ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2022, Volume 11, Number 1: 241-245
P-ISSN.2089-1180, E-ISSN: 2302-2914

# Clinical and radiological profiles of metastatic brain tumor in Indonesia: A study at Dr. Soetomo Hospital, Surabaya

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Received: 2022-02-01
Accepted: 2022-04-06
Published: 2022-04-14

## ABSTRACT

**Background:** Brain metastases have increased over time, and imaging has been considered an important diagnostic tool. In Indonesia, the record of metastatic brain tumors is limited. Therefore, understanding the epidemiology and the imaging characteristics of brain metastases will provide insights into a better diagnosis, management, and therapy towards the disease. This study aimed to evaluate the characteristics of patients with metastatic brain tumors.

**Methods:** A cross-sectional study was conducted in Neurology Unit at Dr. Soetomo Hospital in Surabaya, Indonesia from August 2018 - July 2019. Patients with metastatic brain tumors were enrolled in the study. Data demographics, clinical, and brain imaging characteristics were collected from the patients' Brain Tumor Registry. Computerized tomography (CT) scan and magnetic resonance imaging (MRI) was used to assess the images of the brain metastases. Mini-Mental State Exam (MMSE) was used to assess the patient's cognitive function.

**Results:** Of the total 22 subjects, 14 (63.6%) were male, 13 (59.1%) aged ≥50 years. Headache was the most common clinical symptom, reported by 78.2% of patients. Most of the patients (63.3%) had MMSE score of ≤ 23. CT-scan and MRI imaging suggested that multiple lesions were the most common, 57.8% and 71.4%, respectively. The brain tumor's most frequent was in the parietal and temporal lobes (CT-scan imaging) and temporal and cerebellar lobes based on MRI. Lung tumors were the most common source of brain metastases (50%), followed by breast and nasopharynx cancers (13.6% each); 9% had unknown sources.

**Conclusions:** Our study suggests that the frequency of metastatic brain tumors is gender and age-specific. Headache with early stage of dementia is common among patients with metastatic brain tumor. Multiple lesions in parietal and temporal lobes with lung cancer as the source are common.

**Keywords:** Metastatic brain tumor, epidemiology, imaging, brain tumor, lung cancer.
**Cite This Article:** Anandito, N.A., Ardiansyah, D. 2022. Clinical and radiological profiles of metastatic brain tumor in Indonesia: A study at Dr. Soetomo Hospital, Surabaya. *Bali Medical Journal* 11(1): 241-245. DOI: 10.15562/bmj.v11i1.3222

## INTRODUCTION

A metastatic brain tumor is a type of tumor caused by cancer cells spreading from different parts of the body to the brain and is reportedly more common compared to primary brain tumor. The incidence of brain metastases has increased gradually due to the increase in cancer cells lifespan and the capability to detect through magnetic resonance imaging (MRI).[1,2] In United States, approximately 170.000 new cases have been reported each year.[3] The exact prevalence of metastatic brain tumors is even assumingly much higher than reported cases since the disease is sometimes asymptomatic and undetected. A high prevalence of undetected lesions is often found through an autopsy.[4]

Imaging plays critical role in intracranial tumor diagnosis, characterization, surveillance, and therapy monitoring. Approximately 22% of brain tumors are diagnosed in Indonesia through imaging examinations.[5] This technique is widely used to detect metastases in patients with known malignancy, signs, or new neurological symptoms. Computed tomography scan (CT-scan) and MRI are the main imaging methods and cornerstones for brain metastases diagnosis.[6]

In Indonesia, however, medical records of metastatic brain tumors are limited. A good understanding of the epidemiology and recognizing the imaging features of brain metastases will provide insight into a better diagnosis, management, and therapy towards brain tumors patients. Therefore, this study aimed to evaluate the clinical and radiological characteristics of patients with metastatic brain tumors.

## METHODS

A cross-sectional observational study was conducted among patients with metastatic brain tumors in Neurology Unit at Dr. Soetomo Hospital, Indonesia, from August 2018 to July 2019. The data including the patients' demographic characteristics (gender, age), clinical data (symptoms of brain metastases and cognitive impairment), and radiological profiles (brain imaging of CT-scan and MRI) were collected. Patients with metastatic brain tumor hospitalized for 1 year during the period of the study were included in this study.

Age was grouped into two categories (<50 and ≥ 50 years). Clinical

symptoms were classified as headaches, consciousness decline, visual disturbance, and seizures. To assess the patients' cognitive function, Mini-Mental State Exam (MMSE) consisting of 30 questions was used. It evaluates several domains, including orientation, attention, memory, calculation, repetition, naming, reading, writing, drawing, and comprehension with total score of 30.[7] We divided the score into two categories (score <23 and ≥ 23). The score <23 indicates cognitive impairment such as dementia, whereas ≥ 23 is considered normal.[7]

Imaging techniques including CT-scan and MRI were used to detect and diagnose brain metastases. The number of lesions, tumor location, and the source of metastases was recorded. The number of lesions was divided into single and multiple. The sites of tumor development included the frontal, parietal, temporal, occipital, and cerebellar lobes. Several possible extracranial metastases, such as lung, breast, nasopharynx, sinus, and ovary tumors, as well non-Hodgkin lymphoma were examined.

We used descriptive analysis to determine the distribution (percentage) of the characteristics (sociodemographic, clinical conditions, and brain radiological imaging features) of the patients with metastatic brain tumor. The analysis was conducted using SPSS version 20.

## RESULTS

In total, 92 brain tumor patients were recruited; however, only 22 were classified as metastatic brain tumors and included in the analysis (Table 1). More than half of the patients (59.0%) aged ≥50 years and 63.6% were male. Headache was the most common clinical symptom (78.2%), followed by consciousness decline (39.1%), visual disturbance (21.7%), and seizures (17.39%). The average duration of the symptom onset was 50.4 days. Of the total 22 patients, only 11 were available for MMSE examination since half of them experienced decreased level of consciousness during the initial treatment. More than half of the patients (7 out of 11, 63.6%) had MMSE score of ≤23, whereas 4 (36.6%) had MMSE score of >23 (Table 1).

Table 2 shows metastatic brain tumor imaging characteristics with CT-scan (19

**Table 1. Demographic characteristics, clinical symptom, and MMSE examination.**

| Characteristics | n=22 (%) |
|---|---|
| Gender | |
| Male | 14 (63.6) |
| Female | 8 (36.3) |
| Age | |
| < 50 years | 9 (40.1) |
| ≥ 50 years | 13 (59.0) |
| Clinical symptoms | |
| Headache | 18 (78.2) |
| Consciousness decline | 9 (39.1) |
| Visual disturbance | 5 (21.7) |
| Seizure | 4 (17.3) |
| The average duration of symptom onset (days) | 50.4 |
| Mini-Mental State Exam score (n=11) | |
| ≤ 23 | 7 (63.6) |
| > 23 | 4 (36.3) |

**Table 2. General characteristics of CT scan imaging and MRI of metastatic brain tumor.**

| Criteria | CT-scan n=19 (%) | MRI n=14 (%) |
|---|---|---|
| Number of lesions | | |
| Single | 8 (42.1) | 4 (28.5) |
| Multiple | 11 (57.8) | 10 (71.4) |
| Tumor location | | |
| Frontal lobe | 7 (31.8) | 4 (28.5) |
| Parietal lobe | 8 (36.3) | 5 (35.7) |
| Temporal lobe | 8 (36.3) | 4 (28.5) |
| Occipital lobe | 3 (13.6) | 3 (20.6) |
| Cerebellum | 2 (9.1) | 5 (35.7) |

**Table 3. Age and gender distributions based on the source of tumor metastases (n=22).**

| Source of metastases | Gender n (%) | | Age n (%) | |
|---|---|---|---|---|
| | Male | Female | < 50 years | ≥ 50 years |
| Lung tumor | 8 (72.7) | 3 (27.2) | 4 (36.3) | 7 (63.6) |
| Breast cancer | 0 (0.0) | 3 (100.0) | 1 (33.3) | 2 (66.6) |
| Nasopharynx cancer | 3 (100.0) | 0 (0.0) | 1 (33.3) | 2 (66.6) |
| Non-Hodgkin lymphoma | 1 (100.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) |
| Sinus tumor | 1 (100.0) | 0 (0.0) | 1 (100.0) | 0 (0.0) |
| Ovary tumor | 0 (0.0) | 1 (100.0) | 1 (100.0) | 0 (0.0) |
| Unknown source of tumor | 1 (50.0) | 1 (50.0) | 1 (50.0) | 1 (50.0) |

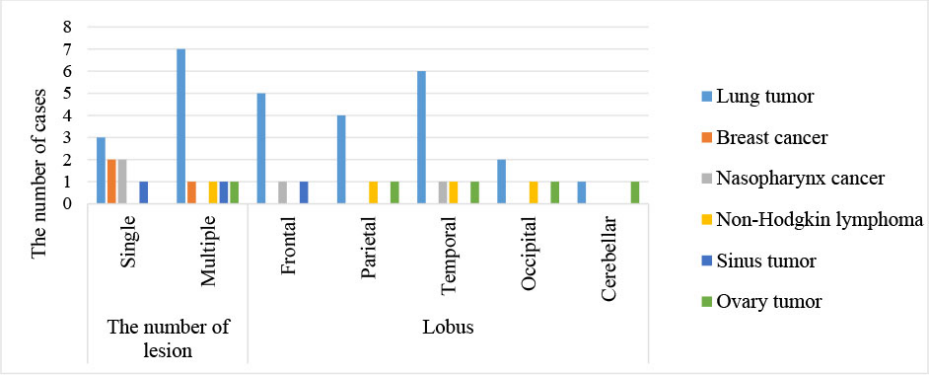


**Figure 1.** The distribution of CT-scan imaging characteristics of metastatic brain tumor based on the sources of metastases.

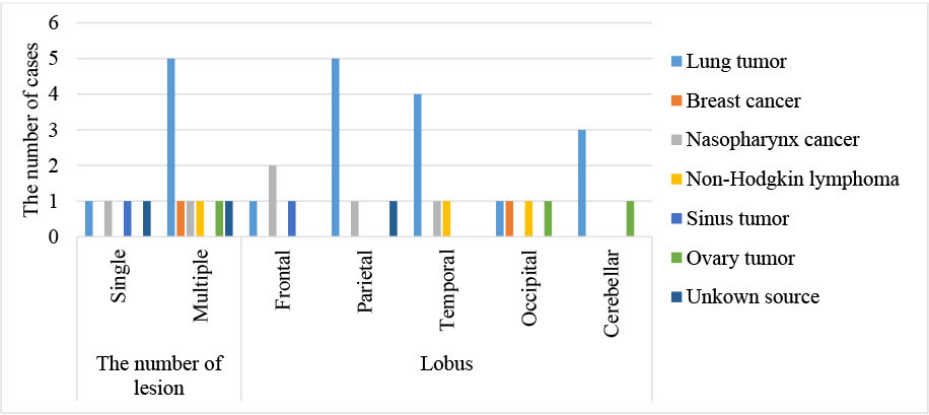


**Figure 2.** The distribution of MRI features of metastatic brain tumor based on the sources of metastases.

cases) and MRI (14 cases). The occurrence of multiple lesions was reportedly higher based on both imaging techniques: CT-scan (57.8% multiple vs. 42.1% single lesion) and MRI (71.4% multiple vs. 28.5% single lesion). In terms of lesion location, CT-scan showed the highest lesions percentage in the parietal and temporal lobes (36.3%), while parietal and cerebellar were the most common sites according to MRI (35.7%).

The highest incidence of brain metastases occurred in patients with primary lung tumor (50.0%), followed by breast and nasopharynx (13.6% each), sinus, ovary, and non-Hodgkin lymphoma (4.54% each) (Table 3). Unknown source metastases contributed to 9% of metastatic brain tumor. Further, age over 50 seemingly appeared to be a risk factor for secondary brain tumors.

Both CT-scan and MRI characteristics suggested that primary lung tumors were the most common source of both single and multiple lesions in secondary brain tumors (Figure 1 and 2). Based on CT-scan, the temporal lobe was the most common site for the lesions (6 cases), followed by the frontal (5 cases), parietal (4 cases), occipital (2 cases) and cerebellar lobe (1 case). In patients with primary nasopharynx cancer, the lesions were found in the frontal and temporal, whereas those with primary non-Hodgkin lymphoma, the lesion was observed in the parietal, temporal, and occipital lobes. In patients with sinus-originated brain tumors, the lesion emerged in the frontal, while those of ovary origin located generally in parietal, temporal, occipital, and cerebellar lobes (Figure 1).

MRI features suggested the parietal lobe as the most common site for lesion formation originating from lung tumor (5 cases), followed by temporal (4), cerebellar (3), occipital (1), and frontal (1) lobes. Lesions from nasopharynx cancer developed mainly in the frontal lobe (2 cases), while those arising from non-Hodgkin lymphoma were found in the temporal and occipital. Furthermore, sinus tumor-associated lesion was shown in the occipital lobe, whereas those from ovary cancer were detected in the occipital and cerebellar regions (Figure 2).

## DISCUSSION

An increased incidence and prevalence of metastatic brain tumors has been widely observed and imaging has become a cornerstone for its diagnosis.[8] Understanding epidemiological, clinical, and radiological characteristics of brain metastases are critical. Our data revealed that of the total 92 brain tumor cases, 22 cases were metastatic brain tumors. This finding was contrary to a previous study, suggesting that metastatic brain tumor has assumingly 10 times higher incidence than primary brain tumor.[9] A small sample in our study, since the patients were limited only to those hospitalized in inpatient settings, might have contributed to these contradicting findings.

We found that male and above 50 years were more likely to develop metastatic brain tumors. Studies in Indonesia and Tunisia also reported a higher incidence of brain metastases in males compared to females by a ratio of 1.26 and 1.24, respectively.[10,11] However, despite different results reported in India, in which the number of females suffering from the disease was higher than that of males by 29.0%, no significant association has been found between gender and the incidence of metastatic brain tumor. A higher incidence of brain metastases among males was presumably due to higher prevalence of males to suffer from lung cancer which has been recognized as the main source of brain metastases in males.

The incidence of brain metastases has been reportedly increased with age, with the highest incidence occurring at the age of 65-74 years.[12,13] Other studies in Tunisia and Southern India reported that the average age for metastatic brain tumors was 54 and 50-70 years, respectively.[11,14] In the present study, the oldest patient was 55.6 years with primary lung cancer, while the youngest was 48.3 years with primary

breast cancers. Primary breast cancer has been reported to contribute to the highest cumulative of brain metastases incidence among individuals with the youngest age category.[13]

The highest incidence of brain metastases was observed in patients with primary lung tumors, followed by primary breast and nasopharynx cancers (Table 3). The source of metastases was determined based on lumps in other parts of the body identified previously through supportive examinations. Lung cancer has been considered the most frequent source of cancer metastasizing to the brain.[9,13] In fact, two-thirds of undiagnosed-cancer patients had their cancer originated from lung cancer based on an autopsy test.[9] The most common type of metastasizing lung cancer cells to the brain was non-small cell lung carcinoma (NSCLC).[15]

The type of lesion in metastatic brain tumor patients, according to CT scan, were often multiple (Table 2 and Figure 1). However, several other studies also reported a high number of single lesion formation in secondary brain tumors with 25-45%.[10,16] Patients with primary lung cancer and melanoma tends to form multiple lesions, while those with primary breast, kidney, large intestine, and thyroid tumors tend to develop single lesion.[6] In terms of location, the most common site for lesion development was the temporal lobes, followed by the frontal and occipital (Figure 1). In a previous study, the highest incidence was reported in the posterior of Sylvian fissure near the region where the temporal, parietal, and occipital meet. Many metastases were found to develop in the boundary area of substantia grisea and alba.[10]

A higher frequency of multiple lesions was detected from MRI examination compared CT-scan (Table 2). This suggests that MRI had higher sensitivity in examining intracranial lesions and revealed 80% of multiple brain tumor cases, with 50% of which had three or more lesions.[17] Conversely, CT-scan had been reportedly fail to exhibit metastatic brain tumor in 30% of the patients.[18]

## CONCLUSION

Our results suggest a higher prevalence of metastatic brain tumor incidence among males and individuals above 50 years of age. Headache was the most common self-reported symptom and most of the patients are in the early stage of dementia. Multiple lesions are the most common lesion type among the patients found dominantly in parietal and temporal lobes, with the metastases originating mainly from lung cancer. These findings might provide insight on several characteristics of metastatic brain tumor, thus subsequently will help to improve the diagnosis of brain tumors.

## ETHICS APPROVAL

The Research Ethics Committee approved this study of Medical Faculty Universitas Airlangga, Surabaya, Indonesia (EC/KEPK/FKUA).

## ACKNOWLEDGMENT

The authors would like to thank Airlangga University and all the staff at Neurology Department of Dr. Soetomo Hospital for their assistance during the study.

## DISCLOSURE OF CONFLICTS OF INTEREST

The authors declared no conflict of interest.

## FUNDING

This study received no external funding.

## AUTHORS CONTRIBUTION

Both authors contributed to the research process, including preparation, conceptualization, data collection and analysis, drafting, and publishing approval.

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