

**STUDYING CLINICAL CHARACTERISTICS OF BRAIN
MAGNETIC RESONANCE IMAGE IN NON-SMALL CELL LUNG
CANCER PATIENTS WITH BRAIN METASTASES**

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SUMMARY

Objectives: To give a description of clinical characteristics of brain magnetic resonance image in patients with brain metastases from non-small cell lung cancer. Subjects and method: A prospective study on 104 patients with brain metastases from non-small cell lung cancer, from 2 - 2017 to 9 - 2018. Results: Mean age was 59, most of them under 65 years old (75.3%), male occupied 89.4%, adenocarcinoma 93.3%. EGFR (+) 52.9%. Asymptomatic patients explained 59.6%. Size of brain metastases ≤ 2 cm made up 73.1%, 1 - 2 tumors constituted 55.8%. Conclusion: Most patients with brain metastases from non-small cell lung cancer were males, under 65 years old with adenocarcinoma and asymptomatic histology. Size of brain metastases ≤ 2 cm and 1 - 2 tumors in brain were common. Brain metastases with ring enhancement was 73.1%, peritumoral edema was 60.6%.

** Keywords: Non-small cell lung cancer; Brain metastases; Brain magnetic resonance image; Clinical characteristics.*

INTRODUCTION

Lung cancer remains a leading cause of mortality with 1.69 million deaths worldwide. An estimated 234,030 new cases occurred in the United States in 2018 with a median age at diagnosis of 70 and 64% of predominance for males. Approximately 84% of these lung cancers are non-small cell lung cancers (NSCLC). Despite improvements in systemic therapy, the survival rate for patients with stage IV disease is poor, with fewer than 5% of 5-year survival after diagnosis. The frequency of central nervous system involvement in NSCLC patients is reported

to reach 40% and 25% to 30% of NSCLC patients have synchronous brain metastases (BMs) at the time of diagnosis [5, 8].

The recent, widespread use of magnetic resonance image (MRI) has led to the increased identification of asymptomatic BMs. NSCLC patients with BMs often receive various forms of treatment, including surgery, radiosurgery, whole brain radiation therapy (WBRT) and chemotherapy, depending on the clinical status and clinical practice [6, 7, 8].

The aim of this study was to: *Give some description of clinical characteristics of brain MRI in NSCLC patients with BMs.*

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SUBJECTS AND METHOD

We retrospectively and prospectively reviewed the medical records of 104 patients with histopathologically proven NSCLC with BMs treated in Respiratory Medicine Department, 108 Military Central Hospital between February 2017 and September 2018. BMs were defined as those diagnosed by MRI at the time of initial evaluation. Pretreatment work-up included taking of clinical history, Eastern Cooperative Oncology Group PS determination, physical examination, blood tests, chest radiography, computed tomography (CT) of the thorax and upper abdomen, bone scintigraphy or PET/CT and brain MRI. Staging was performed according to the TNM classification of the American Joint Committee on cancer (AJCC - 2010). Histological analysis of the tumor was based on the World Health Organization classification for cell types. Description on the basis of neurological symptoms and determined the number, size, and location of the cranial metastatic lesions [6]. Statistical analysis was performed using SPSS 16.0 for Windows.

RESULTS

1. Patients' characteristics.

Table 1:

Characteristics	Number of patient	p
Age	59.11 ± 8.80	
< 65	79 (75.9%)	< 0.05
≥ 65	25	

Male	93 (89.4%)	< 0.001
Female	11 (10.6%)	
Stage I + II	8 (7.7%)	< 0.05
Stage IIIA	7 (6.7%)	
Stage IIIB	13 (12.5%)	
Stage IV	76 (73.1%)	< 0.001
Adenocarcinoma	97 (93.3%)	
Squamous cell carcinoma	7 (6.7%)	> 0.05
EGFR (+)	45 (52.9%)	
EGFR (-)	40 (47.1%)	

There was no difference in EGFR, $p > 0.05$.

2. Clinical characteristics of brain metastasis.

* Symptoms ($n = 104$):

Asymptomatic: 62 patients (59.6%); headache: 40 patients (38.4%); nausea and vomiting: 15 patients (14.4%); seizure: 1 patient (0.9%); weakness of arms or legs: 5 patients (4.8%); problems with speech: 2 patients (1.8%); problem with memory and confusion: 3 patients (2.7%); cognitive impairment: 10 patients (9.6%).

3. Detection time of brain metastasis compared with detected lung cancer.

Before lung cancer treatment: 4 patients (3.8%); after lung cancer treatment: 50 patients (38.6%); the same time as lung cancer treatment: 60 patients (57.6%).

4. Detection time of brain metastasis by stage (n = 50).

Table 2:

Group	Shortest	Longest	Medium	p
Stage I	24	50	37	< 0.05
Stage II	7	30	15	
Stage IIIA	5	24	11.7	
Stage IIIB	2	24	7.7	
Stage IV	1	24	7.4	

In 50 patients with brain metastases from NSCLC: patients in later stages had earlier time to detect brain metastasis, with $p < 0.05$.

5. Characteristics of brain tumor on MRI.

Table 3:

Brain tumor characteristics		n	Percentage (%)	p
Size of tumor: T	≤ 2	76	73.1	< 0.05
	2 < T ≤ 3	17	16.3	
	3 < T ≤ 5	10	9.7	
	> 5	1	0.9	
Location	Two cerebrals	40	38.5	< 0.05
	Right side	33	31.7	
	Left side	16	15.4	
	Cerebellum	15	14.4	
Number	1 tumor	46	44.2	> 0.05
	2 tumors	12	11.6	
	≥ 3 tumors	46	44.2	
Ring enhancement		76	73.1	
Homogeneous enhancement		20	19.2	
Peritumoral edema		63	60.6	
Tumor haemorrhage		1	0.9	

Most of the patients had tumor size ≤ 2 cm (73.1%), only one patient had tumor size > 5 cm. The majority of patients had brain tumor in two cerebrals (38.5%), in the right side: 31.3%. There were no significant differences in the number of brain tumor metastases.

6. Type of treatment for brain tumor metastases.

Majority of patients was treated by Cyberknife radiosurgery (58 patients = 55.8%), whole brain radiation therapy was 37.5% (39 patients); 7 patients (6.7%) refused treatment.

DISCUSSION

1. Clinical characteristics in NSCLC patients with brain metastases.

In our study, median age of patients was 59 years old, the majority of patients (75.9%) were under 65 years, similar to Ayabe E's results (2013) [3] in 107 NSCLC patients with brain metastases, 62.6% of the patients were under 65 years old. Our result suggested that NSCLC patients with brain metastases were detected more in younger patients. Males accounted for 89.4%; adenocarcinoma type was mainly (93.3%); many patients with stage IV (73.1%). Previous studies have shown that the incidence of brain metastases is higher with adenocarcinoma than with other subtypes of NSCLC [1, 2, 4]. In particular, it was reported that the incidence rate of brain metastases is higher in epidermal growth factor receptor (EGFR) - mutant lung adenocarcinoma than in EGFR-wild type lung adenocarcinoma and the other types [3, 5, 7], however there had no difference: EGFR (+) in 45/85 patients (52.9%), maybe the number of patients was not large enough.

Brain metastases was an important cause of morbidity in patients with NSCLC. The frequency of central nervous system involvement in NSCLC patients is

reported to reach 40% and 25 to 30% of NSCLC patients had synchronous BMs at the time of diagnosis. However, the majority of brain metastases were detected by brain MRI method. In our study, 59.6% of patients with brain metastases had no symptoms, consistent to Ayabe E's study (2013), this rate was 55.1% [3]; it indicated that brain MRI when lung cancer was diagnosed and interval time to detect brain metastases was very important. Symptoms were dependent on location, size and number of brain lesions and its edema. Patients had headache 38.4%, nausea and vomiting was found in 14.4%. According to Nakahama K (2017), common clinical features include headache, neurological deficit and seizures... [6]. Le Van Nguyen's study (2016) in 44 NSCLC patients with brain metastases treated by Cyberknife radiosurgery, headache symptom was 77.3%, nausea and vomiting were 18.2% [1].

In 104 NSCLC patients were detected brain metastases, we found that 60 patients (57.6%) at the same time as lung cancer treatment, it is no mean 57.6% of NSCLC patients had brain metastases in the time of diagnosing for lung cancer. Because the study only included NSCLC patients with brain metastases; 50 patients had brain metastases after treatment and 4 patients had brain metastases before lung cancer treatment. These results were different from Le Van Nguyen's findings (2016) with percentage of NSCLC patients with brain metastases after lung cancer treatment of 56.8% [1].

In our study, 50 patients had brain metastases after lung cancer treatment, patients in the later lung cancer stages had time metastases to brain earlier: median time of stage IV (23 patients) was 7.4 months, stage III (13 patients) was 7.7 months, stage IIIA (6 patients) was 11.7 months, stage II (6 patients) was 15 months and stage I (2 patients) was 37 months. The presence of brain metastases in NSCLC cases is associated with a poor outcome, with a median overall survival (OS) of approximately 4 months [4, 6, 7].

2. Characteristics of brain tumor on MRI.

On brain MRI images, we found most of patients had tumor size ≤ 2 cm (73.1%), only one patient had tumor size > 5 cm. The majority of patients had brain tumor in two cerebral hemispheres (38.5%), in the right side was 31.3%, in the left side was 15.4%, in cerebellum 14.4%. There were no significant differences in the number of brain tumor metastases, most of patients had brain metastases from 1 - 2 tumors (55.8%).

Brain metastases with ring enhancement was 73.1%, peritumoral edema was 60.6%, equivalent to Le Van Nguyen's results (2016) [1]. The larger the tumor is, the more edema is.

Patients with 2 tumors brain metastases (even 3 tumors) was still treated by Cyberknife method. 58 patients (55.8%) in our study were treated by this method. We think this is the best method to treat for NSCLC patients with little tumor brain metastases. 39 patients (37.5%) were

treated by whole brain radiation therapy. In this study, we don't assess the effectiveness of treatment for tumors brain metastases and median OS of patients.

CONCLUSION

** Clinical characteristics of NSCLC patients with brain metastases:*

- Median age was 59, most of them under 65 years old (75.3%), males was mainly (89.4%), adenocarcinoma was 93.3%, EGFR (+) 52.9%.

- Asymptomatic patients were 59.6%. Majority of patients had headaches (38.4%), nausea and vomiting were 14.4%.

- 57.6% of NSCLC patients were detected brain metastases at the same time as lung cancer treatment. Patients in the later lung cancer stages had earlier time metastases to brain.

** Characteristics of brain tumor on MRI:*

- Most of tumor brain metastases with size ≤ 2 cm (73.1%), majority of patients had brain tumor in two cerebral hemispheres (38.5%), in the right side was 31.3%, in the left side was 15.4%, in cerebellum 14.4%. Most of patients had brain metastases with 1 - 2 tumors (55.8%).

- Brain metastases with ring enhancement was 73.1%, peritumoral edema was 60.6%.

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