Lung Carcinoma.

① Classify. (4).
② Etiopathogenesis (4).
③ Investigation for confirmation.

EPITHELIAL TUMORS.

- Benign
  - papillomas.
  - Adenomas.
- precursor glandular lesions.
  - Atypical adenomatous hyperplasia of lung.
  - adenocarcinoma in situ of lung.
- adenocarcinomas.
  - minimally invasive.

SC

etiopathogenesis

① Tobacco smoking { PHC, nitrosamine }.

- most impt - 80% of lung cancer
- LCa. develops in 10-15% smokers which indicates there are other factors
- women >> men.
- cessation ↓ risk.
- specific P450 variants have ↑ capacity to ⊕ procarcinogens

- polycyclic HC
  - Binds to DNA
    - mutations

Industrial Hazards.

- asbestos, arsenic, chromium, uranium, nickel, vinyl chloride ↑ risk.
- high dose ionizing radiations.

③ Air pollution.

- Chronic exposure to particulates in lung.
  - ↓
  - lung irritation, inflammation, repair
  - ↓
  - ↑ risk.

- radon gas.

④ molecular genetics

(A) adenocarcinoma

- most common in never-smokers
- mutations in.
  - gain of functions mutations in genes coding for.
    - → Epidermal growth factor receptor EGFR
    - → ALK
    - → BRAF
    - → KRAS.

(B) Squamous cell carcinoma.

- deletion of 3p., 9p.
- TP53 mutation
- CDKN2A.
- amplification: FGFR1.

(C) Small cell carcinoma.

- has highest mutational burden.
- TP53, RB.
- deletion 3p.

Lung cancer in Never Smokers.

- more/c - women
- adenocarcinoma - m/c.
- mutations: EGFR mutations.
- in Never smokers KRAS mutations never seen.

Precursor/ preinvasive lesions.

- does not mean inevitable progression to CA.

(1) Atypical adenomatous hyperplasia.

dysplastic type II pneumocytes. lining alveolar walls.

(2) adenocarcinoma insitu.

Composed entirely of dysplastic cells grow along pre existing alveolar septa.

(3) Squamous dysplasia & Carcinoma insitu

→ precurs for sq. CC.

(4) diffuse idiopathic pulmonary neuroendocrine cell hyperplasia.

CELLS OF ORIGIN OF CANCER.

- Neuroendocrine cells → Small cell carcinoma.
- Basal cells in major bronchi → Sq. CC
- mucus glands in terminal Bronchi → adenocarcinoma.

Classification - Simplified.

- adenocarcinoma variants
- Sq. cell ca
- Neuroendocrine tumors
  - SCC
  - Lung cell NECa.
  - Carcinoid.
- Others
  - Lung cell
  - Adenosquamous.
  - Sarcomatoid.
  - salivary gland type tx

Morphology

Adenocarcinoma

- m/c in men & women.

site - central / Hilar.
large, m/c - squamous SCC.

- peripheral
smaller
m/c - adenocarcinoma.

- malignant epithelial tumor with glandular differentiation.

GROSS

- site ✓
- appearance: Irregular mass.
- CS: non-mucinous - grayish-white
mucinous - glistening.

MC - growth pattern

- lepidic → cells grow along surface of alveolar cells.
- acinar → glands lined by cuboidal / columnar cells.
- papillary → single layer covering covering fibrovascular connective tissue core.
- micropapillary → without fibrovascular core.
- solid adenocar → solid sheets.

IHC → most tumours are positive for TTF-1 thyroid transcription factor.

Squamous cell carcinoma.

m/c - men.

- squamous metaplasia
↓
dysplasia
↓
Ca - insitu
↓
Invasive Ca.

MORPHOLOGY

GROSS

pattern

1. peribronchial growth ✓
2. intraparenchymal ✓
3. exophytic growth ✓

CS.
areas of hemorrhage & necrosis.

MC

1. Keratinization
→ Epithelial Keratin pearls or
→ individual cell Keratinization.
2. Intercellular bridges

1 & 2 → diagnostic.

Small cell Carcinoma

- highly malignant, most aggressive lung tumor.

morphology

GROSS → site – (mc) perihilar mass in major bronchi

c/s – haem + necrosis.

Light m/c
- Growth pattern: sheets | clusters.
- small cells – oat cell.
- cells shows fragmentation of brush artifacts

cytoplasm: scanty
ill defined cell border.

nucleus: round/ovoid/spindle.
chromatin: salt & pepper pattern ☆☆
nuclear molding ☆☆☆.

- high mitotic count.
- necrosis: common.

IHC: chromogranin.
synaptophysin
CD56.

Large cell carcinoma

microscopy
- large tumor cells.
- mod. cytoplasm
- vesicular chromatin.

diagnosis by exclusion.

Neuroendocrine tumours

microscopy

* Growth pattern.
  - organoid, trabecular, ribbons, palisading.

* stroma
  tumor cells are seperated by delicate fibrovascular stroma.

Subcategories
1. typical carcinoids → salt & pepper chromatin. → uniform nuclei
2. Atypical carcinoids. → many pleomorphism

IHC

(+) serotonin
neuron specific enolase.
chromogranin A & B.
synaptophysin
Bombesin.
calcitonin
other peptides.

. Neuroendocrine tumors
1. tumorlets.
2. Carcinoids
3. Small cell Carcinoma.
4. large cell neuroendocrine carcinoma

Spread

Local

- pleural surface
- pleural cavity.
- pericardium.
- pancoast tumor
  Apex of lung
  ↓
  neural structures around trachea & cervical sympathetic plexus.
  ↓
  Horner syndrome in same side.

Lymphatic

- brachial, bronchial, hilar, mediastinal nodes.
- Virchow node - supraclavicular node.

Hematogenous

m/c → adrenals (>50%).
liver
brain
bone.

paraneoplastic syndromes

- cushing syndrome
- carcinoid syndrome.
- hypercalcemia
- hypercalcemia
- Acanthosis nigricans.

Investigations

- Radiological Examination of chest
- cytological examination of sputum, bronchial washings, Fine needle aspirations.
- bronchoscopy biopsy
- Trans bronchial needle aspiration (TBNA) → for obtaining cellular material.

→ IHC markers ✡
→ gene mutations ✡