Pattern of distant metastases at presentation in newly diagnosed non-small cell cancer

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Abstract
Background: Extrathoracic metastases (ETMs) are common in non- small cell lung cancer (NSCLC) at presentation.
Objective: Our study was to detect the percentage distribution of ETMs in various organs at presentation in patients with NSCLC.
Methodology: Between January 2017 and November 2018 inpatient records of all NSCLC was retrospectively analysed for ETMs.
Results: We included 71 patients of NSCLC. ETMs were diagnosed in 35.2% (25/71) of the patients at presentation. 18 fluorodeoxy glucose positron emission tomography combined with Computed tomography (FDG PET/CT) played crucial role in detecting unexpected ETMs. Brain was the most common organ involved in extrathoracic metastases.
Conclusions: Distant metastases at presentation are usual in NSCLC and FDG-PET CT is the key imaging modality to be done in all patients of NSCLC to detect unexpected ETMs.

Keywords: Non-small cell lung cancer; Extrathoracic metastases; PET/CT.

Introduction
Majority of the lung cancer patients at presentation have either locally advanced disease or distant metastasis. Matsuda et al. Little et al. and Bain reported that 40-50% of NSCLC patients at presentation have distant metastasis at the time of diagnosis [1-3]. In this study we aim to determine the percentage of NSCLC patients with extrathoracic metastases and the pattern of distribution at presentation.

Materials and Methods
Post ethical committee approval, we retrospectively analysed inpatient records of newly diagnosed primary lung cancer between January 2017 and November 2018. Only histologically and or cytologically proven Non-small cell lung cancer (NSCLC) patients were enrolled. Secondary and Lymphoproliferative lung cancers were excluded. Lung cancers were staged as per 8th edition of The Union Internationale Contre le Cancer (UICC) and American Joint Committee on Cancer (AJCC). As per this TNM classification M Category is classified in M0: no distant metastasis; M1a: malignant pleural or pericardial effusion or pleural or pericardial nodule or separate tumour nodule(s) in contralateral lobe; M1b: single extrathoracic metastasis; M1c: multiple extrathoracic metastases (1 or > 1 organ). The various radiological investigation used to stage the disease were Contrast enhanced Computed Tomography (CECT) of Chest, Ultrasonography (USG) of Chest, Ultrasonography of whole abdomen, 18 Fluoro deoxy glucose positron emission tomography combined with Computed tomography(FDG PET CT) and Magnetic resonance imaging of Brain (MRI). Fibreoptic Bronchoscopy where relevant was used for diagnosis. Pleural fluid and regional lymph node sampling was done to either diagnose or stage the disease where appropriate.

Results
The study included 71 patients of bronchogenic carcinoma. The disease was staged as per 8th AJCC Lung Cancer classification (Table 1). TNM stage I to IIIA was combined due to fewer patients. FDG-PET CT was done in all the patients to detect extrathoracic metastases. Majority of the patients (n=38, 53.5%) were with M1 disease (Table 2). ETM (M1b & M1c) at presentation were observed in 35.2% of the patients (Table 2). The various sites involved in extrathoracic metastases (M1b & M1c) at presentation were noticed with brain being most commonly involved (Table 3). FDG-PET CT detected 9 patients with unexpected ETM with most common site being brain. ETMs frequently occurred in adenocarcinoma subtype of histology.

Table 1: TNM stage of NSCLC as per 8th edition of UICC/AJCC

Stage	No. of patients(n=71)
I -IIIA	5
IIIB and IIIC	28
IVA	18
IVB	20

Table 2: Percentage of M1 disease at presentation

M1a	18.3 (13/71)
M1b	7 (5/71)
M1c	28.1 (20/71)
M1a + M1b +M1c	53.5 (38/71)
M1b +M1c (ETMs)	35.2 (25/71)

Table 3: Distribution pattern of extrathoracic metastases (ETMs)

Site	Percentage of total patients (n=71)
Brain	17
Liver	14
Adrenal glands	6
Axillary lymph nodes	4
Bone excluding spine	3
Renal	1
Pancreas	1
Subcutaneous tissue	1

Discussion

Lung cancers are highly aggressive with high propensity for distant or extrathoracic metastases (ETM). Detection of ETM to stage the lung cancer plays a decisive role in the treatment of lung cancer. Previously detection of distant metastases was possible only on autopsy given the limited radiological screening modality and the sensitivity of the tests available then. Presently with the availability of FDG-PET CT Scan distant metastases can be easily detected and thus help in proper staging of the lung cancer and appropriate treatment. The ETM were more commonly noticed in patients with higher nodal staging as per TNM classification.

Several autopsy studies in the past literature have reported prevalence of distant metastases as high as 93% with end stage disease. Anderson et al., Abrams et al., and Mathews reported major sites of distant metastases in Liver (35% to 40%), adrenal glands (18% to 35%), brain (15 to 43%), bone (19% to 33%), kidney (16% to 23%) and abdominal lymph nodes (29%) [4-6]. Lahde et al., Salvatierra et al., and Sider et al., reported distant metastases at presentation ranging from 11% to 36% [7-9]. In our study based on the 8th AJCC TNM classification the percentage of patient who had distant or extrathoracic metastases i.e. M1b and M1c at presentation was 35.2% (25/71) [Table 2]. If patients with M1a disease were also included then this was 53.5% (38/71)[Table 2]. The various sites of extrathoracic metastases (M1b & M1c) at presentation were noticed in following frequency brain (17%), followed by liver (14%), adrenal glands(6%), axillary lymph node (4%), bone excluding spine (3%) and renal, pancreas and subcutaneous tissue had 1% each (Table 3). Single organ extrathoracic metastases were seen in brain, 8 patients; liver, 6 patients; and axillary lymph nodes, 2 patients. The remaining 9 patient had multifocal extrathoracic metastases. The localized M1a in the form of pleural effusion and contralateral lobe nodule were observed in 13 patients.

The brain metastasis were observed in 12 patients with cerebral metastasis, 5 patients; cerebellar metastasis, 4 patients; and remaining 3 patients with both. The liver metastases were observed in 10 patients with single lesion in 3 patients and remaining 7 patients with multiple lesions. The extrathoracic metastases were more commonly observed in adenocarcinoma subtype of lung cancer. Brain and Liver metastasis was most commonly observed in patient with adenocarcinoma. The patients with bone or brain metastasis are mostly symptomatic and help in further evaluation with specific imaging studies. While majority of patients with adrenal gland, liver, renal and pancreatic metastases are asymptomatic and even biochemical investigation do not indicate the presence of metastasis. Further the organ involved with metastasis at presentation can have impact on the overall survival. Gorg C et al., and Yamamoto et al., observed in their study that NSCLC with liver metastasis do not respond well to chemotherapy [10-11]. Whereas Tamura et al., observed that patients with brain metastasis had better overall survival which can be attributed to stereotactic radiation therapy and use of epidermal growth factor receptor tyrosine kinase inhibitors [12].

Conclusions

ETM are not uncommon at presentation and thus Whole body FDG-PET CT Scan is a must for detection of extrathoracic metastases in NSCLC and prevent underestimation of tumor stage.

Conflicts of Interests: None declared.

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References

1. Matsuda A, Matsuda T, Shibata A, Katanoda K, Sobue T and Nishimoto H; Japan Cancer Surveillance Research Group: Cancer incidence and incidence rates in Japan in 2008: a study of 25 population-based cancer registries for Monitoring of Cancer Incidence in Japan (MCIJ) project. *Jpn J Clin Oncol* 2014;44:388-396.
2. Little AG, Gay EG, Gasper LE and Stewart AK: National survey of non-small cell lung cancer in the United States: epidemiology, pathology and patterns of care. *Lung Cancer* 2007;57:253-260.
3. Bains MS. Surgical treatment of lung cancer. *Chest* 1991;100(3):826-837.
4. Anderson EE. Nonfunctioning tumors of the adrenal gland. *Urol Clin North Am* 1977;4:263-271.
5. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma. Analysis of 1000 autopsied cases. *Cancer* 1950;3:74-85.
6. Matthews MJ. Problems in morphology and behavior of bronchopulmonary malignant disease. In: Israel L, Chahin-ian P, eds.. Lung cancer: natural history, prognosis and therapy. New York: Academic Press, 1976:23-62.
7. Lahde S, Paivansalo M, Rainio P. CT for predicting the resectability of lung cancer. A prospective study. *Acta Radiol Acta Radiol* 1991;32:449-454.
8. Salvatierra A, Baamonde C, Llamas JM, Cruz F, Lopez-Pujol J. Extrathoracic staging of bronchogenic Carcinoma. *Chest* 1990;97:1053-8.
9. Sider L, Horejs D. Frequency of extrathoracic metastases from bronchogenic carcinoma in patients with normal- sized hilar and mediastinal lymph nodes on CT. *AJR* 1988;151:893-895.
10. Gorg C, SchwerkWB, Wolf M and Havemann K. Prognostic value of response to chemotherapy using Ultrasound in lung cancer with metastatic liver involvement. Bildgebung. 1990;57:70-73.
11. Yamamoto N, Tamura T, Fukuoka M, Saijo N. Survival and prognostic factors in lung cancer patients treated in phase I trials: Japanese experience. *Int J Oncol* 1999;15:737-741.

12. Tamura T, Kurishima K, Nakazawa K, Kagohashi K, Ishikawa H, Satoh H, Hizawa N. Specific organ metastases and survival in metastatic non-small-cell lung cancer. *Mol Clin Oncol* 2015;3:217-221.

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