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A Rare Case Report: Widespread Metastases of Lung Adenocarcinoma in an Elderly Man Who Presented with Features of Metastatic Deposits

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Abstract: Lung cancer is a major public health problem. Just over one in eight lung cancer patients will be living 5 years after their diagnosis. Lung cancers are divided into two major groups-small cell and non-small cell. The non–small cell cancer category consists of adenocarcinoma, squamous cell carcinoma, large cell carcinoma, and variants. Metastatic non-small-cell lung cancer is a common condition with a dismal prognosis. Although palliative chemotherapy improves survival and quality of life, nearly all patients die of progressive disease. Metastatic involvement of adrenal glands is not rare, but usually reflects widespread disease.
Keywords: Lung cancer, public health, carcinoma.

INTRODUCTION

Pathologic features, visible on light microscopy, are used to categorize lung cancers. Since the 1980s, the proportions of lung cancers that are adenocarcinomas and squamous cell carcinomas have changed. In North America, approximately 40% of all lung cancers are adenocarcinomas, and 20% to 25% are squamous cell. These figures were reversed in the past. The increased incidence of lung cancer in women (who are more likely to have adenocarcinomas) and changes in smoking habits are believed to account for this change [1].

Adenocarcinoma- Adenocarcinomas are mostly frequently peripheral nodules under 4cm in size.

Microscopically: A malignant epithelial tumour with glandular differentiation or mucin production, showing acinar, papillary, bronchoalveolar or solid with mucin growth pattern or mixture of these patterns compared to other lung cancers [2].

The pathophysiology of lung cancer development is complex and incompletely understood. The genes influenced in the pathogenesis of lung cancer produce proteins involved in cell growth and differentiation, cell cycle processes, apoptosis, angiogenesis, tumor progression, and immune regulation [1].

CASE DISCUSSION

A 59-year-old man presented with headache and anorexia and significant weight loss since last three months. His past medical history was not significant. The patient did not have any family history of cancer. He had no smoking history and uses alcohol occasionally.

He had no past exposure to asbestos or chemicals. He denied cough, shortness of breath or any other respiratory symptoms or bone pain. Physical exam did not reveal any cervical, supraclavicular or axillary adenopathy. Systemic examination were apparently normal.

His initial complete blood count and complete metabolic panel were normal. Chest CT revealed a 2.5cm nodule involving the right upper lobe of the left lung, involvement of bilateral hilar and sub carinal mediastinal lymphnodes noted. CT scan of brain revealed small enhancing isodense to hyperdense lesions in the right superior frontal and at left cerebellar vermian and left occipital regions-s/o metastases. CT scan abdomen revealed enhancing soft tissue mass lesions noted at both adrenals measuring 2.3*2.8cms on right side and 1.8*2.6cms on left side, s/o of bilateral adrenal metastases. Upper GI endoscopy and Colonoscopy were within normal limits.

Fig-1: x ray lung showing –multiple metastases[canon ball appearance]

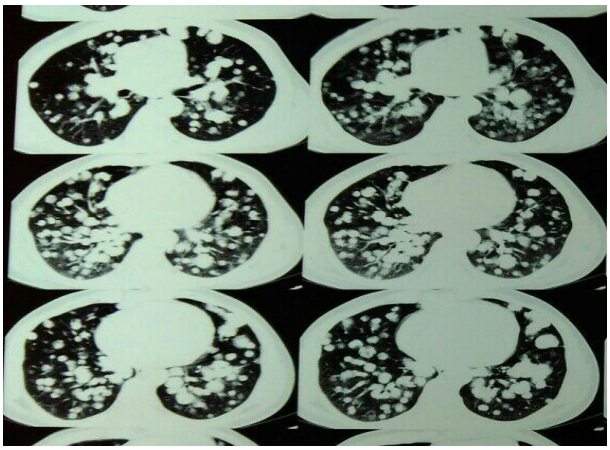

Fig-2: CTscan lung- showing multiple metastases

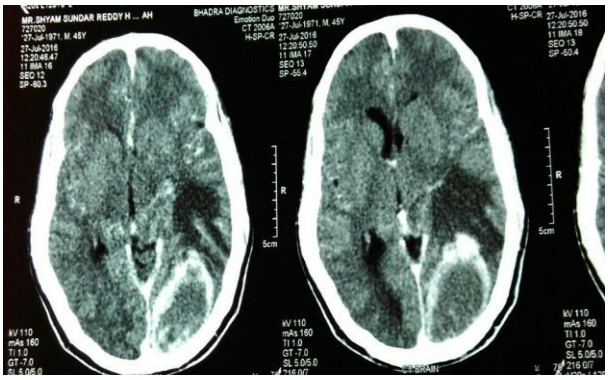

Fig-3: CT scan brain showing metastases

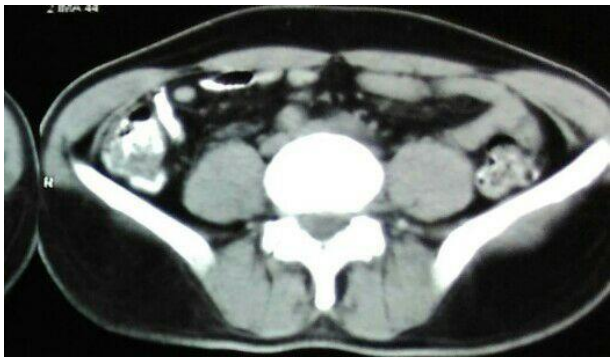

Fig-4: CT scan showing bilateral adrenal metastases

CT guided FNAC from the lung mass revealed the features of Adenocarcinoma lung. Biopsy also revealed features of Adenocarcinoma lung.

DISCUSSION

Broad classification

Dividing lung cancer into small and non-small cell groups is no longer sufficient for clinical purposes. The current standard of care for advanced non-small cell lung carcinoma is to determine the chemotherapies to use on the basis of precise histologic subtype. In advanced, non-squamous cell carcinoma, molecular characterization for epidermal growth factor receptor (EGFR) mutations and/or anaplastic lymphoma kinase (ALK) alterations also helps to guide treatment decisions [1].

Metastases

Why lung metastases should have a predilection for tiny adrenal glands is enigmatic. It is suggested that the slow-flow portal venous structure of the gland (two capillary transitions) may entrap vaso-occlusive tumor emboli. An isolated adrenal metastasis is usually defined as a synchronous metastasis if it is diagnosed within six months of the diagnosis of the primary lung cancer. It is deemed a metachronous metastasis if it occurred more than six months from the time of diagnosis of NSCLC [3].

Risk factors

About 85% to 90% of patients with lung cancer have had direct exposure to tobacco. Many tobacco-related carcinogens have been identified; the two major classes are the *N*-nitrosamines and polycyclic aromatic hydrocarbons [5]. All cell types of lung cancer are associated with smoking. The strongest associations are with small cell and squamous cell carcinomas.

Dietary factors can modify risks. Higher consumption of fruits and vegetables is associated with a reduced lung cancer risk, and an increased dietary fat intake might lead to a higher risk. Supplementation with vitamins A and E, and beta carotene has not positively influenced risk [6].

Signs and Symptoms

The clinical manifestations of lung cancer result from the effects of local growth of the tumor, regional growth or spread through the lymphatic system, hematogenous distant metastatic spread, and remote paraneoplastic effects from tumor products or immune cross-reaction with tumor antigens [1].

Local growth in a central location can cause cough, hemoptysis, or features of large-airway obstruction. Peripheral growth can also cause cough and dyspnea. If the pleura or chest wall becomes involved, pain can occur. Regional growth can lead to esophageal compression (dysphagia), recurrent laryngeal nerve paralysis (hoarseness), phrenic nerve paralysis with an elevated hemidiaphragm (dyspnea), and sympathetic nerve paralysis leading to Horner's syndrome (ptosis, miosis, anhidrosis, and enophthalmos). Apical growth can lead to Pancoast's syndrome, with shoulder pain radiating in an ulnar distribution. The superior vena cava can become obstructed and the heart and pericardium can become involved. Lymphatic obstruction and spread can lead to dyspnea, hypoxia, and pleural effusions [1].

Distant metastatic disease can affect most organs. Neurologic symptoms can suggest brain metastases or spinal cord compression, and pain could indicate bone metastases. Laboratory abnormalities can point to bone marrow or liver involvement. Imaging might detect adrenal involvement.

Paraneoplastic syndromes can occur before the primary tumor appears and thus can be the first sign of disease or an indication of tumor recurrence. Paraneoplastic endocrine syndromes occur when the tumor produces hormones. The three most common are ectopic Cushing's syndrome, the syndrome of inappropriate antidiuretic hormone (SIADH), and humoral hypercalcemia of malignancy [1].

Diagnosis

Approximately 85% of patients with lung cancer are symptomatic at presentation. In the remainder, lung cancer is detected by radiographic evaluation initiated for an unrelated problem like our patient. Chest radiography and computed tomography (CT) are performed at most patients' initial evaluation. Clinical and radiographic features of the presentation dictate further evaluation [1].

Clinical features that suggest malignancy on initial evaluation include older age, current or past history of tobacco abuse, hemoptysis, and the presence of a previous malignancy. Radiographic features suggesting malignancy include the absence of a benign pattern of calcification in the detected lesion, a nodule or mass that is growing, a nodule with a spiculated or lobulated border, a larger lesion (>3 cm is considered malignant unless proven otherwise), and a cavitary lesion that is thick walled. Modern imaging techniques are used to alter the clinical probability of malignancy and hence influence biopsy decisions. Positron emission tomography (PET) using 18F fluorodeoxyglucose is the most-studied ancillary imaging technique. It has a sensitivity of 97% and a specificity of 78% as used in clinical practice [7]. Single-photon emission CT and lung nodule enhancement with contrast-enhanced CT are less well established.

Ultimately, tissue needs to be obtained to confirm the diagnosis of lung cancer. Due to advances in the treatment of non-small cell cancer, appropriate

and sufficient tumor specimens are required to allow accurate histologic subtyping and molecular characterization of the cancer. Flexible bronchoscopy and transthoracic needle biopsy are the invasive, nonsurgical approaches used to obtain tissue. If they fail or are deemed unnecessary, a surgical approach is used.

Flexible bronchoscopy has a high diagnostic yield for endoscopically visible lesions. The addition of endobronchial needle aspiration to conventional sampling techniques (washing, brushing, and endobronchial biopsy) improves this yield. The diagnostic yield from peripheral lesions is lower. Conventional sampling techniques and peripheral transbronchial needle aspiration complement each other [1].

Transthoracic needle biopsy, using fluoroscopic or CT guidance, can be used to obtain tissue. The positive predictive value of this procedure is high, the negative predictive value is modest, and the rate of establishing a specific benign diagnosis is low. Smaller nodules in central locations have lower diagnostic rates. A higher rate of pneumothorax occurs with transthoracic needle biopsy; thus, flexible bronchoscopy is often attempted first [8]. IHC: Epithelial markers [EMA,CEA],CK7>CK20,TTF-1 [2].

Staging

Accurately characterizing the anatomic extent of disease in a patient with lung cancer guides the treatment and prognosis. Non-small cell lung cancer is staged using the TNM system (T for extent of primary tumor, N for regional lymph node involvement, and M for metastasis) (Figure 5). The most recent revision to this staging system occurred in 2009 (Tables 1 and 2) [9]. Small cell lung cancer can also be staged with the TNM system

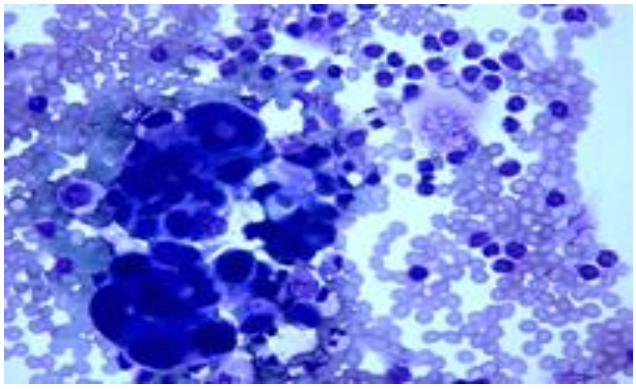

Fig-5: Cytology smear showing Adenocarcinoma pattern

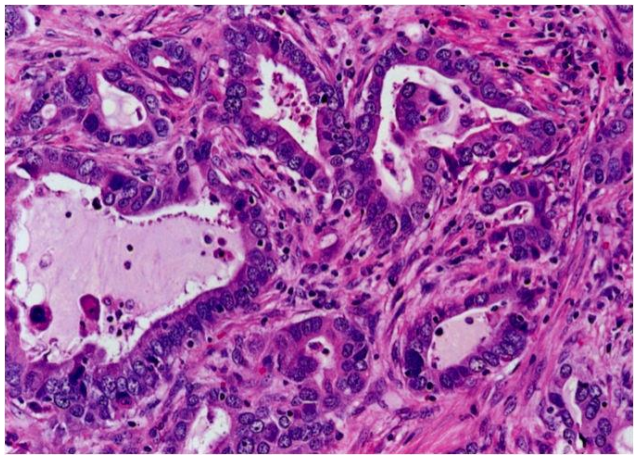

Fig-6: HPE Adenocarcinoma lung

Table 1: TNM Descriptors

Descriptor	Description	Criteria
Primary Tumor (T)		
T1	A small tumor that is not locally advanced or invasive	<3 cm in diameter; T1a ≤2 cm; T1b >2 cm ≤3 cm Surrounded by lung or visceral pleura Does not extend into the main bronchus
T2	A larger tumor that is minimally advanced or invasive	>3 cm in diameter, ≤7 cm; T2a >3 cm ≤5 cm; T2b >5 cm ≤7 cm Might invade the visceral pleura Might extend into the main bronchus but remains >2 cm from the main carina Might cause segmental or lobar atelectasis
T3	Any size tumor that is locally advanced or invasive up to but not including the major intrathoracic structures	>7 cm or Might involve the chest wall, diaphragm, mediastinal pleura, parietal pericardium, main bronchus within 2 cm of the main carina (not involving the main carina) Might cause atelectasis of the entire lung Presence of satellite tumor nodule(s) within the primary tumor lobe
T4	Any size tumor that is advanced or invasive into the major intrathoracic structures	Any size Invades the mediastinum, heart, great vessels, trachea, esophagus, vertebral body, main carina Presence of satellite tumor nodule(s) in a different ipsilateral tumor lobe
Regional Lymph Node Involvement (N)		
N1	Metastatic disease to nodes within the ipsilateral lung	Direct extension to intrapulmonary nodes Metastasis to ipsilateral peribronchial and/or hilar nodes (nodal stations 10 through 14)
N2	Metastatic disease to nodes beyond the ipsilateral lung but not contralateral to the primary tumor	Metastasis to the ipsilateral mediastinal and/or subcarinal nodes (nodal stations 1 through 9)
N3	Metastatic disease to nodes distant to those included in N2	Metastasis to contralateral mediastinal and/or hilar nodes ipsilateral or contralateral scalene and/or supraclavicular nodes
Metastases (M)		
M0	Local or regional disease	No distant metastases
M1	Disseminated disease	m1a – Presence of satellite tumor nodule(s) in contralateral lung malignant pleural or paranodal effusion m1b – Distant metastases present

Table 2: Non–Small Cell Lung Cancer Staging

Stage	Description
IA	T1a, b N0 M0
IB	T2a N0 M0
IIA	T1a, b N1 M0; T2a N1 M0; T2b N0 M0
IIB	T2b N1 M0, T3 N0 M0
IIIA	T3 N1 M0, T(1-3) N2 M0, T4N(0-1) M0
IIIB	T4 N(2-3) M0, T(1-4) N3 M0
IV	T(any) N(any) M1a, b

Treatment of choice for patients with stage IV lung carcinoma and good performance status is palliative chemotherapy. Although chemotherapy improves survival and quality of life in these patients [10], virtually all patients will die of progressive disease

SUMMARY

- Lung cancer causes more cancer-related deaths
- The most important and easily modifiable risk factor for lung cancer is cigarette smoking.
- Symptoms are often absent until lung cancer has advanced; thus, only 15% of lung cancer patients live for 5 years after their diagnosis.
- The histologic subtype, molecular markers, stage of lung cancer and the patient's performance status

guide treatment decisions and influence the prognosis.

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