Original Article

Characteristics of Lung Cancer Patients with Brain Metastases based on Baseline Head Computerized Tomography (CT)-scan in Arifin Achmad Hospital October 2022 - June 2023

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Abstract

Background: The majority of lung cancer cases are often discovered at a late stage because it frequently develops without symptoms in the early stages. Many lung cancer deaths are caused by metastases to other organs. The purpose of this study was to examine the features of lung cancer patients with brain metastases using baseline CT-scan data.

Method: Between October 2022 and June 2023, a cross-sectional study was conducted at the Arifin Achmad General Hospital in Pekanbaru on all newly diagnosed lung cancer patients with brain metastases who also met the inclusion and exclusion criteria.

Results: Eight subjects of lung cancer with brain metastasis were found from 49 patients. All subjects were male with age mostly in between 40 and 60 years. Three subjects (37.5%) were Squamous Cell Carcinoma (SCC), four subjects (50%) were adenocarcinoma and 1 (12.5%) were SCLC.

Conclusion: This study discovered that 16.3% of subjects who met the inclusion criteria had lung cancer with brain metastases. Further research should be done on a cohort study and a preventive strategy for lung cancer with brain metastases.

Keywords: adenocarcinoma, brain metastases, CT-scan, lung cancer, SCC

INTRODUCTION

Lung cancer typically develops without symptoms in early stages and is frequently detected at a late stage. Many lung cancer deaths are caused by metastases to other organs. Lung cancer often metastasizes to the brain, liver, bones, and adrenal glands. Cancer spreading to brain is often lung cancer, which accounts for 30% to 60% of all brain metastases and has a 10:1 ratio to initial brain tumours. Delay in diagnosis risks causing brain herniation, resulting in disability and death.[1,2] Research conducted by Yosephine et al at Cipto Mangunkusumo Hospital and Dharmais Cancer Hospital found metastases in the brain 93.8% and 8.3% in the leptomeningeal.[3]

With improvements in systemic medication that can prolong survival, the prevalence of brain metastatic lung cancer is rising. Patients with untreated brain metastatic lung cancer had a survival time of one to three months. The combination of Whole Brain Radiotherapy (WBRT) and corticosteroids can increase the survival rate.

When Non-Small Cell Lung Carcinoma (NSCLC) patients with brain metastases were evaluated, Ali et al discovered an average survival rate of 7.8 months. Both metastases were detected both at the time of the initial diagnosis and as the disease advanced. On that study, the highest incidence of adenocarcinoma type brain metastases was 52%.[4] Research on the characteristics of lung cancer patients with brain metastases based on the baseline head CT-scan is required because incidence of brain metastatic from lung cancer is high.[1]

Lung cancer is a malignancy originating from the bronchial epithelium. In a broad sense, lung cancer refers to all forms of lung cancer, including tumour metastases in the lung and cancers that develop both inside and outside of the lung tissue.[1] Metastasis is the process by which cells from the main tumour escape, travel through the bloodstream to the tissue, and develop additional cancers.[2]

Metastasis in lung cancer includes intrapulmonary, extrapulmonary intratoracal and extratoracal metastasis. The brain, bone, liver, and adrenal glands are among the organs that extratoracial lung cancer can spread to. The most frequent malignancy to spread to the brain is lung cancer.[2] Brain metastasis is one of the neurological complications in systemic malignancies.[3]

Most metastases hematogenously (via blood vessels) enter the brain. After passing through the heart and venous circulation, tumour cells will settle in the first capillary they come into contact with, which is the lung. The left heart and later other organs are reached by the circulation of tumour cells. Since 20% of cardiac output goes to the brain, lung cancer, both primary and secondary, is frequently the cause of brain metastases.[5,6]

The grey-white matter border, where blood channels narrow to retain tumour emboli, is where brain metastases are most frequently discovered. The brain hemispheres receive 80% of the cerebral blood flow, followed by the cerebellum and brainstem. Because of this, the cerebrum accounts for 85% of brain metastases, the cerebellum for 10-15%, and the brainstem for 3%. However, the cerebellum is the site of around 50% of isolated metastases from these malignancies.[5,6]

Incidence of new cases of lung cancer in the world ranks highest compared to new cases of other cancers at around 1.8 million and caused 1.31 million deaths in 2012. The World Health Organization (WHO) in 2012 stated that lung cancer is included in five types of cancer with a high incidence rate. Lung cancer is a case that is mostly found in men. Research at the Jakarta Friendship Hospital on 167 lung cancer patients in the period 2004 - 2007 found a distribution of

106 men (63.5%) and 61 women (35.5%).[7–9]

Around 50% to 60% of cases of lung cancer spread to the brain, followed by 15% to 20% of breast cancer cases and 5% to 10% of melanoma cases. Brain metastases from kidney and digestive tract cancer are less prevalent.[10] Although the exact incidence is unknown, metastatic brain tumours are the most prevalent intracerebral tumours.

According to a study by Percy et al, there are 11.1 brain metastases for every 100,000 people. A study by Fogelholm et al in Finlandia found an incidence of brain metastases of 3.4 per 100,000 cancer patients. 20–40% of cancer patients have brain metastases, which are 10:1 more common than the original brain tumour.[6]

Patients with metastatic brain tumours are estimated to be 98,000 to 170,000 annually in the United States.[11] In anatomical pathology, the frequency of metastasis to the brain from lung cancer with a ratio of NSCLC is 36% and SCLC is 56%. In patients with NSCLC, half the population is diagnosed with brain metastases at initial diagnosis, and half the population will suffer from brain metastases at a later stage.[4,10] A study by Bonneta et al found a higher prevalence of adenocarcinoma types with brain metastases by 71% (74 of 103 samples) compared to SCC and large cell carcinoma types.[10]

Tumours that have spread, such as to the lymph nodes in the neck, will be found to be enlarged.[1] Tumours that spread to the brain usually show signs of focal neurological deficits such as hemiparesis, focal seizures, and ataxia. The most common location of lung tumour metastasis is in the frontal lobe of the cerebrum, while the cerebellum is rarely found. Lung tumours can also metastasize to the spinal cord, if they compress the anterior spinal artery causing transverse myelitis. Epidural metastases cause back pain, impaired autonomic function, sensory loss and ataxia.[2,12]

Radiology examination is one of the supporting examinations to determine the image and structure in the human body. Radiologic examination in lung cancer is needed before and after therapy for treatment evaluation. Lung radiology examinations, namely thoracic photographs, thoracic CT-scans, bone scans, bone surveys, abdominal ultrasonography (USG), head CT-scans, Positron Emission Tomography (PET) scans and Magnetic Resonance Imaging (MRI) are needed to determine the location of abnormalities, tumour size and metastases. Thoracic photography is the initial examination to assess suspect of lung cancer, if abnormalities are found, further radiological examinations will be performed. Contrast-enhanced chest CT-scans can more accurately detect cancers smaller than one cm and provide superior images of malignancy.[1]

Contrast thoracic CT-scans are needed for disease staging but are unable to detect metastases outside the thoracic cavity (distant metastases). A contrast-enhanced CT-scan of the head assesses the possibility of metastases to the skull

and brain. Even if there are no complaints or symptoms at the time of first diagnosis, head CT-scans should be performed in operable instances (stage I and II), but in advanced stage cases, they should be performed at the beginning or before two months of therapy. It is done for all cases because the results of the study show that 1/3 of cases with brain metastases do not show symptoms and signs.[1]

MRI is another imaging method to detect abnormalities in the brain and abnormalities in the nervous system or spine but is done at the request of a neurologist.[1,13] MRI is more recommended than CT-scans, especially in providing an anatomical picture of the posterior fossa of the brain adjacent to the base of the skull.[2]

Based on Rahman's research in 2019 on 182,977 NSCLC patients, the results of low specificity in finding brain metastases using head CT-scans were obtained so that additional imaging is needed, namely MRI. Additionally, this is consistent with National Comprehensive Cancer Network (NCCN) recommendations for NSCLC patients who have received a stage 2 or later diagnosis.[14]

The primary method for identifying lung cancer is bronchoscopy. It can be used to pinpoint the original lesion's site, monitor intraluminal tumour progression, and collect samples to confirm the presence or absence of cancerous cells. If abnormal appearance is found, bronchial biopsy, bronchial lavage, bronchial scraping or bronchial scraping should be followed. If the tumour is on the right, TBNA in the lower 1/1 carina or trachea (2 rings above the carina) at the 1 o'clock position will offer double information, including acquiring samples for cytology and details on metastasis to the subcarinal or paratracheal lymph nodes. TBLB if the lesion is small and peripherally located and fluoroscopic facilities are available, a lung biopsy via the bronchus should be performed.[1]

The histological classification of lung cancer according to WHO for clinical needs is NSCLC and SCLC. NSCLC consists of adenocarcinoma, SCC, Large Cell Carcinoma (LCC), and others. NSCLC accounts for 80%–85% of cases, making it the most prevalent form. Adenocarcinoma is the most common type with 40% of all lung cancer cases. It comes from type II alveolar cells, which also release substances like mucus. Adenocarcinoma grows more slowly and is easier to detect before it spreads to other organs compared to other types.[1,13]

There are only two subtypes of SCLC recognized by the current subclassification: pure SCLC and mixed SCLC. Mixed SCLC is a combination of small and large cell carcinoma. According to Nicholson et al, mixed SCLC was identified in 28% of cases, along with 16% LCC, 9% adenocarcinoma, and 3% SCC.[15]

Management of brain metastases from lung cancer generally consists of surgery, Stereotactic Radiosurgery (SRS) and WBRT. Patients with neurological symptoms caused by the tumour are given steroids. If the diagnosis is unclear or the lesion is substantial and creates a herniation, hydrocephalus, or mass effect, surgery is advised to acquire a histological

diagnosis. Though the prognosis for SCLC patients is often bad, brain metastases are thought to be radiosensitive. Therefore, if the patient presents with a single large lesion, steroid therapy may be given. If symptoms improve, WBRT or SRS is given in the hope of avoiding surgery even for large lesions (e.g. 3 to 4.5 cm).[5,16]

Patients with NSCLC such as adenocarcinoma or SCC are a little more complicated in decision making. Surgery is not an option for management in NSCLC patients with small brain lesions. If there is a single lesion less than 2 or 3 mm, therapy is often postponed for 6 to 8 weeks, and imaging is done again. This delay allows the lesion to increase in size and facilitates more accurate SRS. Data also suggest that SRS is a useful method in the management of NSCLC metastasizing to the brain, especially in patients with advanced systemic disease, small lesions (3 cm or smaller), or up to 5 lesions where craniotomy is not medically feasible.[5]

The purpose of this study was to examine the features of lung cancer patients with brain metastases using baseline CT-scan data.

METHOD

The study was conducted at Pulmonary ward of Arifin Achmad Hospital October 2022-June 2023. Based on baseline head CT-scans, characteristics of lung cancer patients with brain metastases are identified. Conceptual framework of the research is shown in Figure 1.

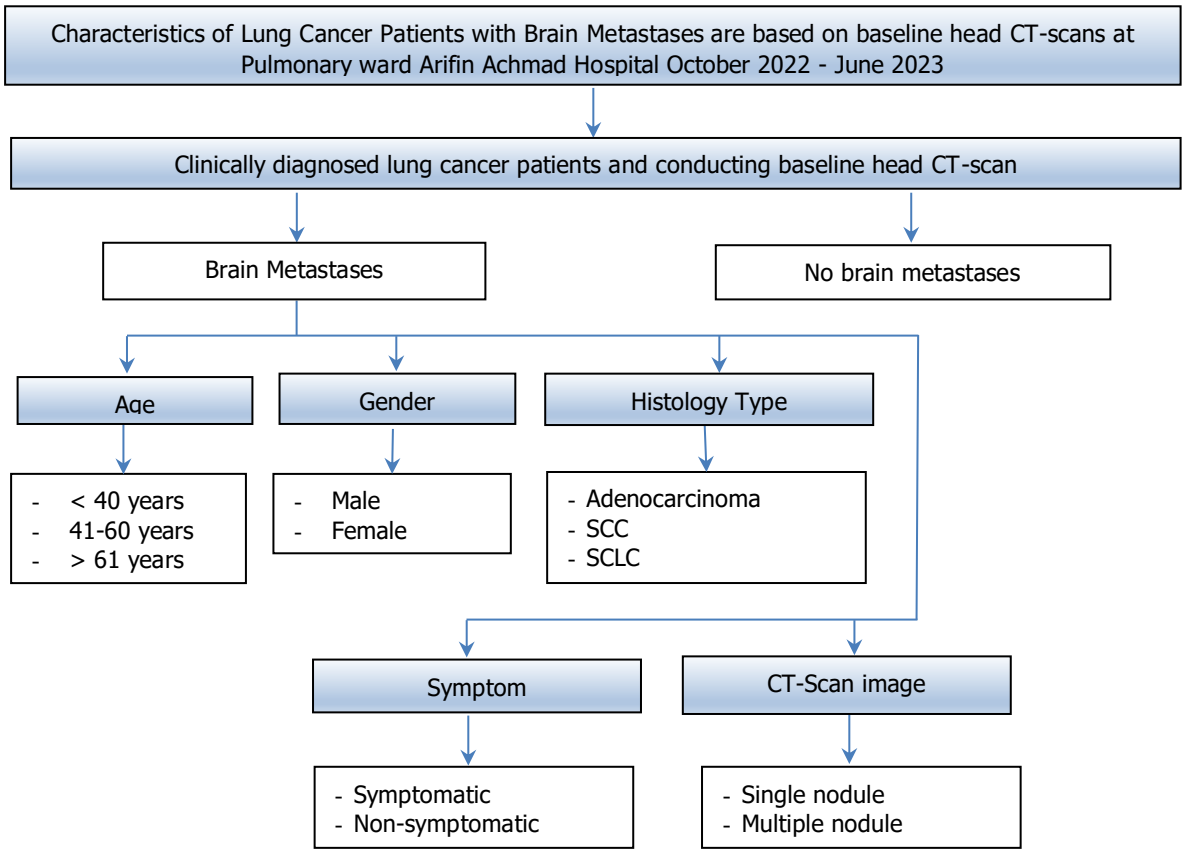

Figure 1. Research Conceptual Framework

The study population was all lung cancer patients who had an upright type based on the results of anatomic pathology and had performed a baseline head CT-scan with contrast. The research sample was lung cancer patients who were histologically upright and had met the inclusion and exclusion criteria by using total sampling technique.

Inclusion criteria were lung cancer patients whose type had been established and had a head CT-scan with contrast before undergoing second cycle first-line chemotherapy. Exclusion criteria were lung cancer patients during the diagnostic procedure, but the type was not established yet, lung cancer patients whose type was decided but had not had a head CT-scan with contrast. Other exclusion criteria were those who had an upright type and had a head CT-scan with contrast but after second cycle of first-line chemotherapy.

This research is an observational descriptive study, which analyses the results of head CT-scans with contrast from radiological data of lung cancer patients. Data was collected through radiological data and medical records of patients being treated.

The data is processed manually and then presented in the form of a frequency distribution table which is calculated as a percentage. The variables in this study were age, gender, symptom, and histological type of lung cancer based on head CT-scan with contrast in the pulmonary ward of Arifin Achmad General Hospital.

RESULTS

The inclusion criteria were met by 49 patients. From 49 patients that meet inclusion criteria, 41 people (88.2%) were no brain metastases and 8 (11.8%) were brain metastases.

In category no brain metastases patients, 12 subjects (29.2%) were SCC, 27 people (65.9%) were adenocarcinoma and 2 patients (4.9%) were SCLC. From metastases patients, 3 subjects (37.5%) were SCC, 4 people (50%) were adenocarcinoma and 1 patient (12.5%) were SCLC (Table 1).

Table 1. Characteristics of Research Results.

Variables	N (%)
Baseline head CT-Scan	
No brain metastases	41 (88.2%)
Brain metastasis	8 (11.8%)
Histology Type of no brain metastases	
SCC	12 (29.2%)
Adenocarcinoma	27 (65.9%)
SCLC	2 (4.9%)
Histology Type of brain metastases	
SCC	3 (37.5%)
Adenocarcinoma	4 (50%)
SCLC	1 (12.5%)
Age	
<40 years	0 (0,0%)
40 - 60 years	7 (87.5%)
>60 years	1 (12.5%)
Gender	
Male	8 (100%)
Female	0 (0,0%)
Nodule	
Multiple	5 (62.5%)
Single	3 (37.5%)
Symptom	
With Symptom	2 (25%)
Without Symptom	6 (75%)

Note: SCC=Squamous Cell Carcinoma; SCLC=Small Cell Lung Carcinoma

DISCUSSION

This study result is consistent with other studies by Waqar et al, who discovered that 10.4% of 457,482 NSCLC patients had brain metastases and 89.6% were not brain metastases.[17] Another study by Li et al in SCLC patients, found 15.5% had brain metastases and 84.5% without brain metastases from 11,093 SCLC patients.[18]

The percentage of lung cancer with brain metastases with adenocarcinoma was higher compared to SCC and SCLC. This study result is same to the study conducted by Ramadhaniah et al, the distribution of morphological types of brain metastatic lung cancer patients was dominated by adenocarcinoma 67.9%.[10] Another study by Yulianti et al found that adenocarcinoma was the most common type, around 77.1% (27 out of 35 patients).[19] In this study, no conclusions could be drawn on the comparison of the proportion of brain metastases between the types of NSCLC (adenocarcinoma and SCC) and representative SCLC because of the small number of samples for this type of SCLC.

All lung cancer patients who experienced brain metastases from the results of baseline head CT-scans during the period October 2022 - June 2023, were all male with most of the age range in between 40 and 60 years. The study's findings agreed with those of Waqar et al, whose investigation found that males had a 59.8% incidence rate for brain metastases.[20] This is consistent with the higher incidence of lung cancer in men, which is linked to smoking risk factors in Indonesia, where men are more likely than women to smoke.[21] An et al's study found that women were more likely than men to get lung cancer brain metastases.[22]

Based on nodule, 5 patients (62.5%) were multiple, and 3 (37.5%) subjects were single. 6 people (75%) were without symptom and 2 subjects (25%) were with symptom. The most common symptom are headache and dizziness.

CONCLUSION

Based on the findings of the baseline CT-Scan with contrast from 49 lung cancer patients, this study identified 8 lung cancer patients with brain metastases. To identify the data profile of lung cancer patients at Arifin Achmad Hospital with brain metastases from baseline and contrast head CT-scan images after 6 cycles of chemotherapy and link them with other preexisting risk factors, a further investigation with a bigger sample size is required.

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