

LUNG CANCER

Non-small-cell lung carcinoma

The three main subtypes of NSCLC are adenocarcinoma, squamous-cell lung carcinoma, and large-cell lung carcinoma. Nearly 40% of lung cancers are adenocarcinoma, which usually originates in peripheral lung tissue. Most cases of adenocarcinoma are associated with smoking; however, among people who have smoked fewer than 100 cigarettes in their lifetimes ("never-smokers"), adenocarcinoma is the most common form of lung cancer. A subtype of adenocarcinoma, the bronchioloalveolar carcinoma, is more common in female never-smokers, and may have different responses to treatment.

Squamous-cell carcinoma accounts for about 30% of lung cancers. They typically occur close to large airways. A hollow cavity and associated necrosis are commonly found at the center of the tumor. About 9% of lung cancers are large-cell carcinoma. These are so named because the cancer cells are large, with excess cytoplasm, large nuclei and conspicuous nucleoli.

Small-cell lung carcinoma

In small-cell lung carcinoma (SCLC), the cells contain dense neurosecretory granules (vesicles containing neuroendocrine hormones), which give this tumor an endocrine/paraneoplastic syndrome association. Most cases arise in the larger airways (primary and secondary bronchi). These cancers grow quickly and spread early in the course of the disease. Sixty to seventy percent have metastatic disease at presentation. This type of lung cancer is strongly associated with smoking.

Others

Four main histological subtypes are recognized, although some cancers may contain a combination of different subtypes. Rare subtypes include glandular tumors, carcinoid tumors, and undifferentiated carcinomas.

Metastasis

The lung is a common place for metastasis of tumors from other parts of the body. Secondary cancers are classified by the site of origin; e.g., breast cancer that has spread to the lung is called metastatic breast cancer. Metastases often have a characteristic round appearance on chest radiograph.

Primary lung cancers themselves most commonly metastasize to the brain, bones, liver, and adrenal glands. Immunostaining of a biopsy is often helpful to determine the original source.

Signs and symptoms

Symptoms and signs that may suggest lung cancer include:

- coughing
- weight loss
- dyspnea (shortness of breath)

- chest pain
- hemoptysis (coughing up blood)
- bone pain
- clubbing of the fingernails
- fever
- fatigue
- superior vena cava obstruction
- dysphagia (difficulty swallowing)
- wheezing

If the cancer grows in the airway, it may obstruct airflow, causing breathing difficulties. The obstruction can lead to accumulation of secretions behind the blockage, and predispose to pneumonia.

Depending on the type of tumor, so-called paraneoplastic phenomena may initially attract attention to the disease. In lung cancer, these phenomena may include Lambert–Eaton myasthenic syndrome (muscle weakness due to autoantibodies), hypercalcemia, or syndrome of inappropriate antidiuretic hormone (SIADH). Tumors in the top (apex) of the lung, known as Pancoast tumors, may invade the local part of the sympathetic nervous system, leading to Horner's syndrome, as well as damage to the brachial plexus.

Many of the symptoms of lung cancer (poor appetite, weight loss, fever, fatigue) are not specific. In many patients, the cancer has already spread beyond the original site by the time they have symptoms and seek medical attention. Common sites of metastasis include the brain, bone, adrenal glands, contralateral (opposite) lung, liver, pericardium, and kidneys. About 10% of people with lung cancer do not have symptoms at diagnosis; these cancers are incidentally found on routine chest radiograph.

Diagnosis

Performing a chest radiograph is one of the first investigative steps if a patient reports symptoms that may suggest lung cancer. This may reveal an obvious mass, widening of the mediastinum (suggestive of spread to lymph nodes there), atelectasis (collapse), consolidation (pneumonia), or pleural effusion. CT imaging is typically used to provide more information about the type and extent of disease. Bronchoscopy or CT-guided biopsy is often used to sample the tumor for histopathology.

Lung cancer often appears as a solitary pulmonary nodule on a chest radiograph. However, the differential diagnosis is wide. Many other diseases can also give this appearance, including tuberculosis, fungal infections, metastatic cancer, or organizing pneumonia. Less common causes of a solitary pulmonary nodule include hamartomas, bronchogenic cysts, adenomas, arteriovenous malformation, pulmonary sequestration, rheumatoid nodules, Wegener's granulomatosis, or lymphoma. Lung cancer can also be an incidental finding, as a solitary pulmonary nodule on a chest radiograph or CT scan taken for an unrelated reason.

The definitive diagnosis of lung cancer is based on histological examination of the suspicious tissue in the context of the clinical and radiological features.

Staging

Lung cancer staging is an assessment of the degree of spread of the cancer from its original source. It is one of the factors affecting the prognosis and potential treatment of lung cancer.

The initial evaluation of non-small-cell lung cancer (NSCLC) staging uses the TNM classification. This is based on the size of the primary tumor, lymph node involvement, and distant metastasis. After this, using the TNM descriptors, a group is assigned, ranging from occult cancer, through stages 0, IA (one-A), IB, IIA, IIB, IIIA, IIIB and IV (four). This stage group assists with the choice of treatment and estimate of prognosis. Small-cell lung carcinoma (SCLC) has traditionally been classified as 'limited stage' (confined to one half of the chest and within the scope of a single tolerable radiotherapy field) or 'extensive stage' (more widespread disease). However, the TNM classification and grouping are useful in estimating prognosis.

For both NSCLC and SCLC, the two general types of staging evaluations are clinical staging and surgical staging. Clinical staging is performed prior to definitive surgery. It is based on the results of imaging studies (such as CT scans and PET scans) and biopsy results. Surgical staging is evaluated either intra- or postoperatively, and is based on the combined results of surgical and clinical findings, including surgical sampling of thoracic lymph nodes.

Surgery

If investigations confirm NSCLC, the stage must be reassessed to determine whether the disease is localized and amenable to surgery or whether it has spread to the point where it cannot be cured surgically. CT scan and positron emission tomography (PET) are used. If mediastinal lymph node involvement is suspected, mediastinoscopy may be used to sample the nodes and assist staging.

Blood tests and pulmonary function testing are also necessary to assess whether the patient is well enough for surgery. If pulmonary function tests reveal poor respiratory reserve, surgery may be contraindicated.

In most cases of early-stage NSCLC, removal of a lobe of lung (lobectomy) is the surgical treatment of choice. In patients who are unfit for a full lobectomy, a smaller sublobar excision (wedge resection) may be performed. However, wedge resection has a higher risk of recurrent disease than lobectomy. Radioactive iodine brachytherapy at the margins of wedge excision may reduce the risk of recurrence. Rarely, removal of a whole lung (pneumonectomy) is performed.

Video-assisted thoracoscopic surgery and VATS lobectomy use a minimally invasive approach to lung cancer surgery. VATS lobectomy is equally effective compared to conventional open lobectomy, and with less postoperative illness.

In SCLC, chemotherapy and/or radiotherapy is typically used. However the role of surgery in SCLC is being reconsidered. Surgery might improve outcomes when added to chemotherapy and radiation in early stage SCLC.

Radiotherapy

Radiotherapy is often given together with chemotherapy, and may be used with curative intent in patients with NSCLC who are not eligible for surgery. This form of high-intensity radiotherapy is called radical radiotherapy.

A refinement of this technique is continuous hyper fractionated accelerated radiotherapy (CHART), in which a high dose of radiotherapy is given in a short time period. Postoperative thoracic radiotherapy generally should not be used after curative intent surgery for NSCLC. Some patients with mediastinal N2 lymph node involvement might benefit from post-operative radiotherapy.

For potentially curable SCLC cases, chest radiotherapy is often recommended in addition to chemotherapy.

If cancer growth blocks a short section of bronchus, brachytherapy (localized radiotherapy) may be given directly inside the airway to open the passage. Compared to external beam radiotherapy, brachytherapy allows a reduction in treatment time and reduced radiation exposure to healthcare staff.

Prophylactic cranial irradiation (PCI) is a type of radiotherapy to the brain, used to reduce the risk of metastasis. PCI is most useful in SCLC. In limited-stage disease, PCI increases three-year survival from 15% to 20%; in extensive disease, one-year survival increases from 13% to 27%.

Recent improvements in targeting and imaging have led to the development of stereotactic radiation in the treatment of early-stage lung cancer. In this form of radiotherapy, high doses are delivered in a small number of sessions using stereotactic targeting techniques. Its use is primarily in patients who are not surgical candidates due to medical comorbidities.

For both NSCLC and SCLC patients, smaller doses of radiation to the chest may be used for symptom control (palliative radiotherapy).

Chemotherapy

The chemotherapy regimen depends on the tumor type.

Small-cell lung carcinoma

Even if relatively early stage, SCLC is treated primarily with chemotherapy and radiation. In SCLC, cisplatin and etoposide are most commonly used. Combinations with carboplatin, gemcitabine, paclitaxel, vinorelbine, topotecan, and irinotecan are also used.

Non-small cell lung carcinoma

In advanced NSCLC, chemotherapy improves survival and is used as first-line treatment, provided the patient is well enough for the treatment. Typically, two drugs are used, of which one is often platinum-based (either cisplatin or carboplatin). Other commonly used drugs are gemcitabine, paclitaxel, docetaxel, pemetrexed, etoposide or vinorelbine.

Adjuvant chemotherapy

Adjuvant chemotherapy refers to the use of chemotherapy after apparently curative surgery to improve the outcome. In NSCLC, samples are taken of nearby lymph nodes during surgery to assist staging. If stage II or III disease is confirmed, adjuvant chemotherapy improves survival by 5% at five years. The combination of vinorelbine and cisplatin is more effective than older regimens.

Adjuvant chemotherapy for patients with stage IB cancer is controversial, as clinical trials have not clearly demonstrated a survival benefit. Trials of preoperative chemotherapy (neoadjuvant chemotherapy) in resectable NSCLC have been inconclusive.

Palliative care

In patients with terminal disease, palliative care or hospice management may be appropriate. These approaches allow additional discussion of treatment options and provide opportunities to arrive at well-considered decisions and may avoid unhelpful but expensive care at the end of life.

Chemotherapy may be combined with palliative care in the treatment of the NSCLC. In advanced cases, appropriate chemotherapy improves average survival over supportive care alone, as well as improving quality of life.

With adequate physical fitness, maintaining chemotherapy during lung cancer palliation offers 1.5 to 3 months of prolongation of survival, symptomatic relief, and an improvement in quality of life, with better results seen with modern agents. The NSCLC Meta-Analyses Collaborative Group recommends if the recipient wants and can tolerate treatment, then chemotherapy should be considered in advanced NSCLC.