**د.سرى سلمان عجام RESPIRATORY DISEASES**

***Lung Tumors***

Avariety of benign and malignant tumors may arise in the lung, but 90% to 95% are carcinomas, about 5% are bronchial carcinoids, and 2% to 5% are mesenchymal and other miscellaneous neoplasms

**CARCINOMAS**

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. This is largely due to the carcinogenic effects of cigarette smoke

***Etiology and Pathogenesis***

**1-Tobacco Smoking.-**

**2-Industrial Hazards.**

High-dose ionizing radiation

Asbestos exposure

**3-Air Pollution.**

Radon is a ubiquitous radioactive gas that has been linked epidemiologically to increased lung cancer

4-**Molecular Genetics.**

**5-Precursor Lesions.**

(1) squamous dysplasia and carcinoma in situ,

(2) atypical adenomatous hyperplasia

(3) diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

**Histologic(WHO) Classification of Malignant Epithelial Lung Tumors**

Squamous cell carcinoma

Small-cell carcinoma

Combined small-cell carcinoma

Adenocarcinoma

Acinar; papillary, bronchioloalveolar, solid, mixed subtypes

Large-cell carcinoma Large-cell neuroendocrine carcinoma

Adenosquamous carcinoma

Carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements

Carcinoid tumor

Typical, atypical

Carcinomas of salivary gland type

Unclassified carcinoma

***Metastasis of carcinoma***

Extension may occur to the pleural surface and then within the pleural cavity or into the pericardium. Spread to the tracheal, bronchial, and mediastinal nodes can be found in most cases. The frequency of nodal involvement varies slightly with the histologic pattern but averages greater than 50%.

Distant spread of lung carcinoma occurs through both lymphatic and hematogenous pathways. These tumors often spread early throughout the body except for squamous cell carcinoma***,***

***Squamous Cell Carcinoma*.**

Squamous cell carcinoma is most commonly found in men and is **closely correlated with a smoking history**. they tend to arise centrally in major bronchi and spread to local hilar nodes but they disseminate outside the thorax later than the other types.

Large lesions undergo necrosis and cavitation

Histologically, this tumor is characterized by the presence of keratinization and/or intercellular bridges. Keratinization may take the form of squamous pearls or individual cells with markedly eosinophilic dense cytoplasm . These features are prominent in the well-differentiated tumors, are easily seen but not extensive in moderately differentiated tumors, and are focally seen in poorly differentiated tumors. Mitotic activity is higher in poorly differentiated tumors. In the past, most squamous cell carcinomas were seen to arise centrally from the segmental or subsegmental bronchi. However, the incidence of squamous cell carcinoma of the peripheral lung is increasing. Squamous metaplasia, epithelial dysplasia, and foci of frank carcinoma in situ may be seen in bronchial epithelium adjacent to the tumor mass

***Adenocarcinoma.***

This is a malignant epithelial tumor with glandular differentiation or mucin production by the tumor cells. Adenocarcinomas grow in various patterns, including acinar, papillary, bronchioloalveolar, and solid with mucin formation. Adenocarcinoma is the most common type of lung cancer in women and nonsmokers

As compared with squamous cell cancers, the lesions are usually more peripherally located, and tend to be smaller. They vary histologically from well-differentiated tumors with obvious glandular elements to papillary lesions resembling other papillary carcinomas to solid masses with only occasional mucin-producing glands and cells.

Adenocarcinomas grow more slowly than squamous cell carcinomas but tend to metastasize widely and earlier

**Bronchiolo alveolar carcinoma** *arises from terminal bronchioloalveolar region It grows on preexisting structure (alveolar wall) without its destruction there is no evidence of stromal, vascular, or pleural invasion*

*it is proposed that adenocarcinoma of the lung arises from* ***atypical adenomatous hyperplasia progressing to bronchioloalveolar carcinoma****,* ***which then transforms into invasive adenocarcinoma***but not all adenocarcinomas arise in this manner, nor do all bronchioloalveolar carcinomas become invasive if left untreated.

***Small Cell Carcinoma*.**

have a strong relationship to cigarette smoking; only about 1% occur in nonsmokers. They may arise in major bronchi or in the periphery of the lung. There is no known preinvasive phase or carcinoma in situ. They are the most aggressive of lung tumors, metastasize widely, and are virtually incurable by surgical means

The occurrence of neurosecretory granules, the ability of some of these tumors to secrete polypeptide hormones suggest derivation of this tumor from *neuroendocrine progenitor cells* of the lining bronchial epithelium. This lung cancer type is most commonly associated with ectopic hormone production

**Microscopic features**

This highly malignant tumor has a distinctive cell type.

The epithelial cells are relatively small, with scant cytoplasm, ill-defined cell borders, finely granular nuclear chromatin (salt and pepper pattern), and absent or inconspicuous nucleoli.

The cells are round, oval, or spindle-shaped,

nuclear molding is prominent.

There is no absolute size for the tumor cells, but in general they are smaller than three small resting lymphocytes.

The mitotic count is high.

The cells grow in clusters that exhibit neither glandular nor squamous organization.

Necrosis is common and often extensive.

***Large Cell Carcinoma*.**

This is an undifferentiated malignant epithelial tumor that lacks the cytologic features of small-cell carcinoma and glandular or squamous differentiation. The cells typically have large nuclei, prominent nucleoli, and a moderate amount of cytoplasm. Large cell carcinomas probably represent squamous cell carcinomas and adenocarcinomas that are so undifferentiated that they can no longer be recognized by light microscopy

***Combined Carcinoma*.** Approximately 10% of all lung carcinomas have a combined histology, including two or more of the above types.

***Clinical Course.***

Lung cancer is one of the most insidious and aggressive neoplasms in the realm of oncology. In the usual case it is discovered in patients in their 50s whose symptoms are of several months' duration. *The major presenting* *complaints are cough* (75%), *weight loss* (40%), *chest pain* (40%), and *dyspnea* (20%). Some of the more common local manifestations of lung cancer and their pathologic bases . Not infrequently the tumor is discovered by its secondary spread during the course of investigation of an apparent primary neoplasm elsewhere.

***Paraneoplastic Syndromes.***

Lung carcinoma can be associated with several paraneoplastic syndromes, some of which may antedate the development of a detectablepulmonary lesion. The hormones or hormone-like factors elaborated include:

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|  | **•** | *Antidiuretic hormone* (ADH), inducing hyponatremia due to inappropriate ADH secretion |
|  | **•** | *Adrenocorticotropic hormone* (ACTH), producing Cushing syndrome |
|  | **•** | *Parathormone*, *parathyroid hormone-related peptide*, *prostaglandin E*, *and some cytokines*, all implicated in the hypercalcemia often seen with lung cancer |
|  | **•** | *Calcitonin*, causing hypocalcemia |
|  | **•** | *Gonadotropins*, causing gynecomastia |
|  | **•** | *Serotonin and bradykinin*, associated with the carcinoid syndrome |

The incidence of clinically significant syndromes related to these factors ranges from 1% to 10% of all lung cancer patients, although a much higher proportion of patients show elevated serum levels of these (and other) peptide hormones. Any one of the histologic types of tumors may occasionally produce any one of the hormones, but tumors that produce ***ACTH and ADH are predominantly small cell carcinomas, whereas those that produce hypercalcemia are mostly squamous cell tumors***..