

Lung cancer

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Aims and objectives

- To understand the epidemiology of lung cancer
- To appreciate the patient experience of lung cancer
- To revise the pathogenesis and classification of lung cancer
- To recognise the clinical signs associated with lung cancer and its sequelae
- To describe the treatment of lung cancer

Why learn about lung cancer?

- 180,000 people per year die of lung cancer in the US
- Commonest cancer in the UK
- Cause of 13% of cancer cases and 18% of cancer deaths worldwide
- 35,000 new cases a year
- 21% 1 year survival
- 5-6% 5 year survival



Richard Doll - Epidemiologist

“The risk of developing the disease increases in proportion to the amount smoked. It may be 50 times as great in those who smoke 25 or more cigarettes a day as among non-smokers”

Conclusion of article in BMJ in 1950

Lead author - Richard Doll (who stopped smoking because of his findings!)



Warnings introduced on cigarette packets in 2003

Patient experience - 1

http://www.healthtalkonline.org/Cancer/Lung_Cancer/Topic/1300/

Please click on the link which takes you to the “healthtalkonline” website where you can view videos of patients describing their experience of being diagnosed with lung cancer

Risk factors

- **Smoking:**
 - 90% of all lung cancers are caused by smoking
 - 40 pack yr history = 20x risk of developing lung cancer of non-smoker
- Radiation therapy
- Environmental toxins:
 - Second hand smoke, asbestos, radon, arsenic
- Pulmonary fibrosis
- HIV
- Genetic factors

Case study 1

- 64 year old woman, presents to GP with a 6 week history of a cough
- She also complains of tiredness, weight gain and weakness general aches and pains
- What do you want to know?

Examination

General inspection:

Observations stable

Respiratory system:

Bronchial breathing RLZ

Decreased percussion note
RLZ

Cardiovascular system:

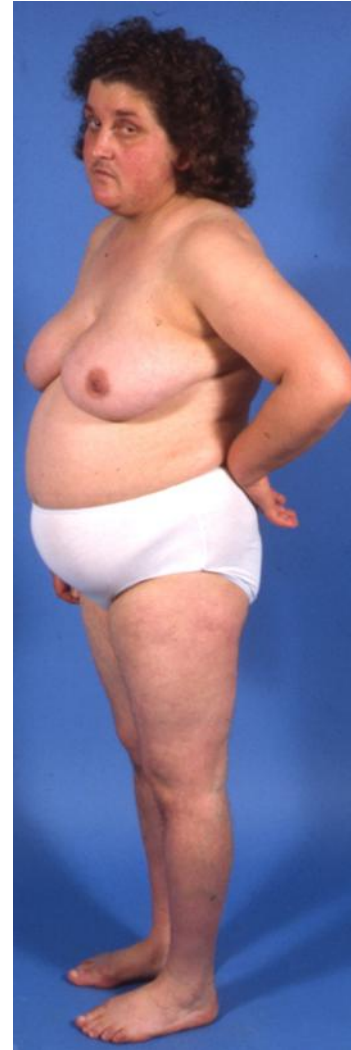
Normal heart sounds

Apex non displaced

Gastrointestinal system:

Soft, non tender

4 cm uneven hepatomegaly



Laboratory results

FBC:

Hb – 10.3

Platelets - 74

WCC – 1.3

U&E's

Na – 136

K – 4.5

Urea – 4

Creat - 90

LFT's:

Alb – 28

ALT – 48

AST – 56

Alk phos – 167

Bilirubin – 74

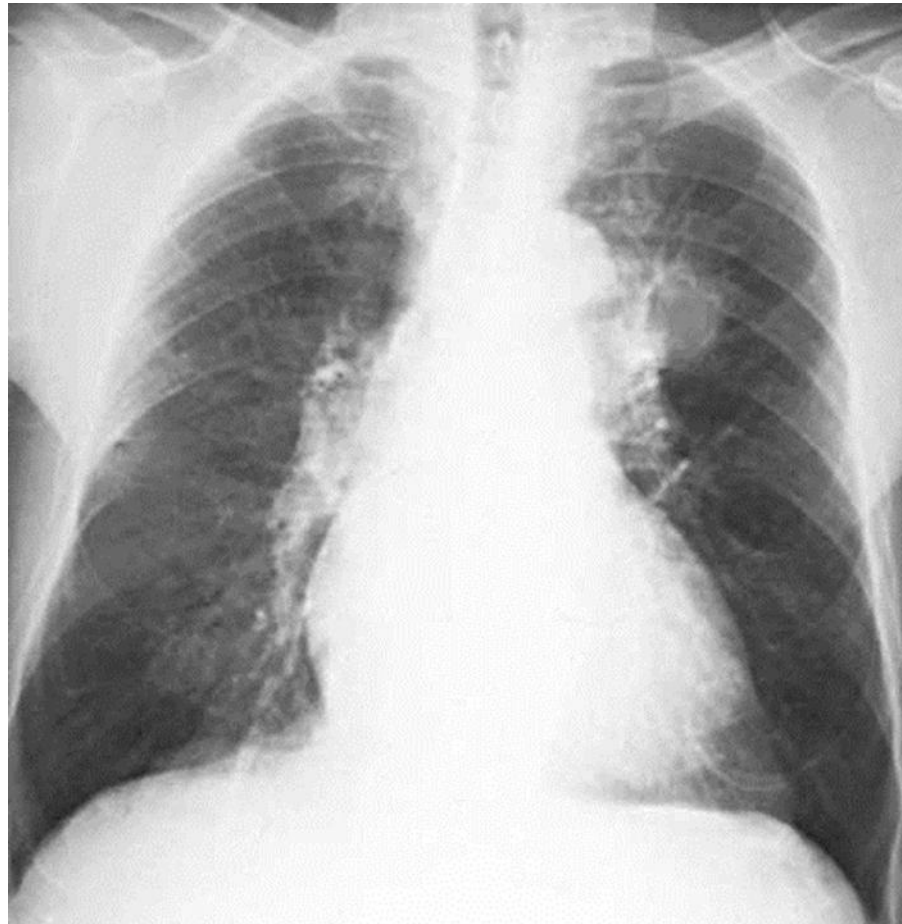
Bone profile:

Corrected calcium – 2.9

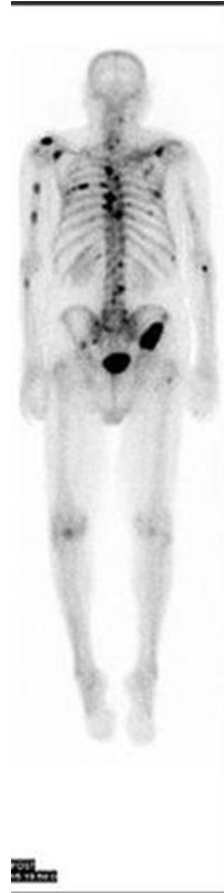
Phosphate – 1.4

24 hour urinary cortisol - high

Investigations



Investigations



What is the unifying diagnosis?

- a) Atypical pneumonia
- b) Large Cell carcinoma of the lung
- c) Small cell carcinoma of the lung
- d) Squamous cell carcinoma of the lung
- e) Tuberculosis

What is the unifying diagnosis?

c) Small cell carcinoma of the lung

The combination of a lung mass, irregular hard hepatomegaly and clinical signs and investigations consistent with paraneoplastic syndromes and bone marrow suppression make small cell lung cancer the most likely diagnosis

What is the cause of the other symptoms?

- a) Cushing's syndrome
- b) Lambert Eaton syndrome
- c) Polymyositis

What is the cause of the other symptoms?

a) **Cushings syndrome**

The patient has a cushingoid appearance with a round face, centripetal obesity and hirsutism.

The raised 24 hour urinary cortisol confirms the diagnosis of Cushings syndrome

What is the cause of the hypercalcaemia?

- a) PTHrP
- b) Bony metastases
- c) Hyperparathyroidism

What is the cause of the hypercalcaemia?

b) Bony metastases

A raised calcium, with a normal phosphate and raised alkaline phosphatase is the classic serological finding in bony metastases. The bone scan shows areas of high pick up consistent with bony metastases.

Small Cell Lung Cancer:

- Rapidly dividing tumour
- 70% have metastases on presentation
 - Bone, liver, adrenals, brain, bone marrow
- Highly responsive to radio- and chemotherapy
- Most patients relapse
- Usually arise in central airways
- Commonly associated with paraneoplastic syndromes
- Almost always associated with smoking

Paraneoplastic syndromes

- Cushing's Syndrome
 - Ectopic ACTH production
 - Classical symptoms and signs
 - Tiredness, weight gain, striae, easy bruising, dower's hump, centripetal obesity
- Diagnosis:
 - Measure urinary cortisol and ACTH levels
 - 24 hr urinary cortisol high
 - High plasma ACTH

Paraneoplastic syndromes

- Dermatomyositis and polymyositis
 - Inflammatory myopathies
 - Gottrons sign, heliotrope rash
 - Interstitial lung disease, inflammatory arthritis
 - Characterised by muscle weakness

Gottrons Papules



Image authors: Elizabeth M. Dugan, Adam M. Huber, Frederick W. Miller, Lisa G. Rider <http://dermatology.cdlib.org/1502/reviews/photoessay/1.jpg>

Heliotrope rash



Source: IMACS

Authors: Elizabeth M. Dugan, Adam M. Huber, Frederick W. Miller, Lisa G. Rider <http://dermatology.cdlib.org/1502/reviews/photoessay/17.jpg>

Paraneoplastic syndromes

- Lambert-Eaton myasthenic syndrome:
 - Disorder of neuromuscular junction transmission
 - Antibodies to voltage gated calcium channel ions
 - Occurs in 3% of SCLC
 - Neurological symptoms precede diagnosis in 80% of cases
 - Slowly progressive proximal muscle weakness
 - Autonomic involvement
 - Rarely cranial nerve involvement (cf myaesthesia gravis)
- Cerebellar degenerative syndromes (Anti-Hu, anti-YO, anti-CRMP-5, anti-Pca-2, Anti-MA1)
- Cerebellar ataxia
- Limbic encephalitis (antibodies to Hu family proteins)

Hypercalcaemia in lung cancer

- Usually secondary to bony metastases
- In SCLC can be caused by tumour secretion of Parathyroid hormone related protein (PTH-rP)
- Symptoms - Anorexia, nausea, vomiting, constipation, lethargy, polyuria, polydipsia, dehydration, confusion, coma

Case study 2

- A 53 year old man
- Trumpeter in working men's clubs
- Presents to his GP with haemoptysis and pain in his joints

Examination

General:

Swollen, plethoric face

Distended neck veins

Clubbing

Tender wrists

Respiratory:

RR = 24/min

Dull PN to left midzone

Reduced breath sounds to left
midzone

CVS:

Normal

GI:

Normal

Investigations

U&E's:

Na – 125

K – 3.6

Urea – 7

Creat – 94

Midnight serum cortisol – 4 m/dl

Urine sodium – 23 mEq/L

Serum osmolality – 240 mOsm

FBC:

Normal

Urine osmolality – 350mOsm

Bone profile:

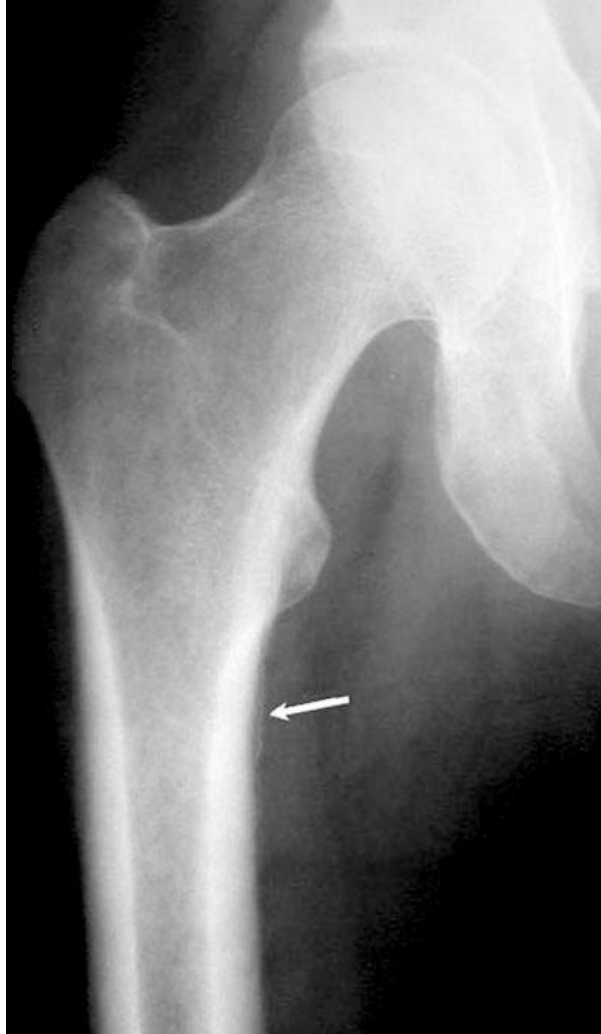
Corr Calcium – 2.1

Phosphate – 0.9

X-ray hands



X-ray right femur



What is the diagnosis?

- a) Atypical pneumonia
- b) Large Cell carcinoma of the lung
- c) Small cell carcinoma of the lung
- d) Squamous cell carcinoma of the lung
- e) Tuberculosis

What is the diagnosis? Answer

c) Small cell carcinoma of the lung

The combination of haemoptysis, superior vena cava obstruction and paraneoplastic signs indicates a diagnosis of SCLC

What is the cause of his joint pain?

- a) Bony metastases
- b) Hypertrophic pulmonary osteoarthropathy
- c) Pathological fractures
- d) Polymyositis

What is the cause of his joint pain?

b) Hypertrophic pulmonary osteoarthropathy

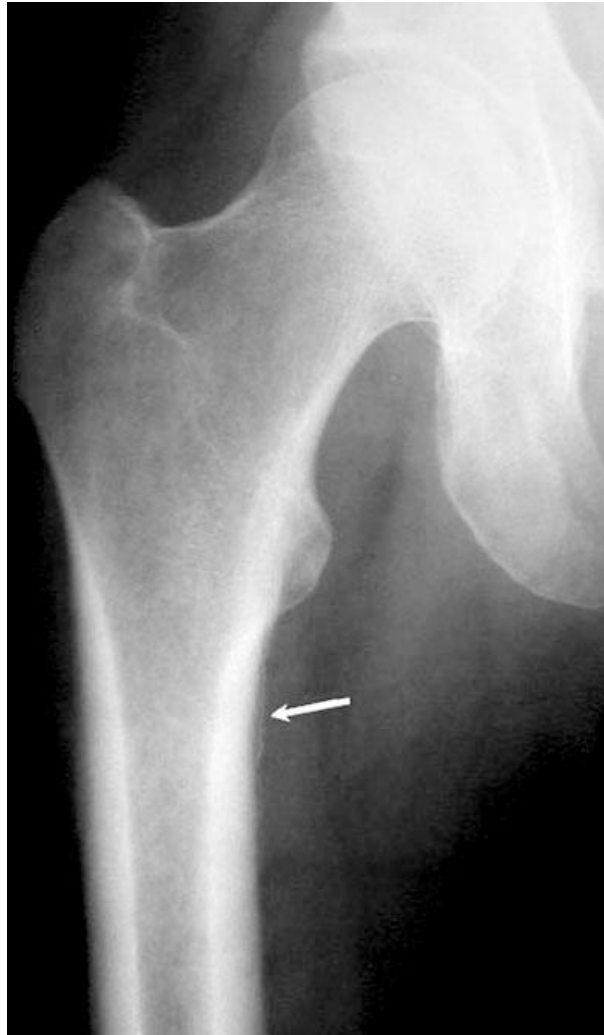
The joint pain is caused by HPOA. The x-rays show clubbing, and new periosteal bone formation on the femur both of which are hallmarks of HPOA. There are no fractures visible and the normal calcium makes bony metastases unlikely

Hypertrophic pulmonary osteoarthropathy (HPOA)

- Presents with clubbing (which is often very marked) and joint pain
- Periosteal proliferation of tubular bones
- Diagnose with x-ray of long bones – show periosteal new bone formation
- MRI and Pet show increase uptake

HPOA – clubbing visible on X-ray





Periosteal new bone formation in HPOA

What is the cause of the hyponatraemia?

- a) Addisons disease
- b) Cushings syndrome
- c) Hypothyroidism
- d) Syndrome of inappropriate ADH secretion (SIADH)

What is the cause of the hyponatraemia?

d) Syndrome of inappropriate ADH secretion (SIADH)

The combination of hyponatraemia, low serum osmolality and high urine osmolality are classical of SIADH

Syndrome of Inappropriate ADH secretion (SIADH)

- Caused by ectopic ADH secretion
- Presentation:
 - May present with confusion and fits or other signs of hyponatremia, but is commonly asymptomatic
- Laboratory findings:
 - Hyponatremia
 - Low serum osmolality (<275mOsm/kg water)
 - High urine osmolality (> 100mOsm/kg water)
 - High urinary sodium (> 40mmol/L with normal dietary sodium intake)
- 15-40% of patients with SCLC have SIADH

Diagnosis of lung cancer - symptoms

- Haemoptysis – 25-50%
- Cough – 50-75%
- Weight Loss
- Hoarse voice
- Chest pain
- Dyspnoea
- Bronchorrhea
- Fullness in the head
- Shoulder pain

Diagnosis of lung cancer - signs

- Systemic:
 - Weight loss
 - Clubbing
 - Wasting of small muscles of the hand
 - Hoarse voice
 - Lymphadenopathy
- Chest:
 - Bronchial breathing
 - Coarse crepitations
 - Wheeze
 - Stridor
 - Pleural effusion
- Other:
 - Horner's Syndrome:
 - Ptosis
 - Miosis
 - Anhydrosis
 - Superior Vena Cava Obstruction:
 - See next page

Superior Vena caval obstruction

- Symptoms:
 - Fullness in the face
 - Headache
- Signs:
 - Plethoric facies
 - Facial swelling
 - Dilated veins of the upper chest wall and face
- Caused by obstruction of the superior vena cava by external compression or thrombosis which results in increased venous pressure, interstitial oedema and retrograde collateral flow
- Most common cause is bronchial carcinoma

Classification of lung cancer

- Small Cell Lung Cancer – 13%
- Non-Small Cell Lung Cancer – 82%
 - Adenocarcinoma – 38%
 - Squamous cell carcinoma – 20%
 - Large Cell Carcinoma – 5%
 - Unclassified – 18%
- Other – 5%

Adenocarcinoma

- Peripheral
- 35-40% lung cancers
- Less commonly associated with smoking
- Bronchoalveolar carcinoma:
 - Manifests from type 2 pneumocytes along alveolar septa
 - Can manifest as solitary peripheral nodule, multifocal disease or rapidly progressive pneumonic form
 - Large amounts of watery sputum

Squamous cell carcinoma

- Usually originates near to a central bronchus
- Necrotic cavity
- 20% lung cancers
- Histologically – keratin pearls
- Can be detected on cytology as it exfoliates

Large Cell Carcinoma

- 5% of lung cancers
- Large peripheral mass
- Highly atypical cells with no evidence of keratinisation

Further investigations

- To stage cancer and distinguish SCLC from NSCLC
- Bloods:
 - FBC, U&E's, LFT's, Calcium,
- Staging CT chest/ abdomen/ pelvis
- +/- CT head
- Bronchoscopy
- Percutaneous transthoracic needle biopsy
- FPG-PET scan

Patient perspective

<http://www.healthtalkonline.org/Cancer/LungCancer/Topic/1298/>

Click on the link above to go to the “healthtalkonline” website where you can view patients with lung cancer talking about their experiences with the medical profession

Treatment of SCLC

- Limited stage:
 - Platinum based chemotherapy
 - Thoracic irradiation
- Extensive stage:
 - Platinum based chemotherapy
- Prophylactic cranial irradiation
- Palliative care

Treatment of NSCLC

- Surgical resection:
 - Stage I/ II NSCLC
 - Adequate lung function and no medical contraindications
 - Lobectomy
- Radical Radiotherapy:
 - Stage I/ II/ III NSCLC
 - Good performance status
 - Need pulmonary function tests prior to this
 - CHART regime
- Chemotherapy:
 - Stage III/ IV disease with good performance status

Prognosis

- SCLC:
 - Limited disease – 15-20 months median survival
 - Extensive disease – 8-13 months median survival
- NSCLC:
 - If resectable (stage 1) - 25-73% 5 year survival
 - Stage 2 – 25-46% 5 year survival
 - Stage 3 – 7-24% 5 year survival
 - Stage 4 – 2-13% 5 year survival

Patient perspective

- <http://www.healthtalkonline.org/Cancer/LungCancer/Topic/1302/>

Click on the link above to go to the “healthtalkonline” website to view patients with lung cancer talking about their thoughts on recurrence, death and dying

Palliative care

- Palliative radiotherapy for relief of symptoms
- Opioids to reduce cough
- Debulking bronchoscopic procedures for relief of large airway obstruction or bleeding
- SVCO:
 - Chemotherapy/ radiotherapy dependant on stage of disease
- Cerebral metastases:
 - Steroids/ radiotherapy
- Pleural effusion drainage/ aspiration

Summary

- Lung cancer is common
- It has a poor prognosis
- Differentiation between small cell and non small cell is important for prognosis and treatment
- Palliative care is important, as most patients will require it

Further reading

- www.healthtalkonline.org
- Van Meerbeeck JP et al Small-cell lung cancer *Lancet* 2011; 378: 1741–55
- Goldstraw P et al. Non-small-cell lung cancer *Lancet* 2011; 378: 1727–40
- Hoffman PC Lung cancer *Lancet* 2000; 355: 479–85