Diagnosis, management and prevention of carcinoma lung
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Introduction
Cancer, as a common disease, injured human health grievously. Though people generally regarded cancer as an “Incurable disease”, in fact, it cancers are found or treated at an ear?” stage, more than 85% of them can be cured. Nevertheless, due to people’s ignorance of the regular pattern of cancer’s occurrence, when patients receive medical advice, most of them have reached the late stage and reduce chances of successful treatment.” The rising wind forebides the coming storm”, as the old saying goes. Everything has certain signs before appearing and developing. Therefore we can discover cancer at an early stage as long as we explore it conscientiously. Lung cancer is the most common cause of cancer death in both men and women world wide. Though nicotine is the key etiology factor, has been known for years, the long lag between exposure and the clinical symptoms of tumor has hampered the initiation of preventive programs in this disease. In addition, reducing tobacco use has major economic and political ramifications.

In the United States alone, 178,000 new lung cancer cases were expected in 1998 and 160400 deaths. The incidence of lung cancer has increased rapidly during the last four decades. The continuous increase in the incidence of lung cancer makes the understanding of etiology, prevention and treatment of this disease more important than ever.

Although genetic factors may predispose patients to develop lung cancer, environmental exposure to carcinogens is responsible for the vast majority of cases. It is well established that dominant risk factor for lung cancer is cigarette smoking.

Tobacco smoking accounts 3° for 85% of all lung cancer 3° cases, and the risk of developing lung carcinoma is directly proportional to the amount of tobacco smoked. After cessation of smoking, after cessation and asymptotically approaching that of non-smokers after 15 years. In addition, passive exposure to cigarette smoke increases the risk of lung cancer in non-smokers 2-3 times and accounts for 25% of lung cancer cases in non-smokers. Previous pulmonary pathology may be associated with lung cancers such as bronchitis and emphysema (COPD) appear to be at a substantial risk of developing lung carcinoma as many as 8.8% developing cancer within 10 years. Many of these are “scar carcinoma with adenocarcinoma histology. Progressive systemic disease such as scleroderma significantly increased the risk of developing lung cancer, especially broncho-alveolar carcinoma.

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Some occupations have been linked to an increased risk of lung cancers. Increases in lung cancer risk accompany exposure to carcinogens, such as asbestos, radon, bis(chloromethyl) ether, polycyclic aromatic hydrocarbons, chromium, nickel, and inorganic arsenic compounds. Asbestos exposed personnel have been suffered from all types of lung cancer, although small and squamous cell carcinoma are the most commonest. The association with occupational exposure to these agents appears to be independent of cigarette smoking.

Air pollution has been incriminated in the development of lung cancer.

Pathology
Histogenesis
Evidence is increasing that lung cancer is derived from a pluripotent stem cell that is capable of expressing a variety of phenotypes. This epithelial stem cell, in normal histogenesis, differentiates to those cells found in the tracheobronchial tree, including pseudostratified reserved cells, ciliated goblet columnar cells, neuroendocrine cells, and type I and II pneumocytes seen lining the alveoli. Cells that are ‘hyperplastic, metaplastic or neocapable of division can express plastic change.

Four main histological types are as follows
- Squamous cell carcinoma (50%)
- Adenocarcinoma (10%)
- Large cell carcinoma (Anaplastic type (20%)
- Small cell carcinoma 20%

Location
Carcinoma lung is common in the right than in the left. The upper lobes are involved more than the lower lobes. Location of the lesion generally depend on histology. Squamous cell carcinoma commonly occur centrally and invade the bronchial cartilage and causing obstruction. Metastases relatively in late. Adenocarcinoma mostly arise peripherally and tend to invade pleura. The bronchoalveolar variant are associated with previous lung damage from various chronic pulmonary diseases. But papillary adenocarcinoma developed from scar.

Large cell carcinoma anaplastic type consists of poorly differentiated squamous and adenocarcinoma components and occur both centrally and peripherally. Giant cell variant is very fatal and clear cell type may be confused with metastatic renal cell carcinoma. Small cell carcinoma is composed of submucosal anaplastic cells. Types are - Oat cell type, combined type. Anaplastic tumours arise centrally and metastasize early. Metastases to bone may osteoblastic in appearance.

Clinical features
Loco-regional manifestation
Local manifestation
Central tumour produces cough, hemoptysis, respiratory difficulty (wheezing, dyspnea, stridor), pain and symptoms of pneumonia.
Peripheral tumour produces cough, pain in the chest wall, respiratory difficulty (dyspnea), Pleural effusion, symptoms of lung abscess (cavitary squamous tumour); and Pan coast tumor presenting with pain in the shoulder and arm and Homers syndrome (ipsilateral miosis, ptosis and anhydrosis).

Regional manifestation
Direct extension from the primary tumor can result in hoarseness of voice (paralysis of recurrent laryngeal nerve). Superior Vena Caval Obstruction Syndrome from compression or invasion to superior vena cava and pericardial tamponade (pulsus paradoxicus, distended neck veins, tachycardia, pericardial rub, distant heart tones and kussmals sign).

Nonmetastatic Generalized Features
The anorexia-cachexia syndrome and generalized weakness and fatigue are the most common and least understood nonmetastatic complications of lung cancer. In addition, a variety of paraneoplastic syndromes associated with epithelial lung cancer have been identified. Hypertrophic Pulmonary Osteoarthropathy (HPO) occurs frequently in NSCLC patients. Symptoms of bone and joint pain herald the onset of this condition and can be the presenting signs of lung cancer. Clubbing of the digits is observed. The alkaline phosphatase level is commonly
elevated, while serum hepatic enzyme levels are normal.

**Metastatic Manifestations**
Lung cancer metastasize through lymphatics and blood circulation. Nearly all patients with advanced inoperable NSCLC demonstrate symptoms referable to their disease at the time of initial presentation. Most patients, in fact, have more than one symptom at the onset of their illness. Fatigue and decreased activity were reported by more than 80%, and most patients also experienced cough, dyspnea, decreased appetite, and weight loss.

Although lung cancer can metastasizes to virtually any organ, the most common sites of spread that are clinically apparent are the pleura, lung, bone, brain, pericardium, liver and adrenal glands. The presenting complaints of a patient with metastatic spread are largely determined by the specific metastatic organ site involved. For example, bone metastases present with pain and limitation of function in the affected area.

**Diagnostic work up**
A. *Medical History and physical examination*: A detailed history and accurate physical examination remain the most important in assessing a patient with lung cancer. Smoking history, past exposure to environmental carcinogens and family history may suggest a higher probability of lung cancer.

New symptoms, including a change in cough, hemoptysis, or history of recurrent respiratory infection, are of concern. Symptoms suggesting locoregional spread include chest pain, symptoms of recurrent nerve palsy, or superior vena cava obstruction. Symptoms suggestive of metastatic disease frequently include focal neurologic symptoms, bone pain or weight loss. Occasionally, patients suffering from NSCLC present with symptoms and signs of a paraneoplastic syndrome but not as frequently as with small cell tumors. Physical examination should look for signs of partial or complete obstruction of airways, atelectasis or pneumonia, and pleural effusions. Examination of the head and neck, including the draining regional lymph node areas in the supraclavicular area, may demonstrate lymphadenopathy, indicating regional lymphatic (N3) spread.

B. *Primary tests and procedures*: All patients with suspected lung cancer should have the following tests performed.

1. **Blood tests**
2. **Sputum cytology**: With sputum samples, up to 80% of central tumors can be diagnosed. The yield is much smaller for peripheral tumors, dropping to less than 20% for peripheral tumors smaller than 3.0 cm in diameter. A 3-day collection of early morning sputum, preserved in Saccamano’s solution, appears to be the optimal method of assessment. Squamous cell tumors, being more proximal, are more frequently diagnosed by cytology than adenocarcinoma or large cell tumors.
3. **Pulmonary function tests**
4. **Imaging Studies**:
   a. **Chest Radiography**: Chest radiography is probably the most valuable tool in the diagnosis of lung cancer. A perfectly normal chest radiograph rules out this diagnosis in most instances, except for the rare occult tumor.
   b. **Computed Tomography of thorax**: CT imaging can confirm abnormalities seen on pain chest radiographs, can often detect early (<1 cm) lesions that cannot be seen on chest radiographs, and has played an important role in staging of lung cancer, especially spread to
areas of the mediastinum undetected on plain films.

Fig. CT Scan shows bronchial carcinoma in right paravertbral gutter demonstrating cavitation and spread to hilum and chest wall.

c. Magnetic Resonance Imaging (MRI): Magnetic Resonance Imaging MRI investigation of pulmonary lesions has been disappointing and has offered no improvement over CT scan.

II. Invasive Procedures
a. Fine Needle Aspiration Cytology from:
   • Lung Tumour
   • Regional Lymph Node
b. Bronchoscopy
c. Transthoracic percutaneous needle biopsy

Management
A. Surgery: Excluding small cell lung cancer, surgery provide the best chance of cure in lung cancer patients. Generally resection is indicated in patients whose gross disease and those do not having any surgical or medical contraindication can be resected technically (Stage I, II or I1k without mediastinal or subcarinal lymph node metastases). Whose existing pulmonary reserve (an compensate (Karnofsky performance > 80; status FEV1>O.9 1) adequately for the loss of pulmonary parenchyma required by resection. There are many different procedures such as segmental resection, lobectomy, pneumonectomy.

B. Radiofrequency Ablation: It is a new technique to destroy tumour by radiofrequency energy, local temperature in the targeted tumour is increased beyond 50 degree Celsius. In this temperature all the proteins of the neoplastic cells become coagulated and tumour dies.

C. Radiation Therapy: Radiotherapy can be delivered as external beam, brachytherapy, intraluminal even intraoperatively. Radiation therapy is indicated in non small cell lung carcinoma with curative intent in patients with stage I or II disease who refuse or medically unfit for surgery and in patients with stage IIIa (N2) or IIIb (unresectable disease). In the postoperative setting, it is used as an adjuvant treatment to improve local control. Total doses of 5500-6000 cGY through small ports but encompassing the entire tumour with 2cm margins. Radiation therapy is indicated with palliative intent in patients with advance disease for symptomatic relief for hemoptysis, cough, dyspnea and bone / brain metastases.

D. Chemotherapy: Chemotherapy can be used as an induction concurrent or sequential with radiotherapy.

1. Non-Small Cell Lung Cancer:
   • Neo-adjuvant chemotherapy
   Recent report demonstrate that preoperative chemotherapy showed a high number of responses. Increased resectability rate and possible survival advantages in Stage I, II and III disease.

   • Adjuvant chemotherapy
   Postoperative chemotherapy had significantly longer median survival. Combination of chemotherapy with cisplatin or arboplatin based chemotherapy is usually considered as an option. Paclitaxel, Vinorelbine, Irinotecan, Topotecan, Gemcitabine, Docetaxel have shown higher response rate with above mentioned settings.

2. Small Cell Lung Cancer:
   Choice of treatment is chemotherapy: There are various combinations of drugs are used: such as Cisplatin and Etoposide (CE), Adriamycin, Cyclophosphamide and Etoposide (ACE), Ifosfamide, Carboplatin and Etoposide ICE), Cisplatin and Irinotecan (CI).

Prognosis
The 5 year survival rate of patients with non small cell lung cancer 43-54% for stage I disease, 27%-31% for stage II ,15-25% br stage IIIA, 5-7% for stage IIIB, and less than
2% for stage IV. Small cell carcinoma survival depends on extends of disease. Patients with small cell lung cancer with limited disease have a median survival of 12-16 months and 2 year survival of 5-25% while those with extensive disease achieve a median survival of 7-11 months and 2 year survival of 1-3%.

**Prevention of lung cancer**

**Primary:** With the solid tisse of scientific information linking cigarette smoking habits to the development of lung cancer, many countries have launched programs to decrease tobacco use and educate the population. Included in these programs are legislative activity (e.g., increased taxes, smoke-free areas, banning tobacco advertisement), educational activities through mass media and schools, and interventional approaches (e.g., smoking-cessation clinics) targeted to groups at the highest risk for developing tobacco-related cancer. The greatest impact on decreased smoking habits appears to be the social stigma directed at smokers. These activities have reduced the percentage of the U.S. population who smoke from a high of approximately 40% to approximately 30%.

**Secondary:** The following key warning sign can help in early diagnosis of lung cancer.

**Reference**

3. Cullen JW The National Cancer Institute’s smoking, tobacco and cancer program chest 1989;96:9S.