Doctor.021

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RS
PATHOLOGY

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LUNG TUMORS

❖ SPREAD AND METASTASIS

- **Each of the tumor types that we discussed before tends to spreads to nodes around the carina, mediastinum, and in the neck and clavicular regions (sooner or later they also metastasize to distant sites).**
- **Left supraclavicular node (Virchow node) involvement is particularly characteristic.**
- Virchow node involvement is sometimes the first clue that indicates the presence of an occult primary tumor 'the first presentation in a patient who has lung carcinoma is its enlargement'.
- **When advanced Extend into adjacent structures:**
  - **pleural or pericardial space, leading to inflammation and effusion.**
  - **Compress or infiltrate the SVC to cause either venous congestion or the vena cava syndrome.**
- **Pancoast tumors (Pancoast syndrome): Apical neoplasms that may Invade the brachial or cervical sympathetic plexus to cause:**
  - **Severe pain in the distribution of the ulnar nerve.**
  - **Horner syndrome (ipsilateral enophthalmos, ptosis, miosis, and anhidrosis).**
  - **Destruction of the first and second ribs and sometimes thoracic vertebrae.**
- **Tumor-Node-Metastasis (TNM) staging system is used to indicate the size and spread of the primary neoplasm.**
- TNM categories point to the anatomic extent of the lung cancer and predicts the overall survival of patients with non-small cell lung carcinoma and small cell lung carcinoma.

- The ‘T’ stands for the tumor size which has an important prognostic relevance as each centimetre increase in size – from 1 cm to up-to 5 cm- yields a significantly different prognosis. While the ‘N’ stands for regional lymph nodes involvement (assessing their quantitative-their number- and qualitative-anatomic lymph nodes- involvement). And the ‘M’ stands for distant metastasis which includes malignant pleural effusions or malignant pericardial effusions.

❖ CLINICAL COURSE

- **Lung cancer is one of the most insidious and aggressive Neoplasms (Mostly Silent), in most cases it extends and becomes unresectable before producing symptoms.**
- **The major presenting complaints are chronic cough (75%)-or expectoration and they could be the first ones to appear, weight loss (40%), chest pain (40%), and dyspnea (20%).**
- **Other symptoms: Hoarseness, superior vena cava syndrome, pericardial or pleural effusion, or persistent segmental atelectasis (obstruction of the airways causing resorption atelectasis) or pneumonitis.**
    - By the time these symptoms are noted, then the result is most probably poor because they result from the direct extension of the tumor to other structures; such as the recurrent laryngeal nerve causing hoarseness of voice, the SVC and the pleural and pericardial spaces causing malignant pericardial or pleural effusion.
    - **All these symptoms are an indication of poor prognosis.**
- **Not infrequently, lung cancer is recognized through biopsy of tissues involved by metastatic disease.**
- **Symptoms from metastatic spread:**
    - **Brain (mental or neurologic changes).**
    - **Liver (hepatomegaly).**

- **Bones (pain).**
- Although the adrenal glands may be nearly obliterated by metastatic disease, adrenal insufficiency 'Addison's disease' is uncommon because the island of the cortical cells stays functional regardless of the extensive infiltration of the adrenal gland.

❖ PROGNOSIS

- **Prognosis is poor for most patients.**
- **Even with thoracic surgery, radiation therapy, and chemotherapy: the overall 5-year survival rate is only 18.7%.**
- **The 5-year survival rate is:**
  - **52% for cases detected when the disease is still localized.**
  - **22% when there is regional metastasis.**
  - **only 4% with distant metastases.**
- **Adenocarcinoma and squamous cell carcinoma carry a slightly better prognosis than SCLCs.**
- **SCLCs, invariably spread by the time they are first detected even if the primary tumor appears to be small and localized.**
- **Surgical resection is not a viable treatment.**
- **Most patients present with advanced stage disease.**
- **Despite excellent initial responses to chemotherapy, the median survival is approximately 10 months and the cure rate is close to zero.**
- When SCC or adenocarcinoma are detected before metastasis or local spread then the treatment is possible either by lobectomy or pneumonectomy.
- SCLC is very sensitive to chemotherapy, but invariably associated with recurrence. The median survival -even with treatment- remains 1 year and only 5% are alive after 10 years.

❖ PARANEOPLASTIC SYNDROMES

- Paraneoplastic syndromes are a group of clinical disorders that are associated with malignant diseases and are not directly related to the physical effect of the primary or the metastatic tumors; these conditions arise from the secretions of the functional peptides or the hormones from the tumor cells themselves or inappropriate immune cross-reaction between the normal host cells and the targeted tumor cells.
- These syndromes can be associated with several malignancies, but they're most commonly seen with lung cancers.
- The histology of lung cancer influences the type of the associated paraneoplastic syndrome.
- About 10% of lung cancer patients present with these syndromes.

1. **Hypercalcemia-Most common PNS- (secretion of a PTH related peptide, Parathormone, prostaglandin E). SCC**
2. **Cushing syndrome (production of ACTH). SCLC, Carcinoid (mostly appears with neuroendocrine lung tumors-AKA carcinoid)**
3. **Syndrome of inappropriate secretion of ADH, (production of ADH), hyponatremia. SCLC**
4. **Acromegaly (growth hormone-releasing hormone (GHRH) or growth hormone (GH)). SCLC, Bronchial Carcinoid**
5. **Neuromuscular syndromes, including a myasthenic syndrome, peripheral neuropathy, and polymyositis**
6. **hypertrophic pulmonary osteoarthropathy which is associated with fingers clubbing. Adeno, SCC**
7. **Coagulation abnormalities, including migratory thrombophlebitis, nonbacterial endocarditis, and DIC.**

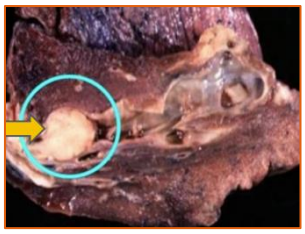
❖ Carcinoid tumors

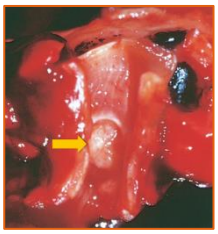
- 5% of all pulmonary neoplasms.
- malignant tumors, low-grade neuroendocrine carcinomas.
- composed of cells containing dense-core neurosecretory granules in their cytoplasm and, rarely, may secrete hormonally active polypeptides.
- subclassified as typical or atypical; both are often resectable and curable.
- May occur as part of the multiple endocrine neoplasia syndrome (MEN syndrome)
- young adults (mean 40 years)
- 5% to15% of carcinoids have metastasized to the hilar nodes at presentation.
- distant metastases are rare.

❖ MORPHOLOGY, macroscopically

- Most carcinoids originate in the main bronchi, peripheral carcinoids are less common.
- They are considered well demarcated.
- The grow in one of two patterns:
    - An obstructing polypoid, spherical, intraluminal mass.
    - A mucosal plaque penetrating the bronchial wall to fan out in the peribronchial tissue- the so-called ‘collar-button lesion’.

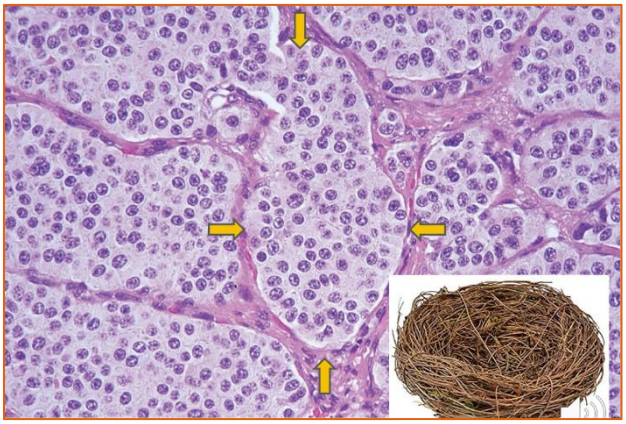
- The figure on the left shows an obstructing polypoid tumor in the lumen of a bronchus (the first pattern).
- The one on the right shows a spherical tumor.





❖ MORPHOLOGY, microscopically:

- **Typical carcinoids: composed of nests of uniform cells that have regular round nuclei with "salt-and-pepper" chromatin, absent or rare mitoses and little pleomorphism.**
- **Atypical carcinoid:**
  - **Tumors display a higher mitotic rate and small foci of necrosis.**
  - **Have a higher incidence of lymph node and distant metastasis than typical carcinoids.**
  - **Have TP53 mutations in 20% to 40% of cases.**



❖ CLINICALLY:

- **Mostly manifest with signs and symptoms related to their intraluminal growth, including cough, hemoptysis, and recurrent bronchial and pulmonary infections.**

- Peripheral tumors are often asymptomatic and discovered incidentally on chest radiographs.
- Rarely induces the carcinoid syndrome:
  - intermittent attacks of diarrhea, flushing, and cyanosis.

❖ PROGNOSIS:

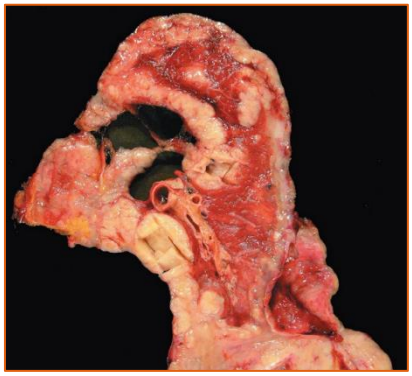
- 5- and 10-year survival rates:
  - for typical carcinoids are above 85%.
  - For atypical carcinoid 56% and 35%, respectively.

❖ MALIGNANT MESOTHELIOMA

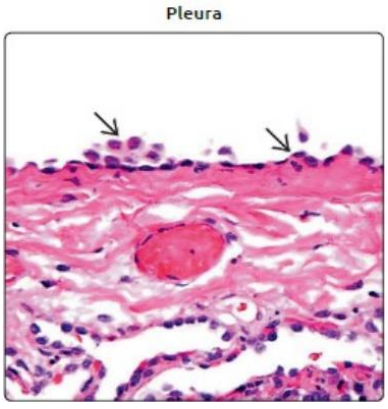
- Rare cancer of mesothelial cells lining parietal or visceral pleura.
- Less commonly in the peritoneum and pericardium.
- highly related to exposure to airborne asbestos (80% to 90% of cases):
  - Not only limit to people working with asbestos **(like shipyard workers, miners, insulators)** but also extends to only exposure was living in proximity to an asbestos factory or being a relative of an asbestos worker.
- Long latent period: 25 to 40 years after initial asbestos exposure.
- The combination of cigarette smoking and asbestos exposure DOES NOT increase the risk of developing malignant mesothelioma <u>BUT INCREASES the risk for developing lung carcinoma</u>.
- Once inhaled, asbestos fibers remain in the body for life.
- the lifetime risk after exposure DOES NOT diminish over time (unlike with smoking, in which the risk decreases after cessation).

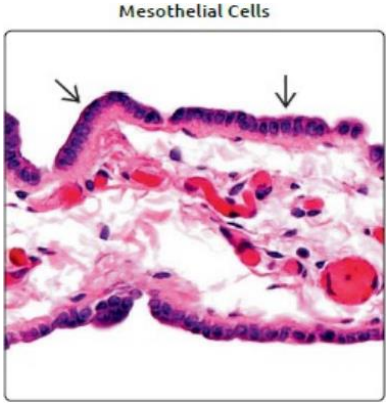
❖ MORPHOLOGY, macroscopically:

- Preceded by extensive pleural fibrosis and plaque.
- begin in a localized area and spread widely, either by contiguous growth or by diffusely seeding the pleural surfaces.
- **The neoplasm might directly invade the thoracic wall or subpleural lung tissue, however,** distant metastases are rare.
- Thick, firm, white pleural tumor tissue that ensheathes the lung.
- At autopsy, the affected lung typically is ensheathed by a layer of yellow, white, firm, variably gelatinous tumor that obliterates the pleural space



- Normally, mesothelial cells are biphasic, giving rise to pleural lining cells as well as the underlying fibrous tissue.
- These figures show benign normal mesothelial cells with aligning epithelial cells and underlying fibrous tissue. The left figure shows the pleura which is lined by a single layer of normal mesothelial cells that are almost flat, they are actually simple cuboidal cells with eosinophilic cytoplasm and indistinct nuclear features. The right one shows the same mesothelial lining, but in this one the cells are much more cuboidal and easier to be identified if compared with the flat ones in the left figure; still in both figures we have the same cytomorphology.



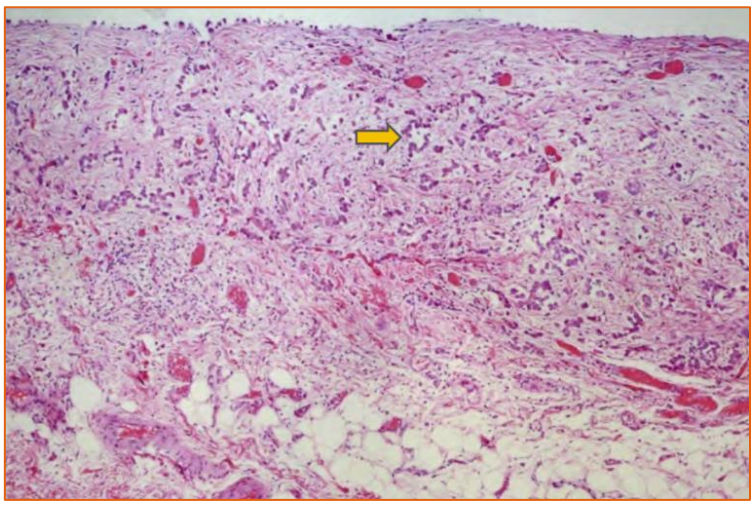


❖ MORPHOLOGY, microscopically:

- **one of three morphologic appearances:**

1. **Epithelial: cuboidal cells with small papillary buds line tubular and microcystic spaces (the most common & confused with a pulmonary adenocarcinoma).**
2. **sarcomatous: spindled cells grow in sheets.**
3. **biphasic: both sarcomatous and epithelial areas.**

- The arrow in the following figure points to a plump-rounded cell forming a gland-like configuration.



ما أجهل الإنسان يضني بعضه

بعضا ويشكو كل ما يضنيه

ويظن أن عدوه في غيره

وعدوه يضحي ويمسي فيه