Bronchogenic Carcinoma — Diagnosis and Treatment

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Bronchogenic carcinomas include small cell carcinoma, squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and undifferentiated carcinoma. Bronchogenic carcinoma is strongly associated with tobacco smoking. Once the diagnosis of bronchogenic carcinoma is confirmed by a biopsy study, disease staging with computed tomography (CT) or fluorodeoxyglucose (FDG)-positron emission tomography (PET) is indicated because treatment is stage-based. While stage I and II disease benefit from surgical lobectomy, chemotherapy is essential for patients with stage III and IV.

Definition

Bronchogenic carcinoma, or lung cancer, is a malignant tumor arising from the epithelial lining of the bronchus or bronchiole.

Epidemiology and Etiology

The incidence of bronchogenic carcinoma is estimated to be over 200,000 cases per year,
making it the 2nd most common malignancy in the United States, after prostate cancer in men and breast cancer in women. Mortality-wise, it causes the highest cancer-related deaths in the United States: about 160,000 deaths per year are related to bronchogenic carcinoma. The average age at the time of diagnosis is about 65 years.

Tobacco smoking is the most important etiologic risk factor for bronchogenic carcinoma. The risk of bronchogenic carcinoma has a direct relationship to the duration and dose of tobacco smoking. Passive (secondhand) smoke is also a risk factor.

Other known risk factors include exposure to asbestos, radon, arsenic, beryllium, chromium, nickel, and soot.

**Classification**

Bronchogenic carcinoma is histologically divided into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), with the latter further subdivided into 3 main subtypes: squamous cell carcinoma, adenocarcinoma, and large cell carcinoma:

- **Adenocarcinoma** is the most common type of bronchogenic carcinoma, representing about 35%-40% of cases. It is more common in women and in nonsmokers. Adenocarcinoma is peripherally located and histologically contains glands.
- **Squamous cell carcinoma** is strongly associated with a history of tobacco smoking and is usually located in the center of the lungs. It is also associated with cavitation and parathyroid hormone-related protein secretion.
- **Large cell carcinoma** is peripherally located and is undifferentiated histologically. The cells do not show gland formation as in adenocarcinoma, or keratinization as in squamous cell carcinoma. It is related to tobacco smoking and has a poor prognosis.

- **Small cell carcinoma** is a central tumor and is more common in smokers. It is a very aggressive form of bronchogenic carcinoma. These tumors are more likely to metastasize to distant organs at the time of presentation, and the prognosis is usually grim. They originate from Kulchitsky (neuroendocrine) cells. They may be associated with paraneoplastic syndromes (Lambert-Eaton syndrome, ectopic secretion of antidiuretic hormone, or adrenocorticotropic hormone).

### Clinical Presentation

The clinical presentation of bronchogenic carcinoma depends on the location of the tumor and the histological type. Approximately 10% of patients are asymptomatic; their bronchogenic carcinoma is detected on chest radiographs done for other reasons.

A cough is the most common presenting symptom; hence, any change in the character or severity of a cough in a smoker is always a red alarm for possible lung cancer. Due to the overlap between the symptoms and risk factors of chronic obstructive lung disease and bronchogenic carcinoma, the threshold to suspect lung cancer should always be low in a smoker.

Patients may also complain of anorexia, weight loss, chest pain or discomfort, shortness of breath, and hemoptysis. Secondary bacterial infections of the lung can also be a presentation of bronchogenic carcinoma.

In metastatic bronchogenic carcinoma, the clinical features of the involved organs are also present. These include seizures, headache, personality changes, bone pain, abdominal pain, and jaundice. The common metastatic sites include lymph nodes, bones, liver, central nervous system (brain and spinal cord), and adrenal glands.

Paraneoplastic syndromes are usually identified in bronchogenic carcinoma, and each presentation can be clearly linked to certain histological subtypes. For example:

- **Hypercalcemia** is more common in squamous cell carcinoma due to ectopic secretion of the parathyroid hormone-related peptide.

- Endocrine syndromes, such as the inappropriate secretion of antidiuretic hormone (SIADH), ectopic (adrenocorticotropic hormone; ACTH) production, and Lambert-Eaton syndrome, are associated with SCLC.

- Finger clubbing (hypertrophic osteoarthropathy) can be found in all types of bronchogenic carcinoma.

Physical examination may be normal or may reveal the following:

- Anemia, finger clubbing, enlarged lymph nodes
- Decreased breath sounds due to underlying malignant pleural effusion
- Wheezing accompanying chronic obstructive pulmonary disease
- Facial swelling, plethora, dilated vessels, and upper limb edema due to superior vena cava syndrome
- Hoarseness due to recurrent laryngeal nerve palsy
A chest radiograph is the first step to take in a patient suspected with bronchogenic carcinoma. Any known smoker who presents with a recent-onset cough or a change in their cough and respiratory function should undergo a chest X-ray. If the X-ray reveals a nodule, it should always be compared with a previous chest X-ray, if available.

It should be noted that a normal chest X-ray does not necessarily exclude lung cancer, because a small tumor can be hidden within the mediastinum or elsewhere in the chest. If the suspicion of bronchogenic carcinoma is high, on the basis of history and physical examination, then further imaging with a CT scan and positron emission tomography (PET) scan is advised.

The next diagnostic step depends on the location of the nodule:

- For central nodules, sputum cytology can help aid with diagnosis, as it can reveal malignant cells. Bronchoscopic and transthoracic biopsies are indicated to define the histological type of the bronchogenic carcinoma, as this clearly affects the treatment plan and prognosis.
- For peripheral nodules, CT-guided transthoracic biopsy is indicated to identify the histological type of cancer.
Routine laboratory investigations in lung cancer can reveal hypercalcemia, hypophosphatemia, hyponatremia (due to SIADH), or increased ACTH.

A CT scan of the chest is used for staging purposes. It can also help differentiate between SCLC and NSCLC, as the former is more commonly associated with massive lymphadenopathy.

A PET scan is commonly used in patients with bronchogenic carcinoma to identify possible mediastinal involvement and distant metastasis.

After confirmation of the histological diagnosis, a detailed staging workup should be performed to determine the extent of disease and the presence of distant metastasis and to identify potential candidates for surgery.

The TNM (tumor-nodes-metastasis) system is used for the staging of bronchogenic carcinoma.
Treatment

The management plan for bronchogenic carcinoma is based on its histology, staging, location, and comorbidities of the patient. The available treatment options are evolving and complex, and in broad terms include surgery, radiotherapy, and chemotherapy.

Generally, there are different treatment options for patients with SCLC and NSCLC.

Treatment For NSCLC

In the early stages of NSCLC, surgical resection of the tumor is indicated as an intent-to-cure therapy.

In later stages, a multidisciplinary approach is often indicated along with chemotherapy and radiotherapy.

Palliative care should be initiated early in patients with metastatic disease, or if underlying morbidity prevents potentially curable therapy, as it improves quality of life.

Treatment For SCLC

Since most SCLCs have metastasized at the time of diagnosis, surgical treatment is often not feasible, although it may be an effective option in the rare case when SCLC is localized to the lungs.

Chemotherapy and radiotherapy should be pursued, but have limited success. The 5-year survival rate is virtually zero for extensive-stage SCLC.

As with NSCLC, palliative care should be initiated early to improve the patient’s quality of life.

References


Non-Small Cell Lung Cancer via medscape.com

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