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Malignant Pleural Effusion in Lung Adenocarcinoma Patient: Case Report

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Abstract : ***Lung adenocarcinoma is a widespread primary lung cancer. Lung cancer itself is one of the leading causes of death in human with 159,000 deaths in 2015. Lung cancer can be categorized into two main histological groups where adenocarcinoma falls in the non-SCLC group. Hereby we present a case of a 69 year old woman with lung adenocarcinoma and malignant pleural effusion. This patient presented symptoms of shortness of breath and chest x ray shows a massive right-sided pleural effusion. Pleural effusion is often a marker of progression of the underlying malignancy.***

Keywords: Pleural effusion, adenocarcinoma, lung cancer

1. Introduction

Lung adenocarcinoma is the most common primary lung cancer seen in the United States. It falls under the umbrella of non-small cell lung cancer (NSCLC) and has a strong association with previous smoking. Lung cancer is also widespread globally. Despite new treatments, the 5-year survival is less than 12% to 15%. Over the past 4 decades, there has been a marked increase in lung adenocarcinoma in women, and this has been linked to smoking. Although incidence and mortality have declined since the 1980s, in 2015 there were 221,200 new cases of lung and bronchial cancers and more than 158,000 lung cancer deaths representing the most common cause of cancer death. The mean age of diagnosis of lung adenocarcinoma is 71 years, and this particular cancer is very rare before the age of 20. In the last 2 decades, adenocarcinoma has replaced squamous cell cancer of the lung as the most prevalent non-small cell cancer.[1]

Lung cancer is categorized into two main histological groups: small cell lung carcinoma (SCLC, 15% of all lung cancers) and non-SCLC (NSCLC, 85% of all lung cancers). NSCLCs are generally subcategorized into adenocarcinoma, squamous cell carcinoma (SqCC), and large cell carcinoma. The histopathological classification of lung cancer has recently been revised and published as the 2015 WHO classification. For lung adenocarcinoma, the 2011 International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society classification was mostly adopted in the 2015 WHO classification.[2]

Adenocarcinoma was defined as carcinoma with an acinar/ tubular structure or mucin production, whereas SqCC was defined as carcinoma with keratinization or intercellular bridges. The 2015 WHO classification divides adenocarcinomas into adenocarcinoma *in situ* (AIS, preinvasive lesion), minimally invasive adenocarcinoma (MIA), or (overt) invasive adenocarcinoma based on the extent of invasiveness.[2]

Adenocarcinoma *in situ* is defined as an adenocarcinoma comprising a lepidic pattern with a diameter of ≤3 cm. If the tumor diameter exceeds 3 cm, it is defined as "lepidic predominant adenocarcinoma, suspect AIS" because these tumors are rare and lack adequate characterization. Minimally invasive adenocarcinoma is defined as an adenocarcinoma with a diameter of ≤3 cm and an invasion size of ≤5 mm. Even if the tumor size and invasion size comply with the definition of MIA, the presence of lymphovascular invasion, pleural invasion, or tumor necrosis can be an exclusion factor for an MIA diagnosis. If the tumor size exceeds 3 cm with an invasion size of ≤5 mm, it is defined as "lepidic predominant adenocarcinoma, suspect MIA" because these tumors are rare and lack adequate characterization. The term "invasive adenocarcinoma, mixed subtype" for invasive adenocarcinoma is no longer used. Invasive adenocarcinoma is now classified using five predominant patterns: lepidic, papillary, acinar, micropapillary, and solid adenocarcinoma. The term "invasive mucinous adenocarcinoma (IMA)" replaced mucinous BAC. IMA and mucinous AIS are accurately classified based on invasiveness. Besides IMA, variants of invasive adenocarcinoma comprise enteric, colloid, and fetal adenocarcinoma. Enteric adenocarcinoma is defined as adenocarcinoma with a predominant component that resembles adenocarcinoma arising in the colorectum and often shows CDX2 immunoreactivity.[2]

Carcinomas of the lung frequently cause malignant pleural effusions. Lung adenocarcinoma is especially associated with malignant pleural effusions, indicating advanced stage disease or disease progression. Malignant pleural effusion (MPE) is one of the commonest causes of an exudative pleural effusion, and its incidence is increasing with increasing cancer prevalence and as more effective cancer therapy that prolongs

life. In lung cancer, the presence of a pleural effusion upstages the cancer to stage IV, denoting a worse prognosis. Thoracentesis is necessary for the diagnosis and treatment of malignant pleural effusions. Cancer cells in these cases can be collected via thoracentesis, instead of through other more invasive procedures, such as biopsy or surgery.[3]

2. Case illustration

A 69 year old female came to the Emergency Room (ER) on 13th December 2020 with chief complain of shortness of breath since 2 weeks ago. Shortness of breath felt increasingly worse since 3 days prior to arrival to the ER. Patient had no symptoms of fever, cough, haemoptysis and nose congestion. Patient did not complain of chest pain and dyspnea on effort. There was no history of swelling in the lower extremities, weight loss or anorexia. Patient went to see a general practitioner 2 days prior, she was tested for a complete blood test and ECG. The doctor told her that the results were within normal limit and recommended a chest x-ray examination. Patient has a history of diabetes mellitus and hypertension and routinely consumes Metformin 1x500 mg and Ramipril 1x5 mg daily. History of lung disease and cancer are denied. Patient is a house wife and does not smoke cigarette.

Physical examination revealed compost mental consciousness, blood pressure 120/80 mmHg, pulse of 85 beats per minute, respiration 28 times per minute, axillary temperature 36.7, and oxygen saturation 93% in room air. On physical examination, dypsneu was observed. Physical examination revealed asymmetric chest movement, right part of lung moved slower during breathing, vocal fremitus on the right chest decreased, dullness was found at the right chest. The cardiac examination showed regular rhythm with no rubs, murmurs, or gallops on auscultation. No jugular venous distention was observed, but the patient's large neck precluded proper assessment of jugular venous distension. The remaining systemic examination was unremarkable.

Complete blood test of the patient shows: Leukocytes 9.61 x 10^3 / µL; Erythrocytes 5.03 x 10^6 / µL; Hemoglobin 15 g / dL; Hematocrit 44.2%; Platelets 371 x 10^3 / µL; Monocyte 1.11 %, Neutrophyl 5.82 %. Renal function test was within normal limit; Nonreactive anti SARS CoV 2 IgM and IgG. ECG was within normal limits. Chest X-ray showed a massive right-sided pleural effusion and blunting of the left costophrenic angle [**Fig 1.**]

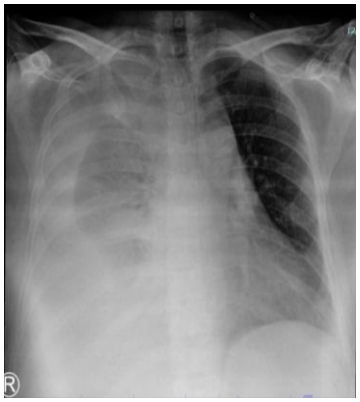

Figure 1: Chest X-ray

Initial therapy addressed to this patient was an infusion of 4 liters of O2 per minute using a nasal canule, budesonide, salbutamol, and ipatoprium bromide inhalation therapy. Patient underwent pleural fluid evacuation by pulmonologist, and around 1 liter of pleural fluid were removed. Thoracentesis revealed serous hemorrhagic pleural fluid. Adenosine deaminase test of pleural fluid showed within normal limit (7 U/L). The cytological examination showed atypical cells, suggesting adenocarcinoma. Furthermore, a CT scan of the thorax demonstrated pleural nodular mass with smooth margin, size 7.1x1.5x6.6 cm involves the parietal and visceral pleural also pleural fissures, pericardium, invade the mediastinal fat (T3) with right pleural effusion; multiple lymph node subcentimeter enlargement (N2); no sign of mass/ nodule metastasis at both lung parenchyma; calcification of aortic arch and descending aorta.

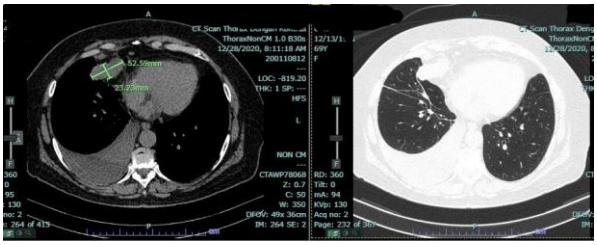

Figure 2: CT-Scan

Computed tomography (CT) head with contrast showed no metastatic nodule or perifocal edema, while CT abdomen and pelvis with contrast showed no metastatic nodule at liver or paraaortocaval. Due to rapid reaccumulation of pleural effusion, the patient underwent additional thoracenteses weekly, around 500-750 of sero-hemorrhagic pleural fluid were removed weekly. The epidermal growth factor receptor (EGFR) mutation test revealed wild type mutation status, while membrane expression of PD-L1 was not detected in tumor cells. Patient was referred to oncologist consultant to provide best medical care possible for chemotherapy.

3. Discussion

We report a case of lung adenocarcinoma, with the presence of pleural effusion in the lung, which is thought to be a complication caused by the tumor.

In this case, the patient came with complaint of shortness of breath for 2 weeks prior to admission. On physical examination, dypsnea was observed. Physical examination revealed asymmetric chest movement, right part of lung moved slower during breathing, vocal fremitus on the right chest decreased, dullness was found at the right chest. Chest X-ray showed a massive right-sided pleural effusion and blunting of the left costophrenic angle. Cytological examination showed atypical cells, suggesting adenocarcinoma. CT scan of the thorax showed pleural nodular mass with smooth margin, size 7.1x1.5x6.6 cm involves the parietal and visceral pleural also pleural fissures, pericardium, invade the mediastinal fat (T3) with right pleural effusion; multiple lymph node subcentimeter enlargement (N2). EGFR mutation test revealed wild type mutation status.

Lung cancer can present with a wide range of symptoms, the most common being cough, haemoptysis, chest and shoulder pain, dyspnoea, hoarseness, weight loss, anorexia, fever, weakness, and bone pain. Cough and dyspnoea were found to be the most common symptoms. Unfortunately, symptoms of lung cancer are largely non-specific and recognition of new symptoms is more difficult in the presence of co-existing respiratory disease.[4]

The initial investigation for possible lung cancer in primary care is a chest X-ray.[5] In this patient, chest x-ray shows massive right-sided pleural effusion and blunting of the left costophrenic angle. Approximately 35% of pleural effusion cases are secondary to lung cancer. At the time of diagnosis, 15% of lung cancer patients have pleural effusions, and over time, this rate increases to 50%. Pleural effusion formation is multifunctional. Pleural effusion formation is associated with i) impaired drainage of the pleural space due to obstruction of vessels and lymphatics of the lung and pleura, ii) increased pleural formation and iii) inflammation and associated vascular increased permeability, resulting in plasma leakage; these are fundamental to the development of exudative, protein-rich pleural effusions. Increased permeability of the pleural microvasculature is generally attributed to factors that are released in inflammatory and malignant pleural diseases.[6]

Cytology is a useful tool in the diagnosis of pulmonary adenocarcinoma. Various sampling techniques are available to procure samples for cytologic evaluation in lung malignancies. These include exfoliative cytology samples such as induced sputum, abrasive cytology samples [bronchial brushing, bronchial washing, bronchioalveolar lavage (BAL)] and fine-needle aspiration cytology (FNAC), which can be endobronchial ultrasound-guided, transesophageal, computed tomography (CT)-guided percutaneous or transthoracic. Accurate cytological diagnosis of pulmonary adenocarcinoma will aid in utilizing the cytological smears and biopsy tissue for molecular testing.[7]

EGFR mutations are commonly detected in adenocarcinoma, with higher rates amongst Asians than Caucasians.[8] EGFR is a glycoprotein that plays a vital role in cell proliferation and apoptosis and has been shown to be important in tumorigenesis.[9] The standard for EGFR mutation testing involved direct sequencing of DNA extracted from samples of tumour tissue gathered during biopsy or resection, usually in the form of formalin-fixed paraffin-embedded diagnostic block.[9] When lung cancer tumor cells do NOT have the EGFR mutation, they are called “EGFR negative” or “EGFR wildtype.”[11]

Based on the staging of lung carcinoma, T3 N 2 M 0 can be classified as stage IIIB. The treatment of lung adenocarcinoma depends on the stage. For early-stage disease, surgery is the treatment of choice. For advanced disease, a combination of surgery, chemotherapy, and radiation is used to manage pain and other complications.[1] In the past, radiotherapy was considered the standard therapy in IIIB patients but demonstrated very low survival, poor local control and early development of distant disease. Patients with inoperable stage III treated only with thoracic radiotherapy experienced a median survival of 9-11 months, 2-year survival of 10-20% and 3-year survival of 5-10%.[12]

Thoracentesis is minimally invasive, can be performed easily in the outpatient setting, provides immediate relief in most patients, and can be repeated if needed in patients with expected shortened survival.[12] Thoracentesis consists in drainage of pleural cavity using small catheters (14–18 G). Although the effect of the procedure may be temporary due to the high chance of recurrence, thoracentesis can be the best option in very frail patients, with poor life-expectancy or in those not fit for pleurodesis or for the use of an indwelling pleural catheter. Its advantages include its technical simplicity, the capacity of adequate drainage of the pleural space, and the possibility of being performed in an outpatient setting.[14]

4. Conclusion

Lung cancer or lung carcinoma is a malignant lung tumor characterized by uncontrolled cell growth in the lung tissues. The two main types of(cancer) are small –cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (NSCLC). The most common clinical manifestations are coughing (including coughing of blood), weight loss, shortness of breath and chest pain. Diagnosis mainly by chest radiographs and computed tomography (CT) scans. Pleural effusion is often a marker of progression of the underlying malignancy. The diagnosis is confirmed with biopsy by bronchoscopy or CT-guidance. Common treatment include surgery, chemotherapy, and radiography. NSCLC is sometimes treated with surgery, whereas SCLC usually respond to chemotherapy and radiotherapy.[15]

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