory result was attained. CT scan was also useful for guidance to determine for the tissue diagnosis and the tumor recurrence.[16] The chosen 4.0 Leveen Needle electrode was able to produce a spherical thermal necrosis up to 4 cm. in diameter. Dupuy and Goldberg[3] postulate that neoadjuvant cytoreduction by RFA could make radiation and systemic chemotherapy more effective. Unfortunately the patient refused other treatments. Guidelines for determining which patients are suitable candidates for

RFA of malignant lung tumors have not been developed, and therefore a careful selections of the treatment options that best serve for the individual patient is necessary. Tacke et al[2] reported that all percutaneous therapies have a significantly shorter hospitalization and recovery time compared with surgery.

In conclusion, percutaneous RFA was performed successfully in our patient. CT image was useful for determination of tumor lysis and recurrence. RFA of malignant lung tumors may reduce tumor burden and may be a complement to surgery, systemic chemotherapy or radiation therapy. The value of CT-guided percutaneous RFA in the treatment of malignant lung tumors is the subject of and ongoing prospective, interdisciplinary study conducted by our institution.

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# PALLIATIVE TREATMENT OF ADVANCED SUBEPENDYMAL OLIGODENDROGLIOMA WITH RADIOTHERAPY AND THAI HERBAL MEDICINE AS SUPPORTIVE REMEDY

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**Sukachart KIRDPON M.D[4] Pongsiri PRATHNADI M.D[5]**

## ABSTRACT

**OBJECTIVE:** To evaluate the supportive effect of Thai herbal medicine, Vilac Plus complementarity to standard palliative radiotherapy in comparison with historic control from the literature reports in subependymal oligodendrogliomas.

**METHOD:** An inoperable subependymal oligodendroglioma in a 14 years old boy being treated by palliative radiotherapy and concurrent with Thai herbal medicine (Vilac Plus) as supportive remedy.

**RESULT:** The result revealed complete response of advanced subependymal oligodendroglioma. The patient shows good quality of life until now, 43 months after the diagnosis and starting the treatment. In addition, there is also improvement of diabetes insipidus and still alive with Karnofsky's performance status 100%. Currently the follow-up time is 43 months after the initial diagnosis and treatment (craniotomy and tumor biopsy).

**CONCLUSION:** The results of radiotherapy of an inoperable subependymal oligodendroglioma using Thai herbal medicine as an adjuvant remedy has been very satisfactory with good quality of life. This combination modality of treatment present a very promising and cost effectiveness therapy, leading to the confirmation of the concept of complementary approaches on cancer therapy.

**Key word:** Subependymal oligodendrogliomas, palliative radiotherapy, Thai herbal medicine

## INTRODUCTION

Subependymal oligodendrogliomas are rare with the character of slow-growing intracranial neoplasms of the subependymal matrix.[1-4] The standard treatments are surgery. But being intraventricular tumors, they are a major challenge for neurosurgeon because of their depth and important adjacent structures. Moreover the operative risks such as visual field defect, postoperative thalamic hemorrage,

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pulmonary emboli, subdural hygroma and neurological deficit have been reported.[1-4] Therefore, in advanced cases, palliative radiotherapy alone is the available method of treatment with not fully satisfactory results due to tumor mass effect or tumor plus peritumoral edema causing increased intracranial pressure. The severe brain edema may produce sudden brain herniation. We are reporting a case with inoperable subependymal oligodendroglioma treated by palliative radiotherapy and the Thai herbal medicine (Vilac Plus) as supportive remedy. The tonic product was proven to have no acute oral toxicity in animal study.[5] No traces of prednisolone and dexametasone were detected.[6] An In Vitro study, the Vilac Plus presents an important antioxidant capacity.[7] 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 Pandurata Holtt (Kra chai) had been found to be effective anti-tumor promoting activities.[8] 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 namely Vilac Plus adjuvant to standard palliative radiotherapy in comparison with historic control from the literature reports in subependymal oligodendrogliomas. This study has been performed at Radiotherapy Division, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002.

## CASE REPORT

A Thai boy 14 years old presented with history of polydipsia, polyurea, behavioral changes for 4-5 months. The computed tomography brain scans revealed subependymal tumor and dilatation of the whole ventricle. The patient had been treated by craniotomy and tumor biopsy. The pathological examination showed to be oligodendroglioma as shown in Figures 1A-1C. The suffering symptoms and complaints of the patient were severe headaches, nausea, vomiting, blurred vision, weakness of all extremities for 1 month and became semiconcious when admitted. These symptoms were due to severe brain edema and increased intracranial pressure from advanced progressive tumor. Computed tomography brain scans found progressive subependymal tumor with dilatation of the whole ventricles as shown in Figures 1D-1G.

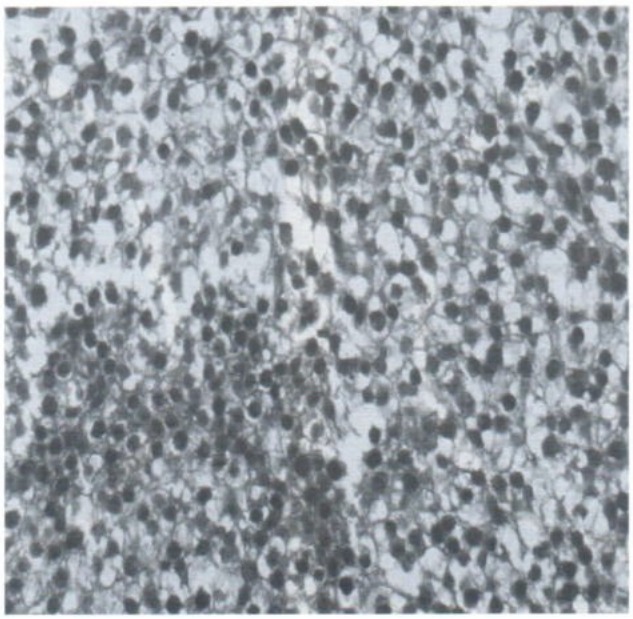

**Fig.1A (x200)** Oligodendroglioma, the tumor composed of uniform round cell with scanty vascular septa.

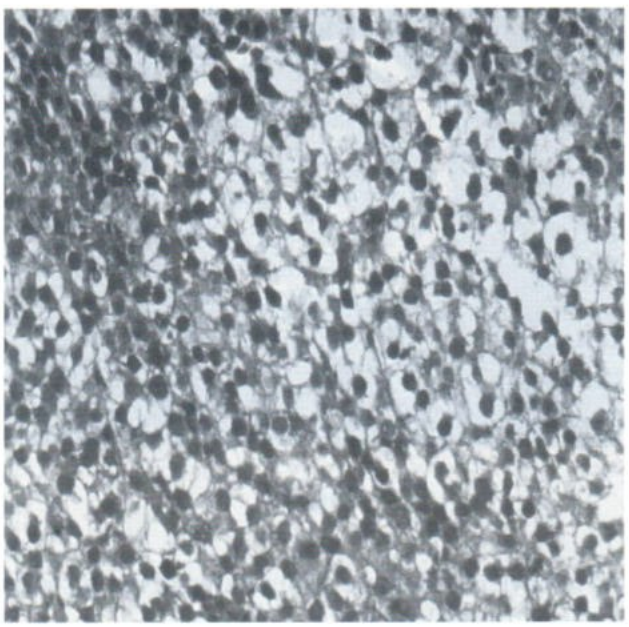

**Fig.1B (x200)** Oligodendroglioma, the cytoplasm was moderate and clear.

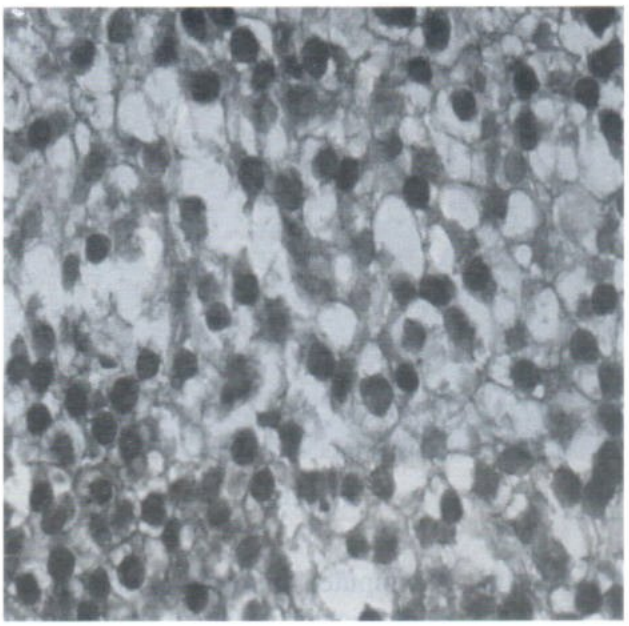

**Fig.1C (x400)** Oligodendroglioma, the nuclei were round and uniform. The nuclear chromatin was rather delicate.

**Fig.1A-1C** Microscopic pictures, Brain, right lateral ventricle: Oligodendroglioma.

Fig.1D

Fig.1E

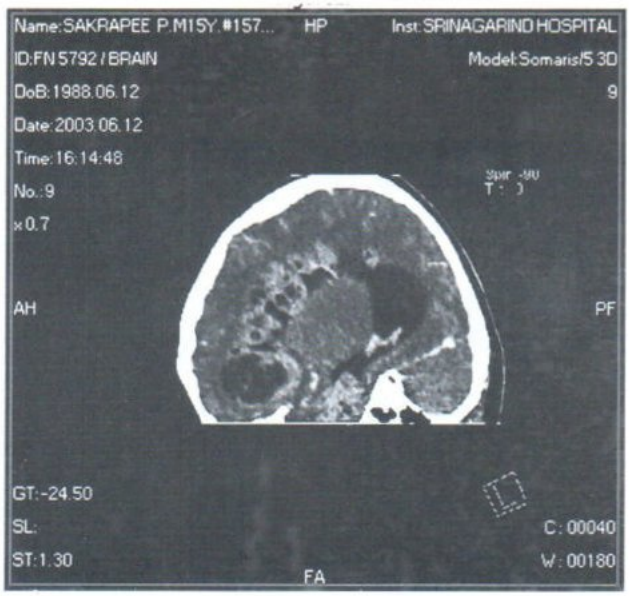


Fig.1F

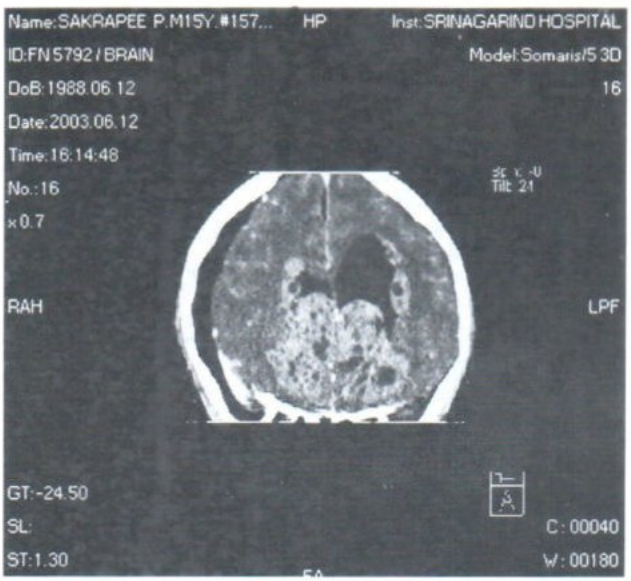


Fig.1G

**Fig.1D -1G** Computed tomography brain scans found to have progressive subependymal tumors with dilatation of the lateral ventricles in both sides of hemisphere before treatment.

## TREATMENT

1. Steroid intravenous therapy to reduce brain edema before radiotherapy.
2. Whole brain irradiation 2850 cGy in 9 weeks (titration dose) with the Thai herbal tonic **Vilac Plus**, dose 15 cc, tid, pc, orally.
3. VP-shunt to relief the symptoms of severe hydrocephalus after a tumor dose of 575 cGy in 4 weeks, titration doses.

## RADIOTHERAPY TECHNIQUE

The target volume is the whole brain and meninges. The prescribed dose is 30 Gy in 3-3.5 weeks by titration doses according to the patient was having a severe brain edema and the VP-shunting can not be performed before radiotherapy. The radiation technique used in this patient were two parallel opposing fields.

The result of treatment in this case showed much improvement. The patient can walk, right after treatment and can be able to communicate with other people. The computed tomography brain scans revealed severe hydrocephalus with no evidence of tumour left in ventricles as shown in Figures 1H- 1I. (tumor dose 575 cGy in 4 weeks) and after follow up computed tomography brain scans as shown in Figures 1J-1M revealed no evidence of tumor left in ventricles after treatment (tumor dose 2850 cGy in 9 weeks). Delayed time of radiation treatment was due to the problem of diarrhea, hypokalemia, hypernatremia, E-colisep-ticemia, poor general condition and the technical and mechanical problems of cobalt-60 unit machine. Follow up computed tomography brain scans revealed hypodense non enhancing soft tissue mass at wall of left lateral ventricle closely to the tip of ventriculostomy which was representing the non functioning of VP-shunt from granulation tissue without residual tumor left in the ventricles as shown in Figures 1N-1W. After performing VP-shunt revision, the granulation tissue had been found at the tip of VP-shunt confirmed by microscopic picture of tissue from tip of VP-shunt that revealed granulation tissue associated with the chronic inflammation as shown in figures 1X-1Z. Another work up on cerebrospinal fluid cytology revealed no malignancy cell and MRI whole spines revealed neither extra or intradural mass lesion nor abnormal enhancement with normal signal of bone marrow of the whole spines.

Computed tomography brain scans revealed no evidence of residual soft tissue tumor. The patient shows good quality of life until now, improving of diabetes insipidus and still alive with Karnofsky's performance status 100%, currently the follow-up time is 43 months after initial diagnosis (craniotomy and tumor biopsy).

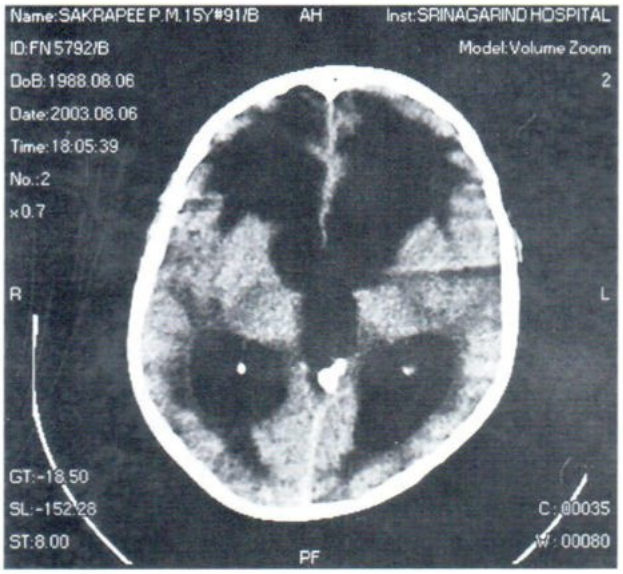


**Fig.1H** After radiation therapy with a dose of 2850 cGy in 9 weeks

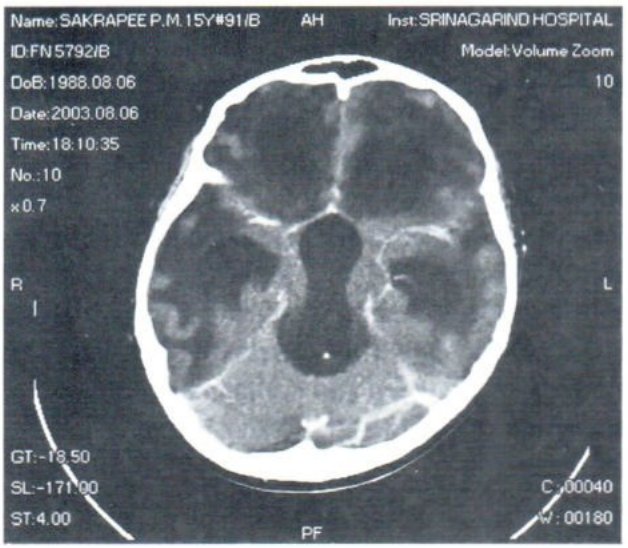


**Fig.1I**

**Fig.1H -1I** Computed tomography brain scans 4 weeks after treatment by radiation with a tumor doses of 575 cGys revealed severe hydrocephalus with no evidence of tumor left in the ventricles.

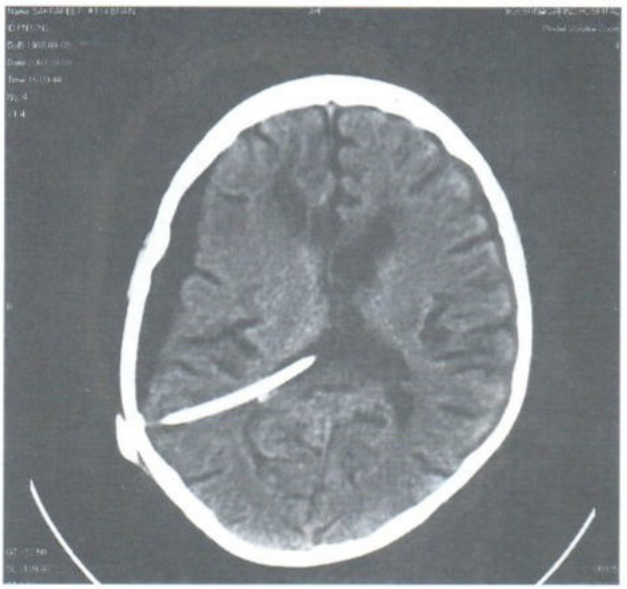

Fig.1J

Fig.1K

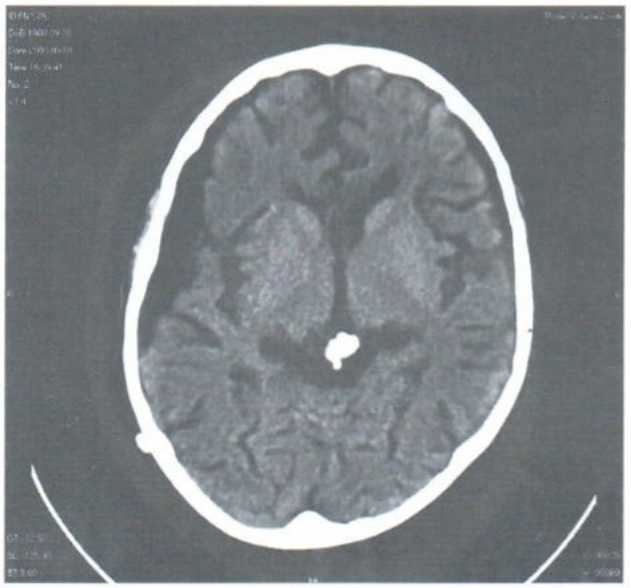

Fig.1L

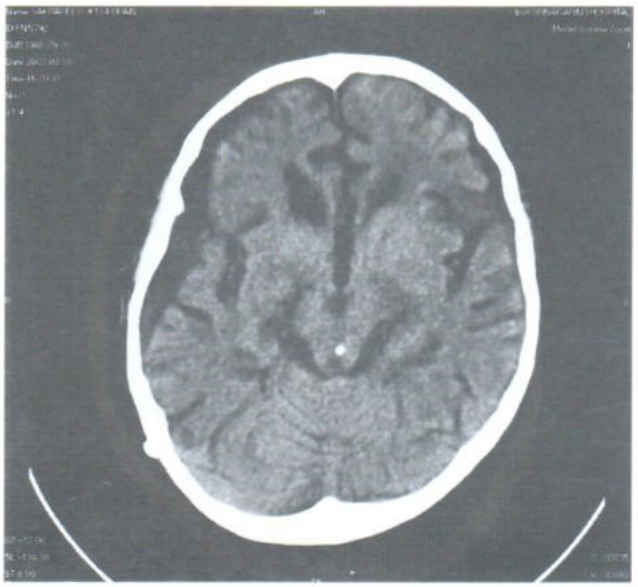

Fig.1M

**Fig.1J-M:** Computed tomography brain scans revealed no evidence of tumor left in ventricles after treatment (tumor dose 2850 cGy in 9 weeks), with improvement of hydrocephalus in comparison with the CT taken 5 weeks before, after having a tumor dose of 575cGy in 4 weeks in Fig.1I and Fig.1K above.

Fig.1N

Fig.1O

Fig.1P

Fig.1Q

**Fig.1N-1Q** Further improvement after craniotomy, biopsy and radiation therapy, followed up 15 months after treatment.

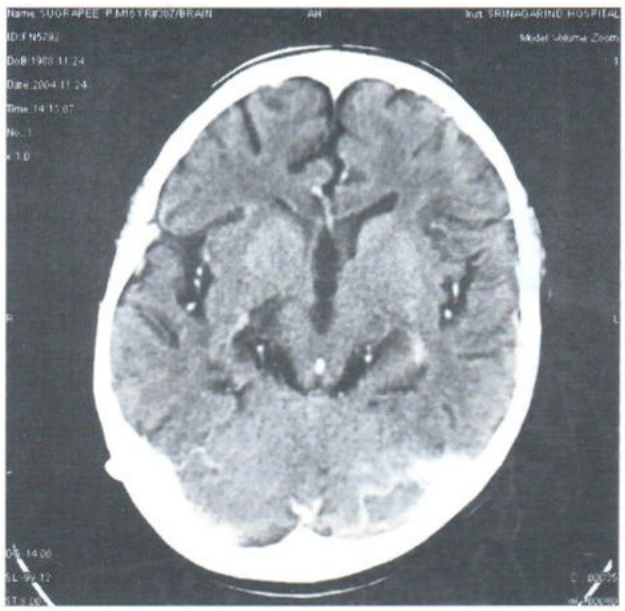

Fig.1R

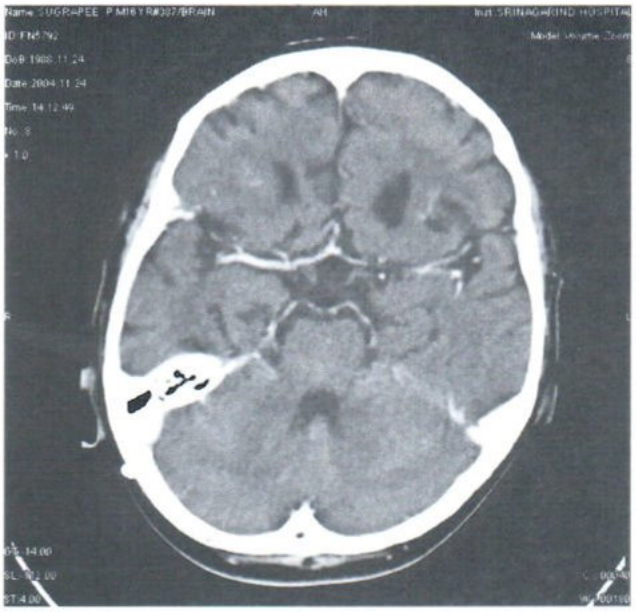

Fig.1S

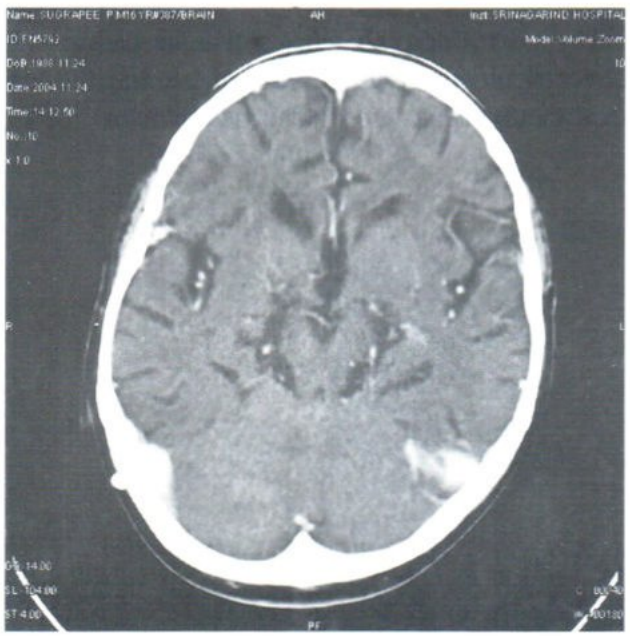

Fig.1T

Fig.1U

**Fig.1R-1U** Further improvement 15 months after having craniotomy, biopsy, and radiation therapy 2852 cGy in 9 weeks with "Vilac" supplementary and supportive therapy.

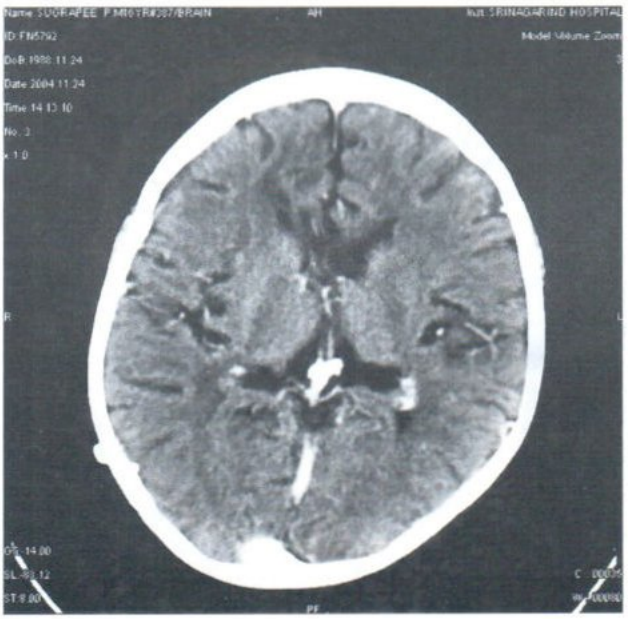

Fig.1V

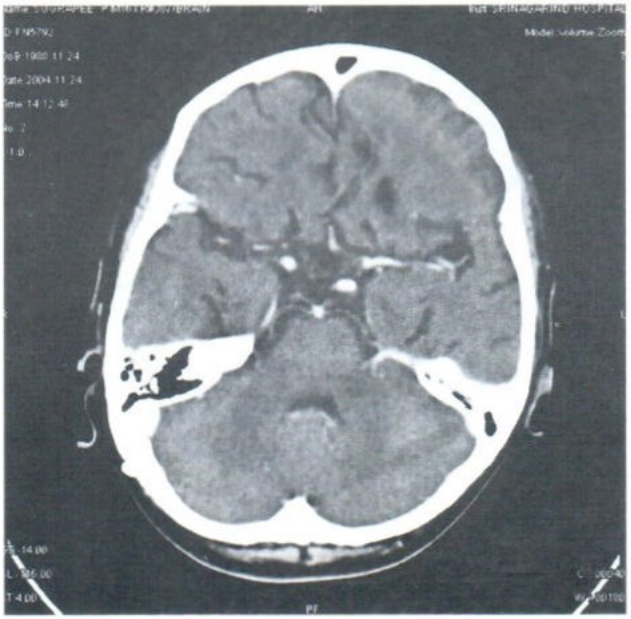

Fig.1W

**Fig.1V-1W:** Computed tomography brain scans revealed hypodense non enhancing soft tissue mass at wall of left lateral ventricle closely to the tip of ventriculostomy which was representing the non function of VP-shunt from granulation tissue without residual tumor left in the ventricles.

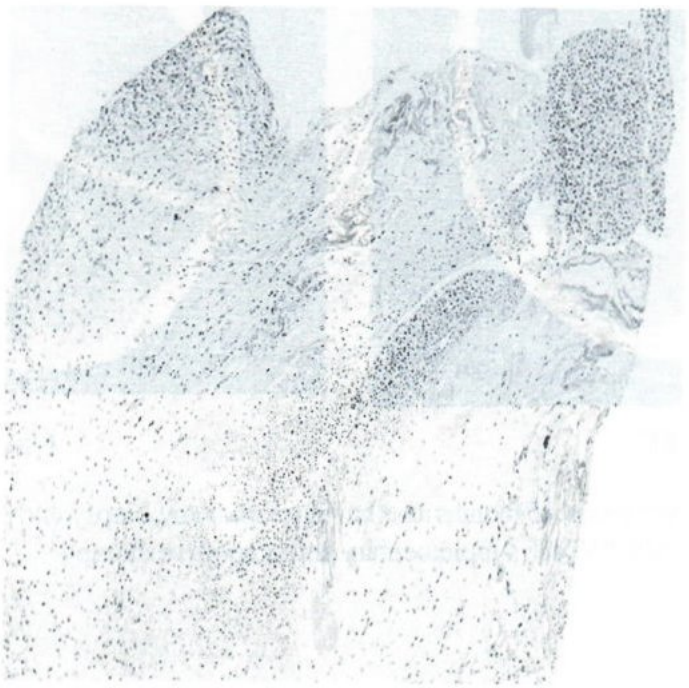

**Fig.1X (x40)**

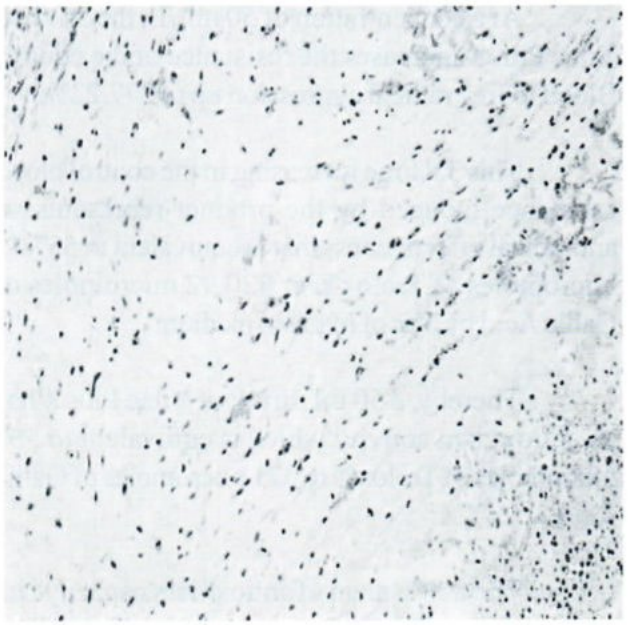

Fig.1Y (x100)

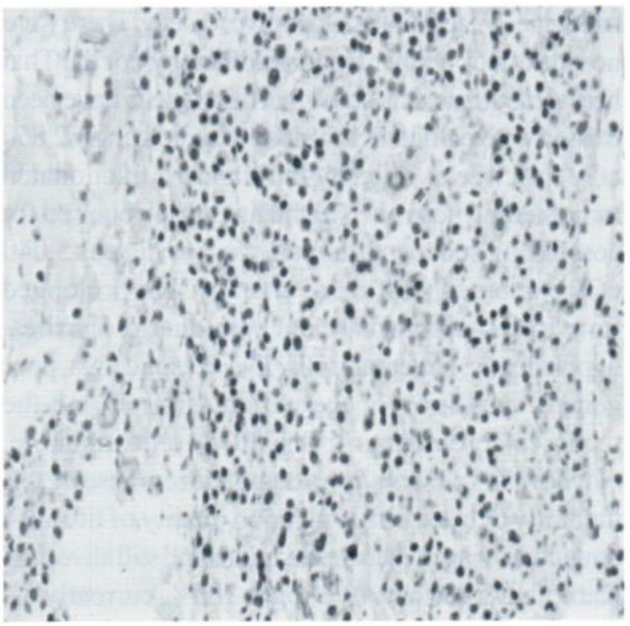

Fig.1Z (x200)

**Fig.1 X, Y, Z** Microscopic pictures of tissue from tip of VP-shunt revealed granulation tissue associated with chronic inflammation.

## RESULT

The result revealed complete response of advanced subependymal oligodendroglioma. The patient shows good quality of life until now, 43 months after treatment, in addition to improving of diabetes insipidus and still alive with Karnofsky's performance status 100%, currently the follow- up time is 43 months after initial diagnosis (craniotomy and tumor biopsy).

## DISCUSSION

Classically, oligodendroglioma are slow -growing brain tumor and have a long natural history with a median survival of over five years following the onset of symptoms. The frontal lobes are the most frequently involved region and abnormal calcifications may be seen on skull radiographs.[9] The standard treatments are surgery. The role of post-operative radiotherapy in these gliomas is not clear. Nevertheless, the limited available data suggest that post-operative radiotherapy improves five year survival of these patients. Five- year survival rates following surgery alone range from 23-82% and surgery with radiotherapy[9] range 53-100 %. Subependymal oligodendrogliomas are a major challenge for neurosurgeon because of their depth and important adjacent structures. Moreover the operative risks such as visual field defect, postoperative thalamic hemorrage, pulmonary emboli, subdural hygroma and neurological deficit have been reported[1-4] Long term results for subependymal oligodendroglioma depend on the size of surgical resection.[1-4] In advanced cases, palliative radiotherapy alone is the available method of treatment with not fully satisfactory results due to tumor plus peritumoral edema causing increased intracranial pressure. The severe brain edema may produce sudden brain herniation. We are continue our study that has been reported[10] with inoperable subependymal oligodendroglioma treated by palliative radiotherapy and the Thai herbal

medicine (Vilac Plus) as supportive remedy. There were no side effect neither from radiotherapy nor the Thai herbal medicine. It is noted that this patient have been treated with palliative low dose of radiotherapy 2,850 cGy in 9 weeks whereby the standard fractionated radiotherapy dose cited in the literature[1] required for controlling subependymoma, were as high as 5,040 cGy combined with chemotherapy. The prolonged time of radiation treatment was due to diarrhea, hypokalemia, hypernatremia, ***E-coli*** septicemia, poor general condition of the patient himself and the technical problems of Cobalt-60 unit machine. Anyhow this patient shows complete response by this modality of treatment with good quality of life until now, improving of diabetes insipidus and still alive with Karnofsky's performance status 100%, currently the follow-up time is 43 months after initial diagnosis (craniotomy and tumor biopsy).

The accomplishment of herbal cancer therapy was reported by Battle TE. et al., Harvard Medical school U.S.A., on the successful of Chinese herbal extract in chronic lymphocytic leukemia with complete remission over 10 years without chemotherapy.[11] However from our study the authors are satisfied with the uses of Thai herbal tonic (Vilac Plus) in a combined mode of treatment simultaneously with radiation therapy in the hopeless advanced cancer cases.

The impressive synergistic effect of Vilac Plus the radiation therapy evidenced by the extended longer survival time particularly in this hopeless case of cancer. This tonic product must contribute a complementarily supportive effect through its powerful antioxidant effect[7] that the analysis report revealed the impressive results of antiradical potency of Vilac Plus®. This Vilac Plus® presents in vitro as an important antioxidant capacity, which increases with the dose of the product until a concentration of 50 mL per liter of the reaction medium.

® = Trolox, Vilac, Patented by Kirial lab SPIRAL-No. Patent FR 2.642.526

At a concentration of 50 mL/L, the drink of Vilac Plus® increases the resistance of the control Blood to free radical aggression up to 277.22%.

This 3.8 time increasing in the control blood resistance induced by the product represents an antiradical effectiveness that is equivalent to 557.45 micromoles of Trolox® or 320.92 micromoles of Gallic Acid by liter of reaction medium.

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 (Spiral Test Patent)

The mechanism of the antioxidants on enhancing the therapeutic effect of cancer can be explained by the biochemical aspect of the antioxidants[12, 13, 14] including Vilac Plus® contributing to potentiate radiotherapy effect can be explained by 3 mechanisms:

(1) 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 (SM) lung cancer patients
(2) Inhibit extracellular signal for lung cancer cell proliferation and antigen production
(3) Blocking the regulation of protein synthesis of lung cancer

3 mechanisms will be the consequence of these evidences by reduction of the tumor size and space or lesion and eventually reduction the chance of distant metastasis of the tumor, where in this study, not only prolong survival time, but also no brain metastasis were noted in all cases.

## CONCLUSION

The results of radiotherapy on inoperable subependymal oligodendroglioma using Thai herbal medicine as an adjuvant remedy is very satisfactory results with good quality of life. There were no side effects either from radiotherapy or the Thai herbal medicine. These combinations are very promising and cost effectiveness therapy leading to confirmation on the concept of complementary approaches for cancer management.

## ACKNOWLEDGEMENTS

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# 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 of 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 recepter (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 staging[6-9] 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 $\leq$ 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 of 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.

**Table1** 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 ≤ 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]

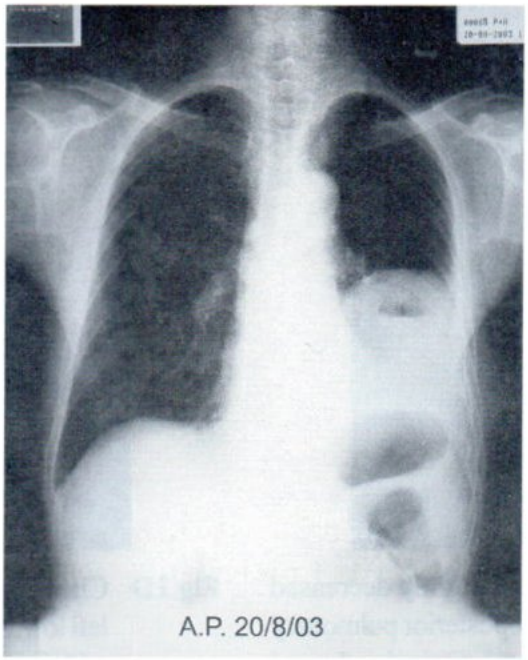



**Fig.1A** Chest film PA revealed the larged left lower posterior pulmonary cavitary mass with irregular inner border and atelectasis of left lower lung before radiotherapy treatment.

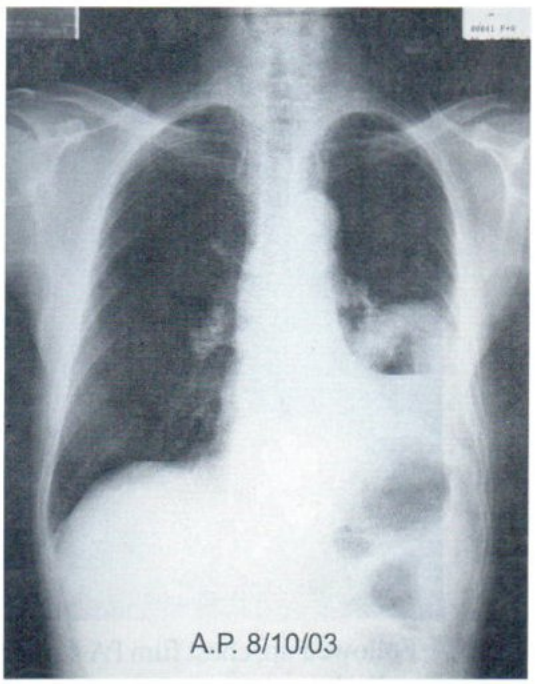



**Fig.1 B1**

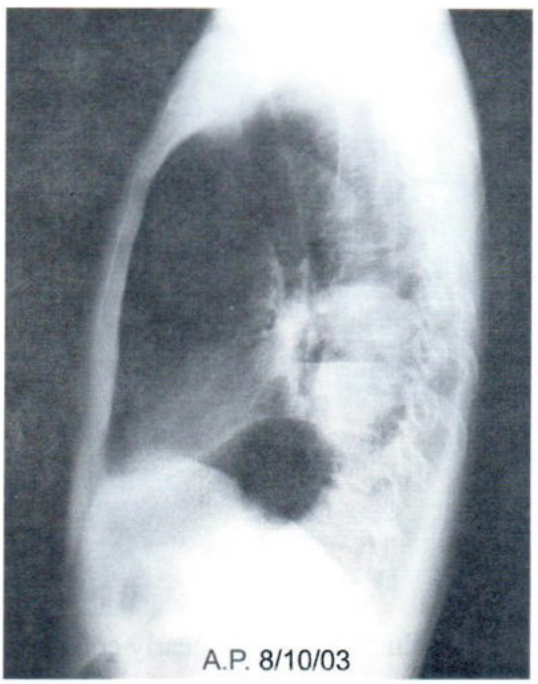



**Fig.1 B2**

**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.

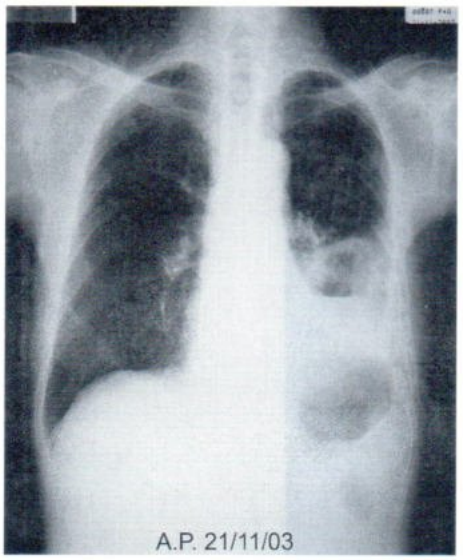



**Fig.1C** Chest film PA revealed slightly decreased in size of the left lower posterior pulmonary cavitary mass with irregular inner border and atelectasis of left lower lung after antibiotic combined with Thai herbal tonic, immediately after radiotherapy with a tumor dose of 2,160 cGy in 2.5 weeks.

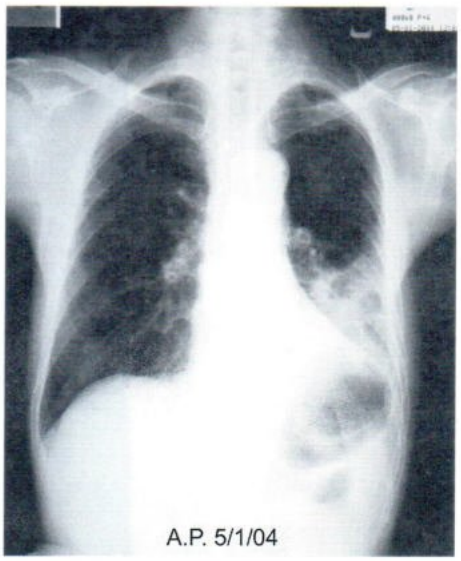



**Fig.1D** Chest film PA revealed decreased in size of left lower posterior pulmonary cavitary mass with irregular inner border and atelectasis of left lower lung after radiotherapy combined with Thai herbal tonic, 2 months after radiotherapy with a dose of 2,160 cGy in 2.5 weeks.

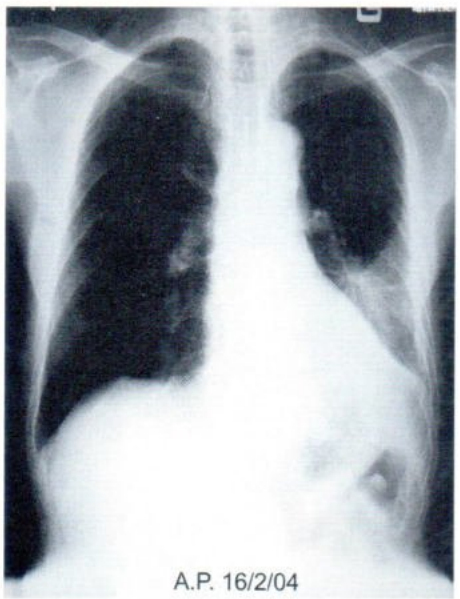



**Fig.1E** Chest film PA revealed nearly complete regression of the left lower posterior pulmonary tumor mass with atelectasis of left lower lung after radiotherapy combined with Thai herbal tonic, 3 months after radiotherapy 2,160 cGy in 2.5 weeks.

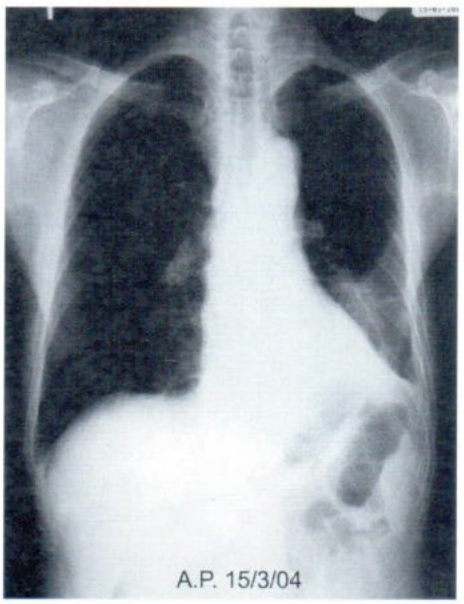



**Fig.1F** Followed up, chest film PA 4 months after radiotherapy revealed nearly complete regression of the left lower posterior pulmonary tumor mass and atelectasis of left lower lung.

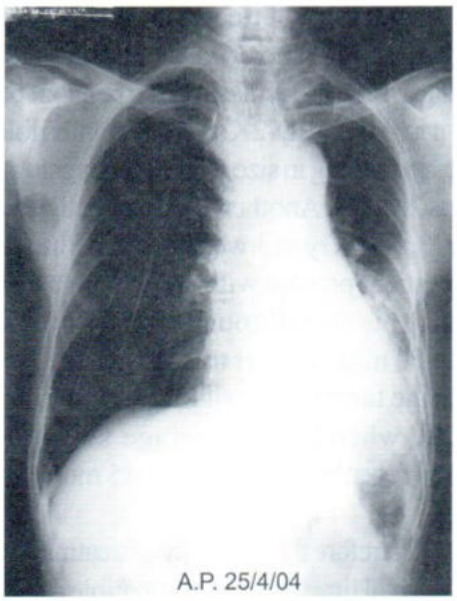



Fig.1 G1

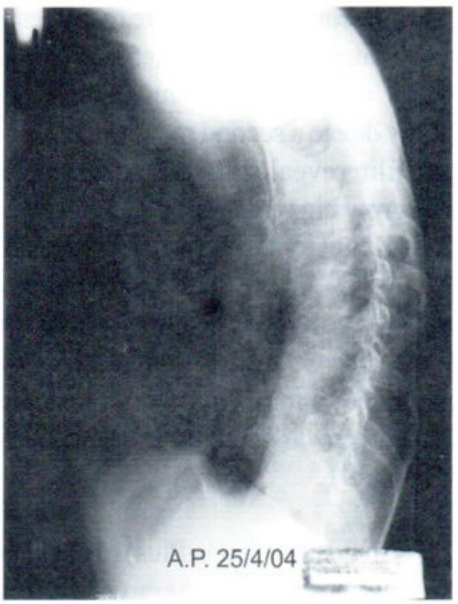



Fig.1 G2

**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($T_3N_2$-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.

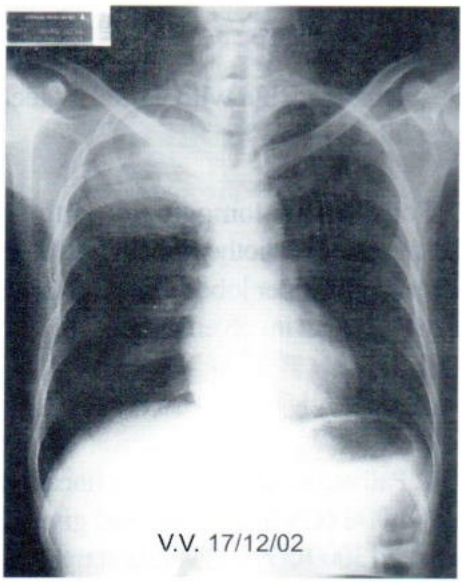
Second course of palliative radiotherapy with linear accelerator (6MV) 2,000 cGy in 2 weeks was given at right upper lung field, 6 months after palliative radiotherapy due to recurrent (1st course) of the tumor.

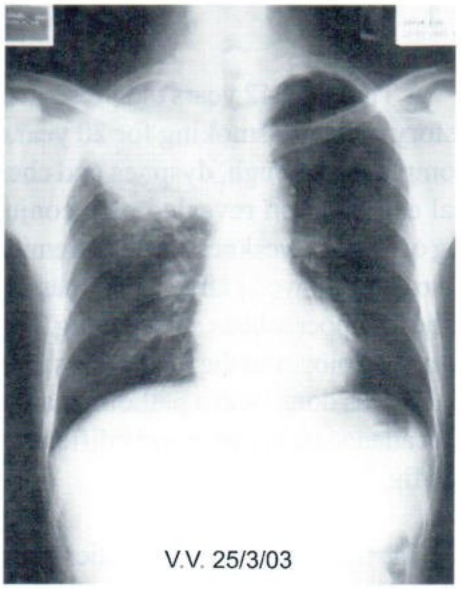
Third course of palliative radiotherapy with linear accelerator 6,600 cGy in 6.5 weeks was given at the right upper lung, 9 months after initial radiotherapy due to a second recurrent of the tumour. P.A. chest film revealed the lung mass in the right upper lobe grow bigger and also the increasing of 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.

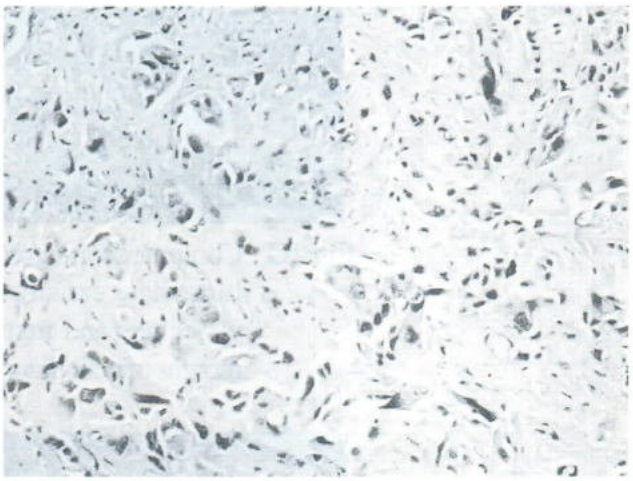


**Fig.2D** Microscopic picture(400x) Tumor cells were pleomorphic. Some of them arranged in gland-like structure. Mucin production was seen, both intracellular and extracellular in microscopic picture of adenocarcinoma, poory differentiated.

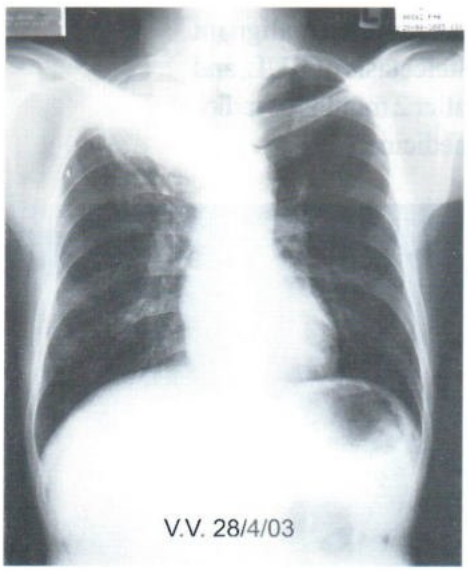



**Fig.2E** Film chest PA revealed partial regression of tumour size after radiotherapy 4,000 cGy in 4 weeks.

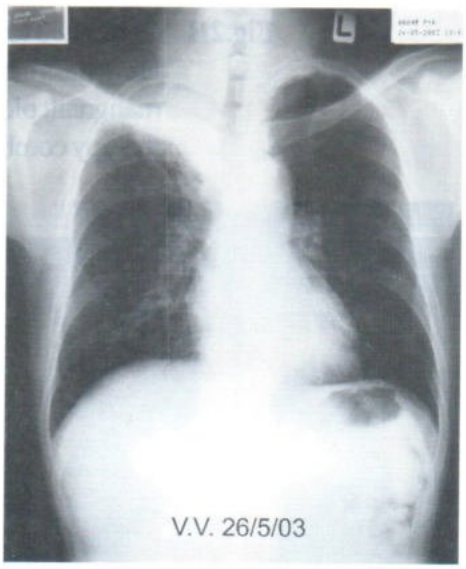



**Fig.2F** Film chest PA revealed partial regression of tumour after 1 month of radiotherapy combined with herbal medicine.

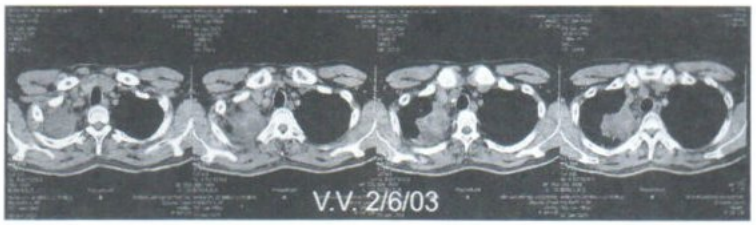



**Fig.2G** Computed tomography chest scan revealed malignant lung mass causing obstructive atelectasis of right upper lung and malignant pleural involvement after 2 months of radiotherapy combined with herbal medicine.

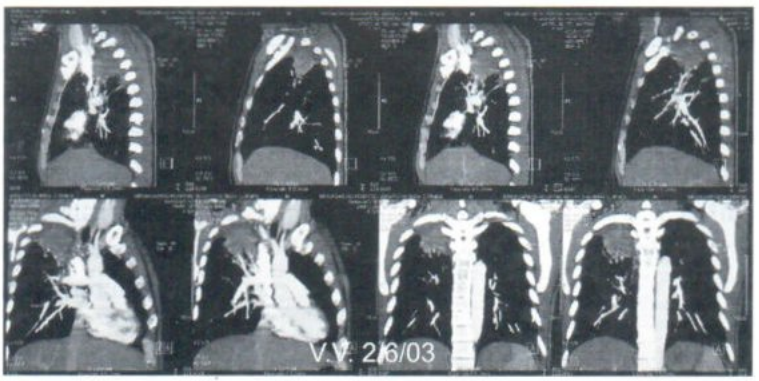



**Fig.2H** Computed tomography chest scan revealed malignant lung mass causing obstructive atelectasis of RUL, and malignant pleural involvement after 2 months of radiotherapy combined with herbal medicine.

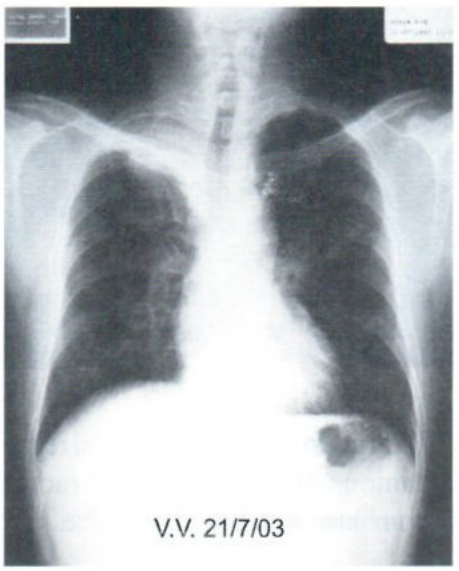



**Fig.2I** Film chest PA revealed partial regression of tumour size after 3 months radiotherapy combined with herbal medicine.

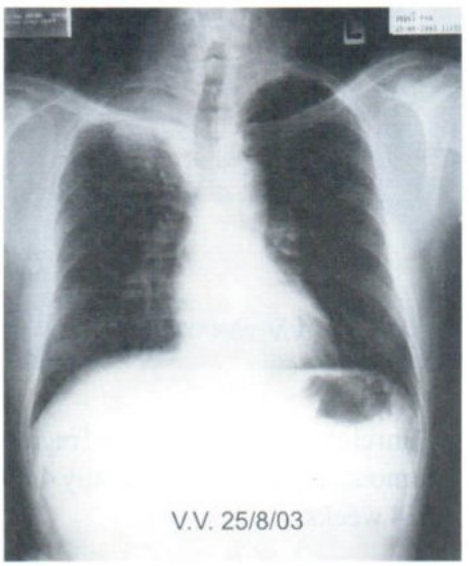



**Fig.2J** Film chest PA revealed partial regression of tumour size after 4 months of radiotherapy combined with herbal medicine.

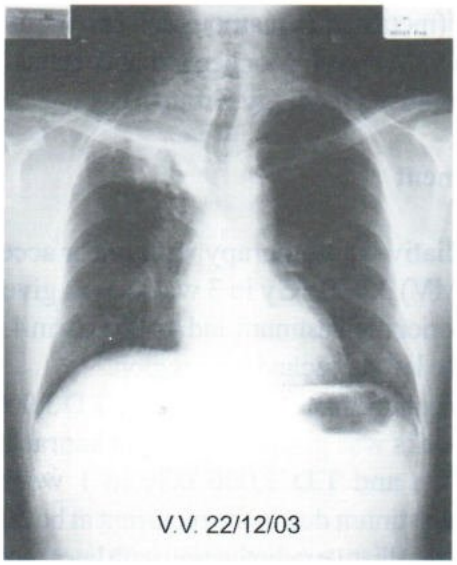



**Fig.2K** Film chest PA revealed partial regression of tumour size after 8 months of radiotherapy combined with herbal medicine.

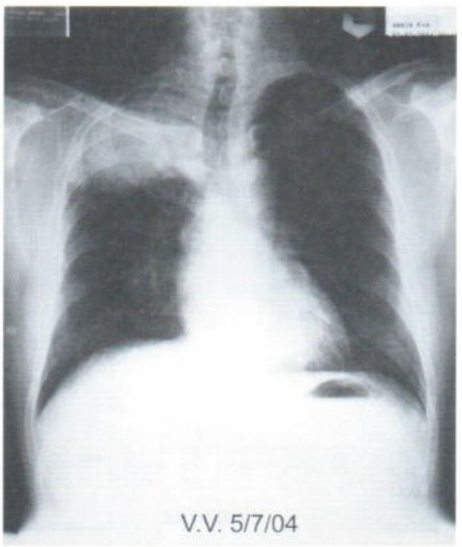



**Fig.2L** Film chest PA revealed decreased in size of tumour after 13 months of radiotherapy combined with herbal medicine.

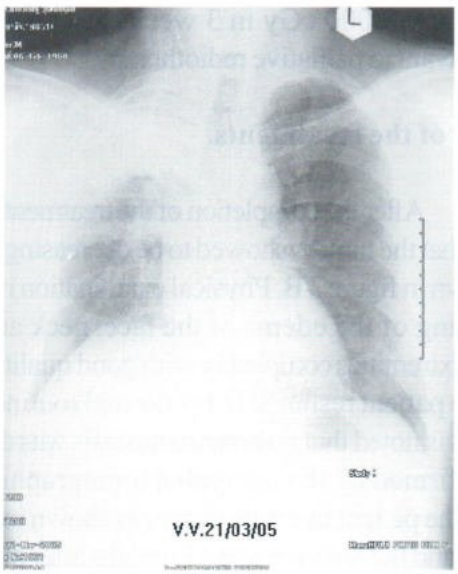



**Fig.2M** Film chest PA revealed slightly decreased in size of the tumour after 27 months of radiotherapy combined with herbal medicine.

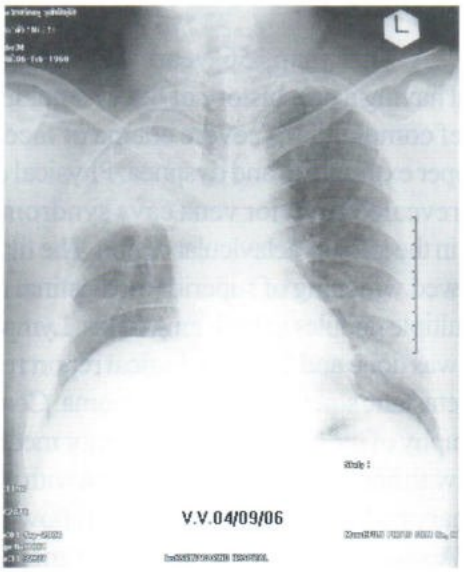



**Fig.2N** Film chest PA revealed stable of the tumour size after 45 months of radiotherapy combined with herbal medicine.

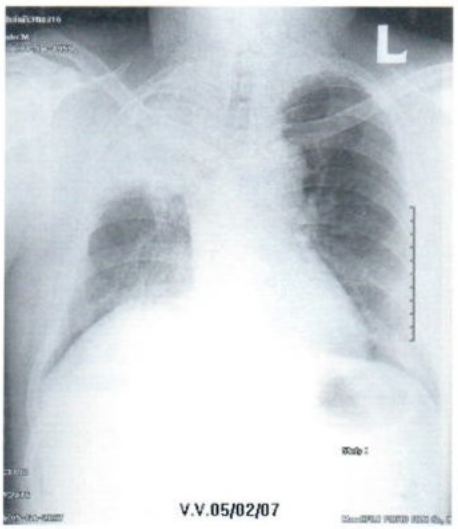



**Fig.2 O** Film chest PA revealed stable of the tumour size after 50 months of radiotherapy combined with herbal medicine .

## 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]

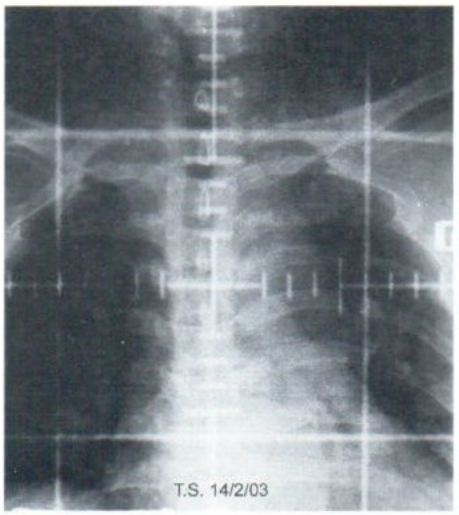



**Fig.3A** Chest film PA showed anterior mediastinal and left supraclavicular masses with multiple nodules both lungs before treatment.

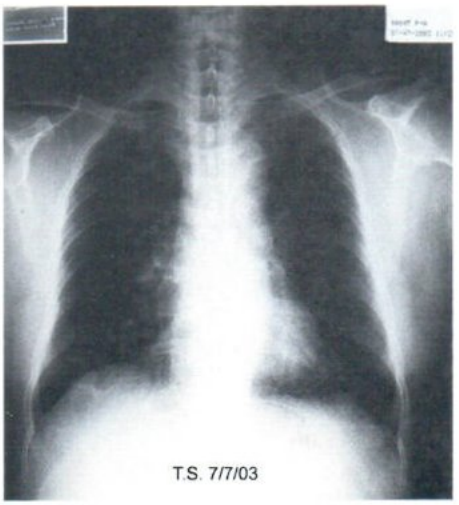



**Fig.3B** Chest film PA revealed nearly complete regression of the masses at left supraclavicular and mediastinum after treatment 4 months.


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

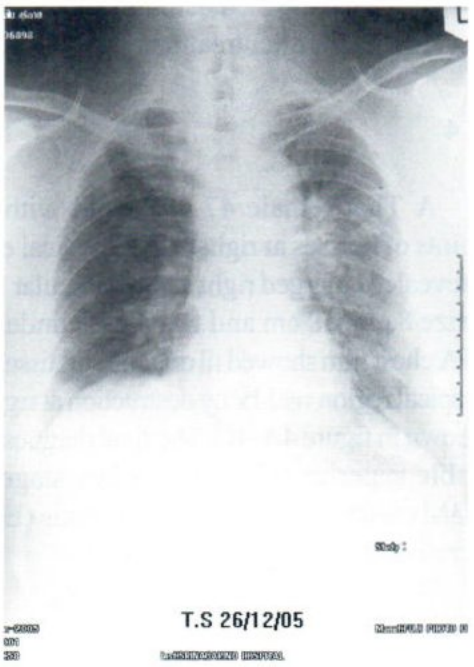



**Fig.3D** Chest film PA revealed stable of the tumour at mediastinum and both lungs after treatment 34 months.

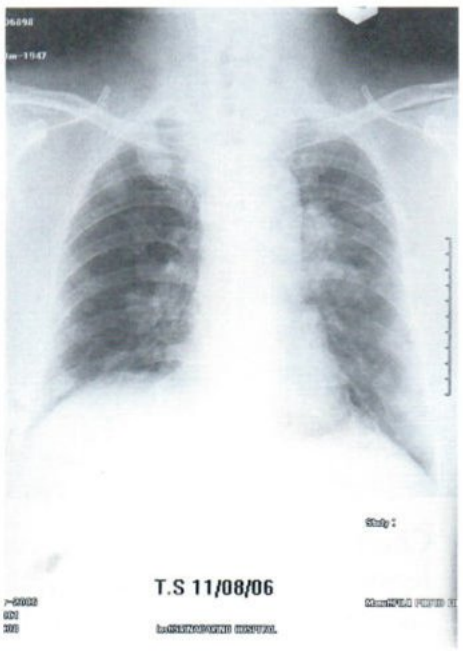



**Fig.3E** Chest film PA revealed progression of the tumors at the mediastinum and both lungs 42 months after treatment .

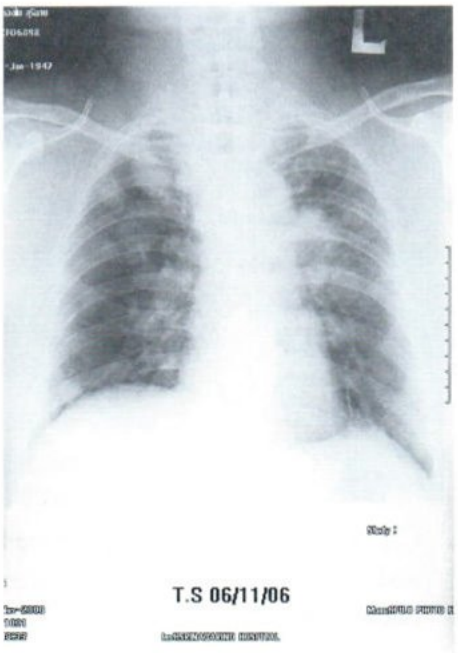



**Fig.3F** Chest film PA revealed progression of the tumors at the mediastinum and both lungs 44 months after treatment .

## 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 ≥ 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.**

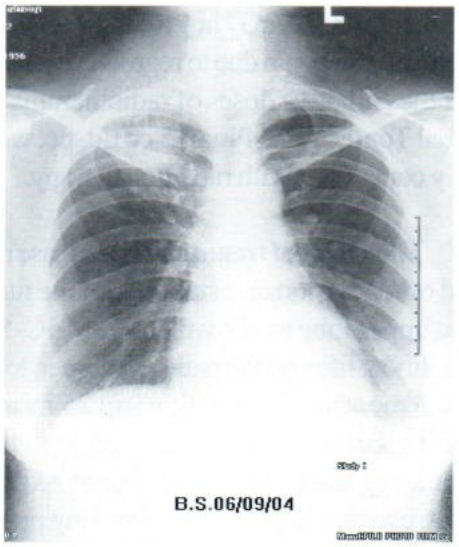



**Fig.4A** Chest film PA showed ill defined soft tissue mass in the apical and supraclavicular region with bony destruction at first rib, right side.

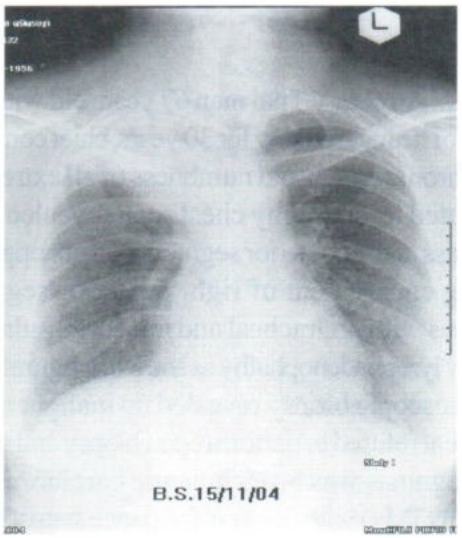



**Fig.4B** Chest film PA, 2.5 months later revealed increasing in size of the mass in the apical and supraclavicular region with bony destruction at the first rib, right side.

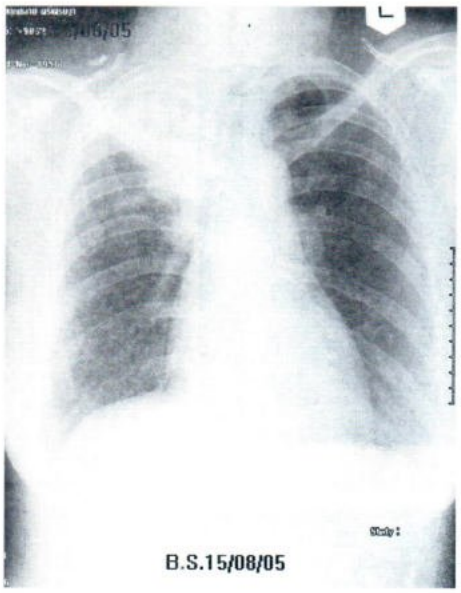



**Fig.4C** Chest film PA revealed ill defined soft tissue mass in the apical and supraclavicular with bony destruction of the first rib, right side.

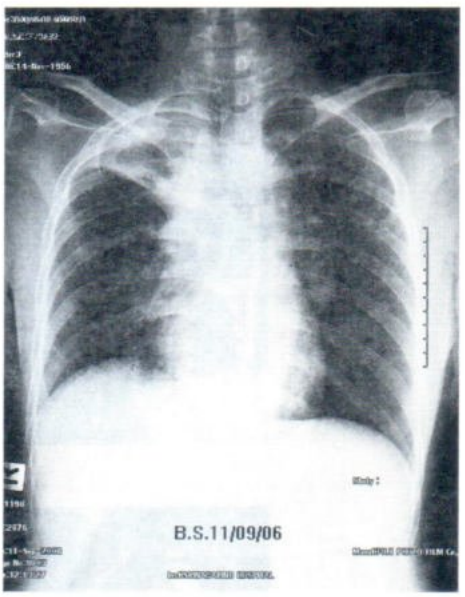



**Fig.4D** Chest film PA revealed decreased in size of the tumour 1 year after treatment.

## CASE 5

An eldery 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 larged lung mass at the posterior segment of right upper lobe causing encasement of right posterior segmental bronchus with pretracheal and left aorto-pulmonary window lymphadenophathy 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 stablility 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 larged 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 afer 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]**

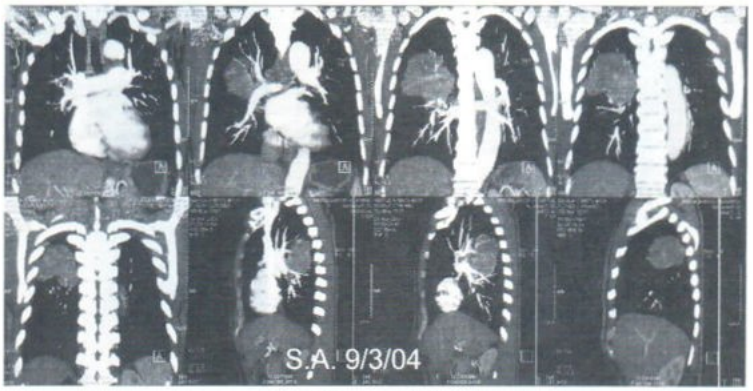



Figure 5A

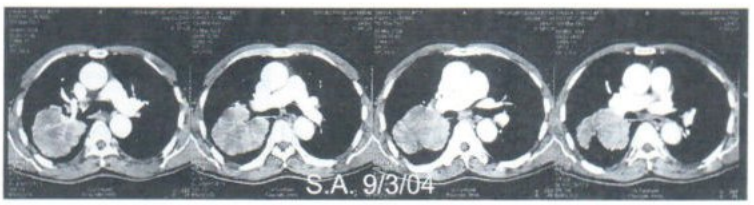



Figure 5B

**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 lymphadenophathy.

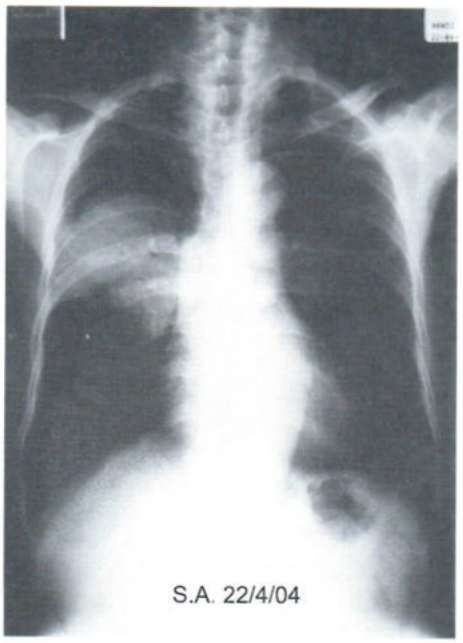



**Fig. 5C** Chest film PA revealed stable of the tumour at right upper lobe.

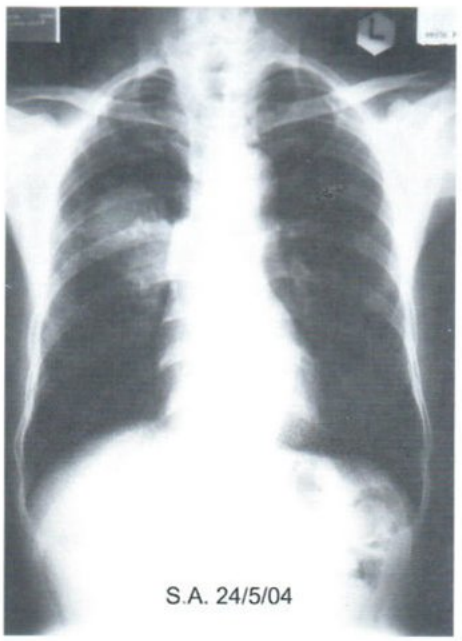



**Fig. 5D** Chest film PA revealed stable of the tumour at right upper lobe.

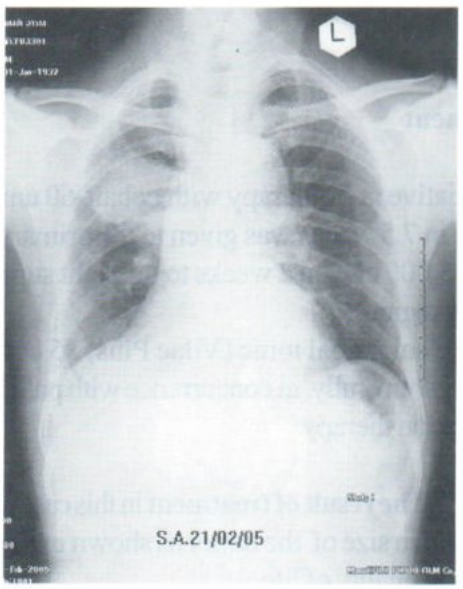



**Fig. 5E** Chest film PA revealed quiescence of tumour at right upper lobe.

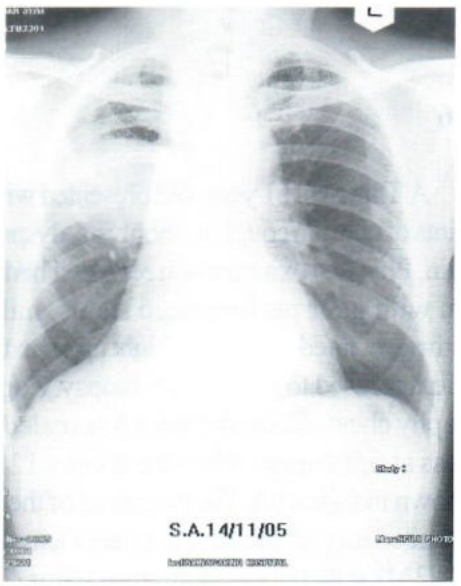



**Fig. 5F** Chest film PA revealed quiescence of tumour at right upper lobe.

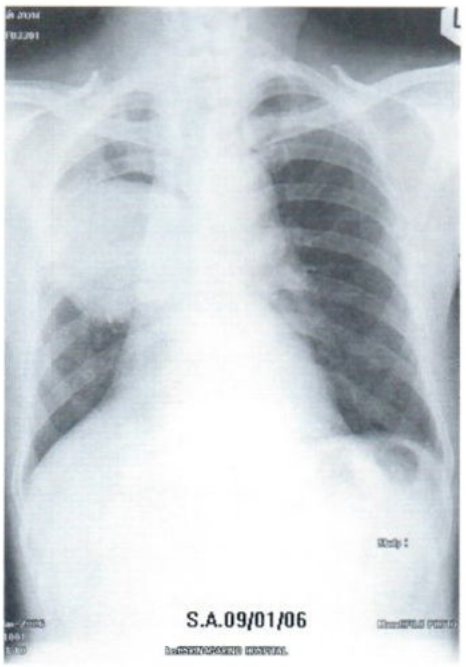



**Fig.5G** Chest film PA revealed quiescence of tumour at right upper lobe.

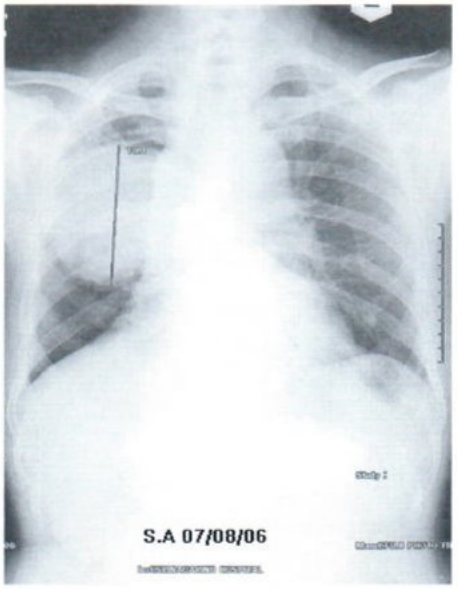



**Fig.5H** Chest film PA revealed the tumour at right upper lobe start to grow bigger.

## 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 ≥ 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]

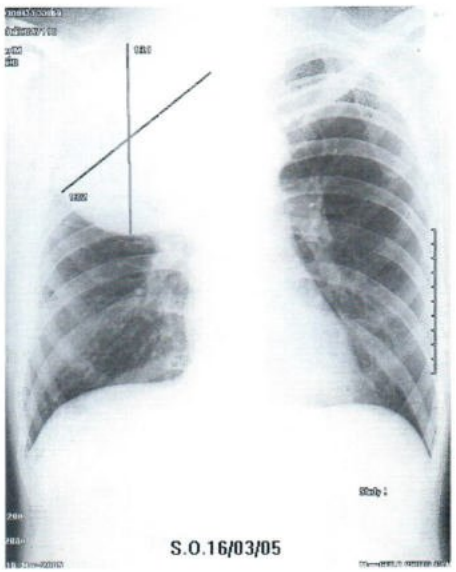



**Fig.6A** Chest PA revealed larged lung mass at right upper lobe size 8 cm x 12 cm. at right upper lobe.

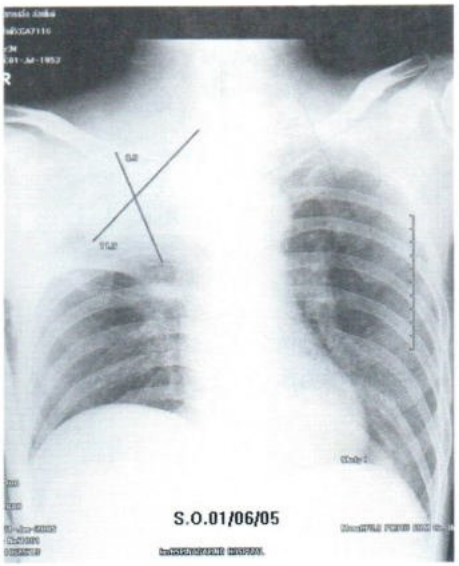



**Fig.6B** Chest PA revealed decreased in size of the tumor at right upper lobe

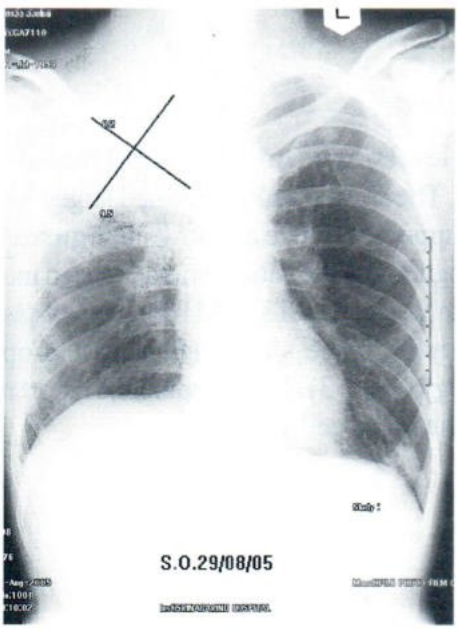



**Fig.6C** Chest film PA revealed stable of the tumour at right upper lobe.

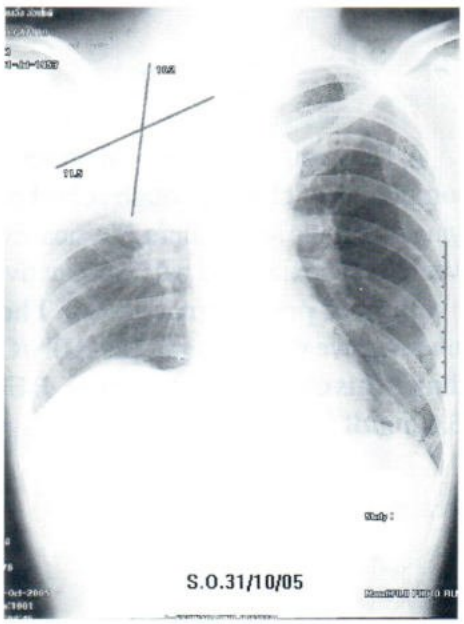



**Fig.6D** Chest film PA revealed stable of the tumour at right upper lobe.

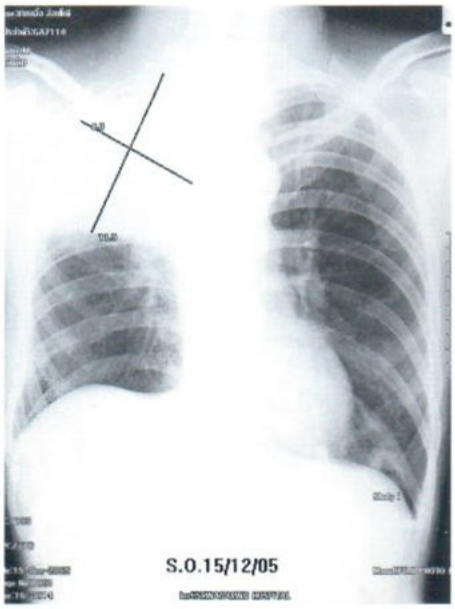



**Fig.6E** Chest film PA revealed stable of the tumor at right upper lobe.

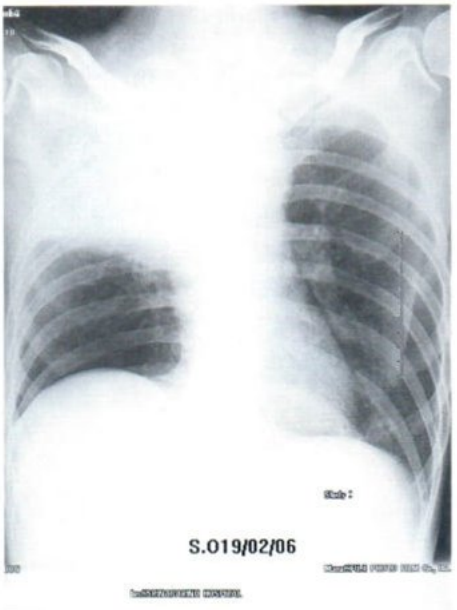



**Fig.6F** Chest film PA revealed tumor at right upper lobe started to grow bigger.

## 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),** 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.

**Cr** = Creatinine

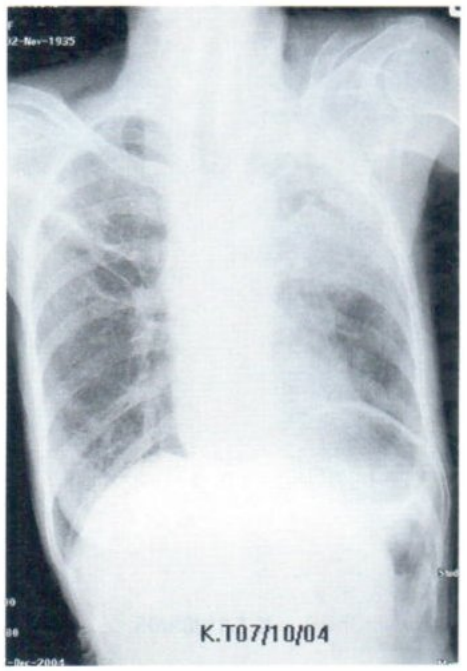



Fig. 7A

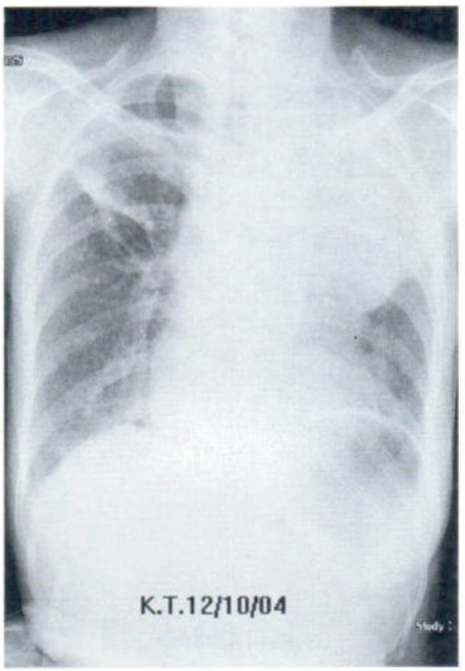



Fig.7B

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

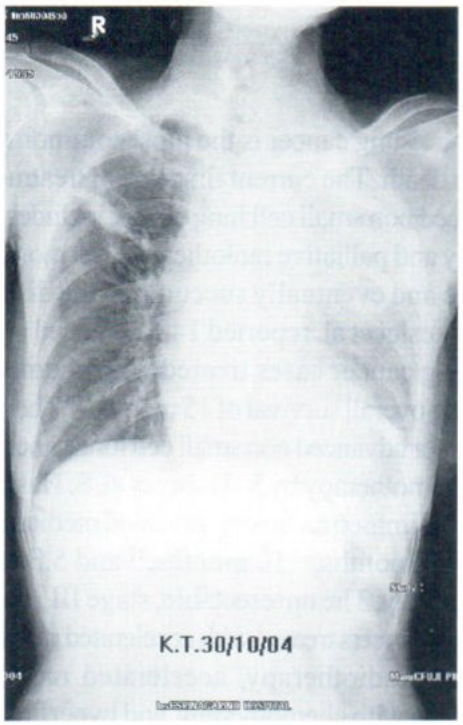



Fig. 7C

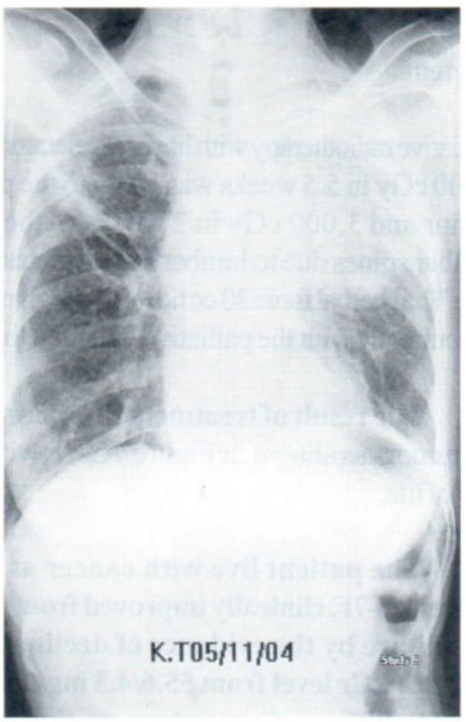



Fig. 7D

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

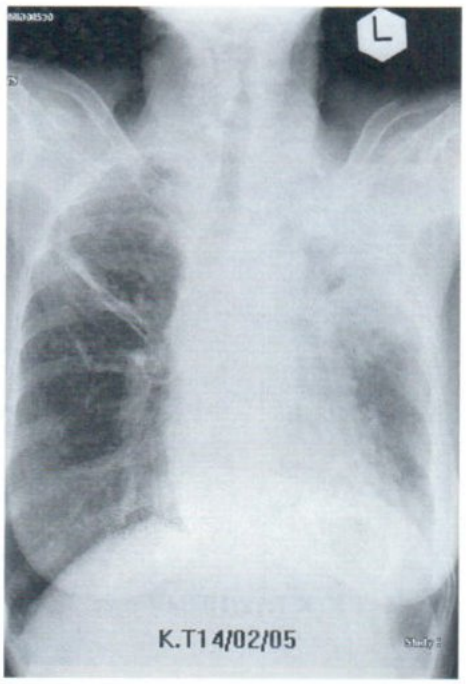



Fig. 7E

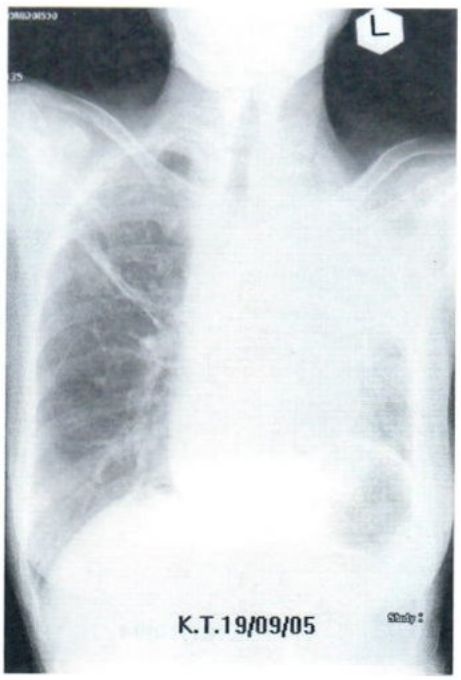



Fig. 7F

**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 months[13] 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 radiotherapy[16] 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 antradical 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 antioxidants [29-31] 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-nitrosaminno)-l-(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 recepter (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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