Bronchogenic carcinoma

- Bronchogenic carcinoma means carcinoma of the bronchi and lung parenchyma.

- Bronchogenic carcinoma refers to carcinoma of the bronchi and lung parenchyma.
- Morphologically bronchogenic carcinoma is divided into 2 types:
  1. small cell (SCLC)
  2. non-small cell bronchogenic carcinoma (NSCLC).
- SCLC accounts for about 20-25%, NSCLC 75-80%.
- Non-small cell carcinoma contains 3 subtypes of tumor:
  1. squamous cell carcinoma,
  2. adenocarcinoma,
  3. large cell carcinoma.
- Lung tumors can also be combined → it contains a component of SCLC and another histological type.

!!! Histological determination of cancer is essential because the prognosis and treatment of small cell and non-small cell carcinomas are diametrically different!

Biological properties

- Small cell carcinoma (SCLC) → grows rapidly and produces distant metastases early.
  - For this reason, surgical treatment options for the tumor are limited.
  - However, cancer responds well to chemotherapy and radiotherapy.

- Non-small cell carcinoma (NSCLC)→ grows more slowly than the previous type of tumor, and therefore the tumor can be treated by surgical resection of the tumor.
  - The sensitivity to treatment is lower in this type of tumor.

Epidemiology

- Worldwide, bronchogenic carcinoma is the most common malignancy in men in incidence and mortality.
- In women, it ranks third in incidence and second in mortality (after breast cancer).
- It accounts for 20% of all cancer deaths worldwide.
- In the Czech Republic, bronchogenic carcinoma has the second-highest incidence (93 / 100,000 inhabitants) among malignant tumors.
- It has an increasing incidence in the female population and is generally at the level of 60 / 100,000 inhabitants.
- The highest incidence is between the ages of 70 and 85.

Etiology

- The influences that cause bronchogenic carcinoma can be divided into endogenous and exogenous.
  - Endogenous effects include increased cytochrome P450 activity (increased production of carcinogens from cigarette smoke), decreased glutathione S-transferase function, decreased activity of cellular DNA repair mechanisms, as well as TP53 gene mutations.
  - The most significant exogenous cause is smoking. 90% of lung tumors are reported to occur in smokers
    - Passive smoking also poses an increased risk.
  - Another risk factor is increased radon exposure.
    - 222Rn is formed by the decay of uranium.
    - In the Czech Republic, there is increased exposure to natural radon in the South Bohemian Region.
  - Other important carcinogens are part of the workload - asbestos, inorganic compounds of arsenic, sulfur, compounds of chromium, nickel, or PVC. Another risk factor is ionizing radiation.

Clinical picture

- Bronchogenic carcinoma does not show early symptoms.
- As soon as the symptoms of the disease appear, it is already advanced cancer.
- We divide the symptoms into three groups: intrathoracic, extrathoracic, and paraneoplastic.

1. Intrathoracic symptoms
   - Intrathoracic symptoms depend on the size and location of the primary tumor.
     - In centrally growing tumors:
       - cough (in 45-75% of patients - initially dry, irritating, then productive);
       - change like chronic cough (greater intensity, frequency, irritability); hemoptysis (20-30%);
       - stridor in narrowing of the main airways;
       - bronchopneumonia in bronchial obstruction;
       - upper vena cava syndrome as a result of oppression by enlarged lymph nodes;
       - hoarseness during compression of the recurrent laryngeal nerve, where paresis of the vocal cords occurs;
       - in advanced stages also shortness of breath.
     - For peripherally growing tumors:
       - chest pain, restrictive dyspnoea.
     - Pancoast tumor → a consequence of the local progression of a tumor growing in the lung tip, which may affect:
       - plexus brachialis → severe upper limb pain, paresis;
       - cervical plexus → Horner's syndrome (miosis, ptosis, enophthalmos) develops.
2. Extrathoracic symptoms
   - In CNS metastases → headaches, visual impairment, neurological or mental disorders.
   - In bone metastasis → anemia, leukoerythroblastosis, pain, pathological fractures.
   - Liver metastases are manifested by jaundice and other hepatobiliary symptoms.
3. Paraneoplastic symptoms
   - They are very common in bronchogenic carcinomas and can also be the first manifestation of the disease.
   - Endogenous paraneoplastic syndromes include hypercalcemia and hypophosphataemia in ectopic parathyroid hormone secretion.
   - Hyponatremia - inadequate ADH secretion.
   - Cushing's syndrome with hypokalemia in ectopic ACTH secretion.
   - Hypertrophic osteoarthropathy - clubbed fingers, periostitis.
   - Dermatomyositis.
   - Neurological - peripheral neuropathy, muscle myopathy.
   - Muscle - myasthenia.
   - Hematological.

Diagnostics

- We cannot diagnose bronchogenic carcinoma alone based on physical examination and imaging methods.
- We can determine the definitive diagnosis only based on histopathological examination.
- For a patient (especially with lung disease), a biopsy is always a burden, so it should be treated only if there is a serious suspicion of cancer.

Physical exam

- The physical finding is often physiological.
- Sometimes we can find shortness of breath and shortened percussion, which indicates a pleural effusion.
- Whistling or squeaking may appear. It is necessary to specifically examine the lymph nodes - the supraclavicular, axillary, and cervical.
- An enlarged liver may already be metastatic.

Imaging methods

1. X-ray - posterior and lateral projections.
2. CT - lungs and mediastinum.
3. MRI - lungs and mediastinum, suitable for Pancoast's tumor.
4. other → PET, abdomen and retroperitoneum, skeletal scintigraphy, brain CT, sternal puncture.

Cytohistological examination

1. Bronchoscopy → a collection of material for histological examination, using a brush for cytological examination, changes can be evaluated macroscopically.
2. Video-assisted thoracoscopy (VATS) → biopsy/resection of a part of the lung parenchyma.
3. Mediastinoscopy.
4. Transparietal biopsy → under X-ray / CT control (mainly peripheral lesions).
5. Cryobiopsy.

If the patient is not allowed to perform a sampling examination, we can cytologically examine the sputum (3-5 doses).

Histology

Small cell carcinoma

- Oat carcinoma → uniform small cells with a narrow cytoplasmic margin are typical.
- Intermediate form (spindle cell) → polygonal cells and spindle cell shapes.
- Small cell carcinomas have a short doubling time, a high growth fraction, and a tendency to early regional and distant metastasis (CNS, bones, liver, adrenal glands, skin).
- Hilar and mediastinal adenopathy, atelectasis, and secondary bronchopneumonia are more common than non-small cell carcinomas.

Non-small cell carcinoma

- Squamous cell carcinomas (epidermoid, squamous cell) → central localization, a tendency to early involvement of mediastinal nodes.
- Adenocarcinomas → peripherally localized, a tendency to both regional and systemic dissemination.
- Large cell carcinomas → less common, also manifest as peripheral lesions and have the same tendency to metastasize as adenocarcinoma.

Therapy

- Treatment for small cell and non-small cell forms differs in many respects.

1. Treatment of small cell carcinoma
   - Chemotherapy, tumor-targeted and metastatic radiotherapy, preventive brain irradiation, and rarely surgery.
   - In practice, SCLC is divided into 2 forms:
     - Limited disease - the disease affects only one pulmonary wing with/without the involvement of ipsilateral or contralateral mediastinal or supraclavicular nodes and with/without ipsilateral effusion, which can be taken up in one irradiation field.
     - Extensive diseases - all other forms.

- The basis of chemotherapy in both forms is chemotherapy for 4-6 cycles of cisplatin + etoposide.
- Cisplatin can be replaced by carboplatin. Topotecan is used as second-line chemotherapy.
- In the limited form, radiotherapy is combined with chemotherapy - a standard treatment procedure.
- Surgical treatment is indicated only in very limited cases. Systemic treatment must always follow.

Treatment of non-small cell lung cancer

- Determining the clinical stage based on the TNM classification is the basis for determining treatment.

Stage	T	N	M	Treatment
0	CIS	N0	M0	
IA	T1	N0	M0	surgery, if surgery is not possible - radiotherapy
IB	T2	N0	M0	surgery and subsequent systemic treatment
IIA	T1	N1	M0	surgery and subsequent systemic treatment
IIB	T2	N1	M0	surgery and subsequent systemic treatment
IIB	T3	N0	M0	surgery and subsequent systemic treatment
IIIA	T1-T3	N1-N2	M0	surgery and subsequent systemic treatment
IIIB	T4	Nx	M0	inoperable, CHT + chest radiotherapy
IIIB	Tx	N3	M0	inoperable, CHT + chest radiotherapy
IV	Tx	Nx	M1	inoperable, palliative CHT or radiotherapy

- In combination chemotherapy, a platinum derivative (cisplatin, carboplatin) with cytostatics III is used. generation (vinorelbine, gemcitabine, paclitaxel).
- Palliative chemotherapy takes 2-6 cycles.
- After the 2nd and 4th cycles, the patient's condition is evaluated

Biological treatment of NSCLC

- Tyrosine kinase inhibitors: erlotinib + gefitinib +afatinib → indicated in patients with a positive activating mutation of the EGFR gene.
- Due to a mutation in the EGFR gene, the receptor is pathologically activated and the properties that make cells malignant are affected
  - inhibition of apoptosis, angiogenesis, the ability of the tumor to metastasize, uncontrolled cell proliferation
- Monoclonal antibody against VEGFR: bevacizumab
- crizotinib → a selective inhibitor of ALK and its oncogenic variants (eg EML4-ALK gene fusion).

Differential diagnostics

- Other lung tumors.
- granulomatous lung processes - tuberculosis, sarcoidosis, pneumoconiosis.

Prognosis

- The prognosis depends on the type and stage of the disease.

1. small cell carcinoma

Stadium	Bez léčby	CHT	CHT + radiotherapy
Limited	median survival 3 months	12–14 months	14–16 months
Extenzivní	median survival 6 weeks	7-8 months	

2. non-small cell carcinoma

- In stage I, the 5-year survival is 40-50%.
- In stage II, the 5-year survival is about 30%.
- Stage III around 10% and stage IV less than 1%.
- The median survival for recurrent stages II and III are about 2 years.
- For stage IV, the median is 12 months.

Links

Related articles

- Malobuněčný karcinom plic (preparát)
- Nádory plic
- Pancoastův tumor

External links

- Pancoastův tumor – video Youtube (https://www.youtube.com/watch?v=BarrQZbsZJI)

Used literature

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- ČEŠKA, Richard, et al. *Interna.* 1. vydání. Praha : Triton, 2010. 855 s. ISBN 978-80-7387-423-0.

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3. ↑ SVOD,. *Incidence bronchogenního karcinomu u mužů* [online]. [cit. 2016-03-11]. <http://www.svod.cz/analyse.php?modul=vek&diag=C34&zobrazeni=graph&incmor=inc&vypocet=c&pohl=&kraj=&obdobi_od=1977&obdobi_do=2013&stadium=&t=&n=&m=&pt=&pn=&pm=&t=&n=&zije=&umrti=&lect
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7. ↑ AMERICAN CANCER SOCIETY,. *Non-small cell lung cancer survival rates, by stage* [online]. [cit. 2016-03-11]. <https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html>.

External links

- Malobuněčný karcinom (medscape) (https://emedicine.medscape.com/article/280104-overview)
- Nemalobuněčný karcinom (medscape) (https://emedicine.medscape.com/article/279960-overview)