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PATHOLOGICAL ANATOMY AND DIFFERENTIAL DIAGNOSIS OF SMALL CELL LUNG CANCER

Lutfullayeva D. L.
1 st year of master of Samarkand State Medical University

Kudratova Z. E.
PhD, Ass. Professor of the department of clinical laboratory diagnosis with the course of clinical laboratory diagnostics of PGD;

Shamsiddinova D. K.
Pediatrician at the Republican Scientific center of emergency care;
Samarkand, Uzbekistan

Relevance

Lung cancer is one of the most common and deadly malignancies worldwide. It originates in the lung tissues, primarily in the bronchi or alveoli, and is strongly associated with smoking, environmental pollutants, and genetic factors. Lung cancer is broadly classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), with NSCLC being more prevalent [1,2].

Keywords: cancer of lung, SCLC, NSCLC,population,deaths, paraneoplastic syndromes.

Introduction

Lung cancer is one of the most common and deadly malignancies worldwide. It originates in the lung tissues, primarily in the bronchi or alveoli, and is strongly associated with smoking, environmental pollutants, and genetic factors. Lung cancer is broadly classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), with NSCLC being more prevalent.

Epidemiology: Global Statistics: Lung cancer is the leading cause of cancer-related deaths, with over 2.2 million new cases reported in 2020 [6,7,8].

Incidence in Uzbekistan. Overall Lung Cancer: In 2021, 1,574 individuals were diagnosed with lung cancer for the first time in Uzbekistan, with an incidence rate of 4.6 per 100,000 population. In 2022, this number increased to 1,676 cases, corresponding to an incidence rate of 4.7 per 100,000 population. SCLC Specific: While specific data on the proportion of SCLC cases in Uzbekistan is not readily available, applying the global estimate of 10–15% to the 2022 data suggests that there may have been approximately 168 to 251 new SCLC cases in Uzbekistan that year [1,2,3].

Risk Factors

1. Tobacco Smoking (accounts for ~85% of cases)
2. Air Pollution and Occupational Exposure (asbestos, radon)
3. Genetic Predisposition
4. Chronic Lung Diseases (COPD, fibrosis)

Pathogenesis and Histology

NSCLC: Includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.

SCLC: A neuroendocrine tumor with rapid progression, high mitotic rate, and early metastasis.

Clinical Features

Persistent cough, hemoptysis, chest pain

Weight loss, dyspnea, fatigue

Paraneoplastic syndromes (especially in SCLC)

Diagnosis.

Imaging: Chest X-ray, CT, PET scan

Histopathology: Biopsy and immunohistochemistry (IHC markers like TTF-1, p40)

Molecular Testing: EGFR, ALK, and PD-L1 in NSCLC for targeted therapy

Treatment

NSCLC: Surgery, chemotherapy, immunotherapy, and targeted therapy

SCLC: Chemotherapy (platinum-based regimens), radiation, and immunotherapy

Prognosis

NSCLC 5-year survival rate: 15–20%

SCLC 5-year survival rate: ~7% (limited-stage)

Small cell lung cancer (SCLC) is a particularly aggressive form of lung cancer, accounting for approximately 10–15% of all lung cancer cases globally [1,2].

Incidence in Uzbekistan: Overall Lung Cancer: In 2021, 1,574 individuals were diagnosed with lung cancer for the first time in Uzbekistan, with an incidence rate of 4.6 per 100,000 population. In 2022, this number increased to 1,676 cases, corresponding to an incidence rate of 4.7 per 100,000 population. SCLC Specific: While specific data on the proportion of SCLC cases in Uzbekistan is not readily available, applying the global estimate of 10–15% to the 2022 data suggests that there may have been approximately 168 to 251 new SCLC cases in Uzbekistan that year [3,4].

SCLC constitutes a significant portion of lung cancer diagnoses both globally and in Uzbekistan. Efforts in early detection, prevention, and treatment are essential to address the burden of this aggressive cancer.Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine carcinoma that originates in the lung and is characterized by rapid growth, early metastasis, and poor prognosis. It accounts for approximately 15% of all lung cancers and is strongly associated with smoking. SCLC has distinct pathological features and requires differentiation from other malignancies with similar morphology [10,11,12].

Pathological Anatomy of Small Cell Lung Cancer

1. Gross Pathology

SCLC typically arises centrally in the lung, near the major bronchi.

The tumor appears as a soft, gray-white, friable mass with areas of necrosis and hemorrhage.

It grows rapidly and often infiltrates the bronchial wall, lymph nodes, and mediastinal structures.

Due to early vascular invasion, SCLC frequently metastasizes to the liver, brain, adrenal glands, and bone.

2. Microscopic Pathology [7,8,9]

SCLC is classified as a poorly differentiated neuroendocrine carcinoma with the following histological features:

Cellular Morphology

Small, round to oval cells with scant cytoplasm.

Hyperchromatic nuclei with finely granular ("salt-and-pepper") chromatin.

Nuclear molding: Overlapping and tightly packed nuclei.

High mitotic rate: Typically >10 mitoses per high-power field.

Frequent necrosis, often extensive, due to rapid tumor growth.

Immunohistochemistry (IHC) [4,5,6]

SCLC expresses neuroendocrine and epithelial markers:

Neuroendocrine markers: Chromogranin A, Synaptophysin, CD56.

Epithelial markers: Cytokeratins (CK7).

Thyroid transcription factor-1 (TTF-1) positive in most cases, supporting lung origin.

Ki-67 proliferation index is typically >80%, indicating high proliferation.

Ultrastructural Features (Electron Microscopy)

Dense-core neurosecretory granules, confirming neuroendocrine differentiation.

Desmosome-like intercellular junctions, though less developed than in NSCLC.

Differential Diagnosis of Small Cell Lung Cancer

Due to its small cell morphology, SCLC must be distinguished from other tumors, including:

1. Non-Small Cell Lung Cancer (NSCLC)

Adenocarcinoma: Larger cells, prominent nucleoli, and glandular differentiation; expresses Napsin A and TTF-1 but lacks neuroendocrine markers.

Squamous Cell Carcinoma: Keratinization and intercellular bridges; positive for p40 and p63, but negative for neuroendocrine markers.

2. Large Cell Neuroendocrine Carcinoma (LCNEC)

Larger cells, more cytoplasm, and coarser chromatin than SCLC.

Still expresses neuroendocrine markers but has lower mitotic activity and less necrosis.

3. Metastatic Small Cell Carcinoma
Bladder or prostate small cell carcinoma can mimic lung SCLC.
Markers: Prostate small cell carcinoma is PSA-positive, while lung SCLC is TTF-1 positive.
4. Lymphomas (e.g., Lymphoblastic Lymphoma, Burkitt's Lymphoma)
Key Difference: Lymphoid origin, CD45 (leukocyte common antigen) positive.
No neuroendocrine differentiation.
5. Merkel Cell Carcinoma (Primary Cutaneous Neuroendocrine Carcinoma)
Primary skin tumor with similar morphology to SCLC.
CK20-positive (dot-like pattern) and TTF-1 negative, unlike lung SCLC.
6. Ewing Sarcoma/PNET (Primitive Neuroectodermal Tumor)
Common in younger patients; associated with EWSR1 translocation.
CD99 positive, neuroendocrine markers negative.

Conclusion

Thus, SCLC is a highly aggressive neuroendocrine tumor with distinct pathological features, including small cells, nuclear molding, high mitotic rate, and necrosis. Immunohistochemical staining (TTF-1, chromogranin, synaptophysin) is essential for diagnosis. Differentiation from NSCLC, LCNEC, lymphomas, and metastatic small cell tumors is critical for appropriate treatment [1,2,3].

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