Lung Tumours

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Primary carcinoma of the lung was an uncommon cancer until the 1930s. At that time a dramatic increase in the incidence of lung cancer began that has not yet abated. Although the overall incidence of lung cancer has dramatically increased over the past 30 years, the relative incidence of squamous cell carcinoma has decreased, and adenocarcinoma has become the dominant cell type—a phenomenon that has been temporally associated with the changes in tobacco blends and the use of filters in cigarettes.

Lung cancer is now the most common cause of cancer mortality in both males and females.
Classification of the malignant lung tumours

- Small cell carcinoma
- Non small cell carcinomas
- Mesothelioma
- Metastases from distant sites (Breast, GIT, Ovarian Ca, Melanoma)
Non malignant causes of a mass in the lung

- Radiographic artefact- eg nipple shadow
- Infection – aspergilloma (X-ray reveals dense round ball, capped by slim meniscus of air, in a cavity)
- Connective tissue disease- Wegeners granulomatosis. (necrotizing granulomatous angiitis involving the lungs. X-ray reveals diffuse or nodular infiltrates that may resemble malignant metastases.)
Aetiology of malignant lung tumours

- Smoking-80% lung cancer occur in active or former smokers.
- 5% occur in passive smokers.
- Much less frequent causes of lung cancer are exposure to:
  - Asbestos (associated with Mesothelioma)
  - Radon
  - Polycyclic aromatic hydrocarbons
  - Nikel
  - Chromate
  - Inorganic arsenicals
WHO pathological classification

A. Squamous Cell Ca 30%
B. Small Cell Ca 20%
C. Adenocarcinama 40%:
   - Acinar
   - Papillary
   - Bronchoalveolar
   - Mucinous
D. Large Cell Ca
E. Mixed
For the purpose of management, lung cancers are grouped as:

- Non-small cell lung cancer (NSCLC)
- Small cell lung cancer (SCLC)
Clinical presentations of malignant lung tumours

1. **Symptoms:**

   Depend on the size, location and metastases

   a. Cough
   b. Haemoptisis
   c. Dyspnea
   d. Chest pain
   e. Recurrent chest infections
   f. Dysphagia
   g. Hoarseness
2. Signs - Local and paraneoplastic

A. Local Signs:

- Chest sign - nil or signs of collapse/consolidation/formation of abscess
- Horner’s syndrome (miosis, ptosis, enophthalmos, and anhydrosis)
- Pancoast’s syndrome (lower brachial plexopathy, Horner’s syndrome, shoulder pain)
- Superior vena cava syndrome (Swelling of the neck, face, and arms especially in the morning, headache, visual disturbance. Fixed engorgement of external and internal jugular veins, collateral veins over the chest wall)
- Supraclavicular mass/Lymph node
B. Paraneoplastic signs

- Clubbing
- Hypertrophic pulmonary osteoartropathy: bone and joint pain, periostal inflammation and elevation on the X-ray, affects the distal end of the long bones, elevated ALP, respond to Aspirin and NSAID
- Proximal myopathy
- Peripheral neuropathy
- Eaton-Lambert myastenic syndrom: weakness affecting the limbs and sparing the ocular and bulbar muscle. Pt. Complain of weakness and pain in the proximal limbs, paresthesias, dry mouth, impotents and ptosis, deep tendon reflexes-reduced
- IADH secretion
Investigations

1. Chest X-ray (AP and lateral)
2. Sputum Cytology
3. Tissue biopsy :
   - Biopsy of mass
   - Bronchoscopy
   - CT-guided biopsy
   - Mediastinotomy
   - Thoracotomy
It is essential to make a definitive diagnosis prior to the treatment. This might be difficult. Cytology can be misleading.

An exception is a life threatening SVC syndrome – Radiation prior to the diagnosis.
Staging

1. Different staging systems used for different tumours.

2. Tests required for adequate staging:
   - FBC/UKE/LFT/Ca- may reveal biochemical paraneoplastic phenomena, eg hyponatremia, hypercalcaemia, or suggest sites of metastases.
   - CT chest and abdomen: size of the tumour, site, relationship to the chest wall, fissures, mediastinal structures, diaphragm, lymphnodes>1cm, involvement of the liver and adrenals.
   - Bone scan- if symptoms suggestive of bone metastases (pain, Elevated ALP and Ca)
   - CT of the brain – if CNS signs
   - MUGA or heart sonar if suspicious of underlying heart disease and cardiotoxic chemotherapy planned.
1. Non small cell lung cancer (NSCLC)

TNM Staging
T- Size of the tumour, structures it invades, closeness to carina. T1-4
N- Nodes (ipsilateral, bilateral, position of nodes) N1-3
M- Presence of distant metastases. M0-1
Stage 1-4
<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM</th>
<th>Survival Rate (%)</th>
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<tr>
<td>Revised staging system</td>
<td></td>
<td></td>
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<tr>
<td>IA</td>
<td>T1, N0, M0</td>
<td>&gt;70</td>
</tr>
<tr>
<td>IB</td>
<td>T2, N0, M0</td>
<td>60</td>
</tr>
<tr>
<td>IIA</td>
<td>T1, N1, M0</td>
<td>50</td>
</tr>
<tr>
<td>IIB</td>
<td>T2, N1, M0</td>
<td>30</td>
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<tr>
<td></td>
<td>T3, N0–N1, M0</td>
<td>40</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1–T3, N2, M0</td>
<td>10–30</td>
</tr>
<tr>
<td>IIIB</td>
<td>Any T4, any N3, M0</td>
<td>&lt;10</td>
</tr>
<tr>
<td>IV</td>
<td>Any M1</td>
<td>&lt;5</td>
</tr>
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</table>
2. Small cell lung cancer

Limited or Extensive stage

1. Limited- tumour confined to ipsilateral thorax and nodes and able to fit in one radiation field.

2. Extensive- disease which can not fit in one radiation field.
3. Mesothelioma

Number of different systems including TNM and Buchart classification.
TNM staging system for MPM

T- reflects the invaded structures by the tumour. T1 limited to the pleura; T2 invades the diaphragmal muscle or pulmonary parenchima; T3 is defined as locally advanced and resectable, T4 is defined as locally advanced unresectable

N-Reflects the involved lymphnode N0-3

M-Reflects the distant metastases. M0-1
<table>
<thead>
<tr>
<th>Stage I</th>
<th>Ia: T1aN0 M0</th>
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<tr>
<td>Ib: T1bN0 M0</td>
<td></td>
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<tr>
<td>Stage II</td>
<td>T2 N0 M0</td>
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<tr>
<td>Stage III</td>
<td>Any T3 M0</td>
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<tr>
<td>Any N1 M0</td>
<td></td>
</tr>
<tr>
<td>Any N2 M0</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T4</td>
</tr>
<tr>
<td>Any N3</td>
<td></td>
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</table>
Performance status (PS)

WHO performance status score:
0-no symptoms
1-Symptoms but normal activity
2-Symptoms causing the pt. to lie in bed < 50% of the day
3-Symptoms causing the pt. to lie in bed > 50% of the day
4-The pt is bedridden
PS is a very important concept in oncology. The PS together with the stage of the disease helps the oncologist to decide whether the patient will benefit from chemotherapy. NSCLC and mesothelioma, PS>2 do very poorly on chemotherapy.
Individual tumors in more details

1. SCLC
2. NSCLC
3. Mesothelioma
1. Small cell lung cancer (SCLC)

- It is one of the most aggressive, fast growing tumors
- Without treatment the median survival is 6-9 weeks
- Refer the patient as soon as you have the diagnosis
Chemotherapy

- Mainstay of treatment, because of the chemo-responsiveness of the SCLC and frequent dissemination at the time of diagnosis.
- Various regimens exist (Adriamycin-based, Cisplatin-based, Ifosfomide-based).
- Substantial activity has been shown by several new agents, including the taxanes (paclitaxel, docetaxel) and the topoisomerase I inhibitors (topotecan, irinotecan), gemcitabine, and vinorelbine.
- Response rates: 75-90% for limited stage and 75% for extensive stage.
- 50% of limited stage have complete response (CR).
- 25% CR for the extensive stage.
Cisplatin-based:
Cisplatin 80 mg/m day 1 and etoposide 80 mg/m days 1, 2, 3
Cisplatin 25 mg/m days 1, 2, 3 and etoposide 100 mg/m days 1, 2, 3

Doxorubicin-based
Cyclophosphamide 1000 mg/m day 1 and doxorubicin 45 mg/m day 1 and
vincristine 1.4 mg/m day 1

Ifosfamide-based
Ifosfamide 1200 mg/m days 1, 2, 3, 4 and etoposide 75 mg/m days 1, 2, 3, 4
and cisplatin 20 mg/m days 1, 2, 3, 4
Mesna required for ifosfamide.
Despite the excellent response rates, cure is very unusual. Median survival for Limited stage is 14 months and for extensive stage 7 months.
Radiation

- 60% of the relapses after chemotherapy are in the thorax. TI reduces the risk of relapse by 50%
- Has role in SVCS and spinal cord compression
- High risk of brain metastases in SCLC (20% have brain involvement at diagnosis, 80% have brain involvement at death) - prophylactic cranial RT increases 3 year survival by 5% and is usually given if the patient is in CR post chemotherapy
- Palliative RT – short course of irradiation to either the primary tumor or site of metastases can provide useful symptom control.
2. Non small cell lung cancer

- Adenocarcinoma
- Squamous cell carcinoma
- Large cell carcinoma
More slow growing than SCLC.

Surgery and radiotherapy have more important role than in SCLC.
Treatment of NSCLC

Surgical removal of NSCLC continues to offer best possibility of cure. Consequently, each patient should be considered where possible for surgical treatment, although advanced stage and significant co-morbidity will preclude this option in many patients.
First group: stage 1, 2, 3A. Surgically resectable

- Surgery (lobectomy) is the treatment of choice - 60-80% cure
- Radiotherapy if contraindication for surgery - 20% cure
- Adjuvant chemotherapy may have a role in stage 1, 2 and 3A providing survival advantage.
Second groupe: T3-T4 and/or N1-N2 (advanced Lung Ca)

Surgery is still the treatment of choice with chemoradiotherapy or chemotherapy

Patients with unresectable N2-3 can be treated with combined Chemo-radiotherapy
Third group: Metastatic disease (M1)

Radiation therapy or chemotherapy for palliation of symptoms

Patients previously treated with platinum based chemotherapy may have survival benefit and symptoms control from Taxol and epidermal growth factor receptor inhibitor.
Stage 4 NSCLC

- Chemotherapy improves survival (10% 1 year if untreated vs 30% if treated)
- Different regimens are used most platinum-based
- Unfortunately median survival remains poor (10 months)
- Palliation is very important - adequate pain control, pleurodesis for recurrent pleural effusion, drugs for dispnoea.
PRINCIPLES OF CHEMOTHERAPY FOR ADVANCED NON-SMALL CELL LUNG CANCER

- Survival: more appropriate measure of outcome than response.
- Baseline prognostic variables (stage, weight loss, PS, gender) predict survival.
- Platinum-based chemotherapy prolongs survival, improves symptom control and yields superior quality of life compared to best supportive care.
- New agent platinum combinations have generated a plateau in overall response rate (ORR) (25-35%), time to progression (TTP) (4-6 mo), median survival (8-10 mo) and 1 y, survival rate (30-40%) in fit patients.
- No specific new agent - platinum combination is clearly superior.
- Fit elderly merit appropriate treatment.
- Unfit of any age do not benefit from cytotoxic treatment.
3. Mesothelioma

1. Malignant pleural mesothelioma (MPM) is an aggressive tumour arising from the serosal lining of the chest and abdomen with survival rates less then 1 year reported following diagnosis.

2. M/F ratio - 5:1

3. High correlation with asbestos exposure

4. Other causative agents include:
   - Radiation
   - Thorium dioxide
   - Silicate fibers
   - Simian virus 40 (SV40), discovered as contaminant of early poliovirus vaccines.
Pathology

Three distinctive subtypes have been identified:

1. Epithelial (50% of all cases)
2. Sarcomatouse
3. Mixed histologies

Distinguishing mesothelioma from other intrathoracic malignancies such as adenocarcinoma is important and requires assistance of experienced pathologist.
**Treatment**

1. Localized MPM
   - Surgery if technically possible
   - Palliative RT

2. Extensive MPM
   - Aim is to palliate symptoms
   - Radiotherapy/Pleurodesis
   - Single agent chemotherapy has 10-20% response rate
   - New agents show more promises Alimta, Gemzar
   - Alimta +Cisplatin improves survival and quality of life in comparison with cisplatin alone
Prognosis for MPM remains very poor
Median survival - 6 to 12 months
Take home message

- Have a high index of suspicion in smoker with suggestive symptoms
- High correlation between MPM and asbestos exposure (>15 yrs. Prior)
- Do appropriate diagnostic tests quickly and try to get histological confirmation as soon as possible
- Refer the patient early- Chemotherapy and/or Radiotherapy improves survival and quality of life.
Novel therapeutic approaches

- Gene therapy
- Immunotherapy
- VEGF & EGFR inhibitors

PRESENTATION