Neuroendocrine tumours (NET) are a various and interesting group of neoplasms considering their common origin, localisation in different organs and ability to secrete hormones, bioactive amines and peptides. This tumours originate from neurosecretive cells (enterochromaffinocytes) termed Kulchitsky cells, that underwent neoplastic transformation. Cells that, during embryogenesis, evolve from neuroectoderm of foregut and localise mainly in the upper part of alimentary system and pancreas, give rise to the diffused neuroendocrine system of the digestive tract termed APUD (amine precursor uptake and decarboxylation). Some of them migrate to lungs and other organs such as: suprarenal glands, thyroid gland, thymus, uterine tubes, vagina, uterus (tab. 1). The enterochromaffinocytes characterise themselves with pale cytoplasm and affinity to silver salts in cytopathological tests. They show expression of antigens found in cells of nervous system such as: chromogranin A, NSE (neurospecific enolase), synaptophysin and PGP 9.5 (1-5).

According to the latest definitions, endocrine tumours group include also neoplasms originating from cells of endocrine glands such as: pituitary gland, parathyroid glands, adrenal medulla (fig. 1) (6). Neoplasms with neuroendocrine etiology, despite common histochemical and structural features, are a heterogeneous group of neoplasms differing with: secretion of distinct biological substances, presence or absence of hormonal activity, difficulties in diagnosing, varied clinical manifestation, biological course, susceptibility to treatment and prognosis (7, 8). Presently, 19 types of APUD cells localised in the alimentary tract mainly, are distinguished. It become identified that they may excrete almost 40 types of pharmacologically active substances, biogenic amines and peptides (3, 5). Nevertheless, hormonal activity is confirmed in up to 50% of tumours (9).

Table 1. Embryologic classification of neuroendocrine tumours

<table>
<thead>
<tr>
<th>Foregut</th>
<th>Midgut</th>
<th>Hindgut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagus</td>
<td>– jejenum</td>
<td>transverse colon,</td>
</tr>
<tr>
<td>Stomach</td>
<td>– ileum</td>
<td>descendingt colon, sigmoid</td>
</tr>
<tr>
<td>Duodenum</td>
<td>– appendix</td>
<td>colon*</td>
</tr>
<tr>
<td>Pancreas</td>
<td>– caecum, ascending colon, transverse colon*</td>
<td></td>
</tr>
<tr>
<td>Extrahepatic bile ducts</td>
<td>– liver</td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td>– ovary</td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td>– cervix</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>– testes</td>
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</tr>
</tbody>
</table>

The variety of neuroendocrine tumours and their multiorgan localisation determined serious difficulties in their classification for several years.

In the year 2000 a group of specialists of WHO (World Health Organisation) elaborated an unified classification of neuroendocrine tumours, then extended in 2004 by introducing a common term: NET (Neuroendocrine tumours). The classification discerns 3 types of neoplasms: neuroendocrine tumours well differentiated – NEWD (WHO type I) located in organs or intestinal wall; well differentiated neuroendocrine cancers with local or distant metastases (WHO type II), low differentiated neuroendocrine cancers of high malignancy (WHO type III), sometimes also a group of mixed glandular and endocrine cancers with prevalence of endocrine component is distinguished (6, 10).

A simple classification of neuroendocrine tumours depending on their excretory properties and clinical manifestation of their activity is used in clinical practice. There is discerned a group of tumours that secrete active substances into the circulation. The substances may be hormonally active and cause manifestation of certain clinical syndromes, for example carcinoid and hormonally inactive tumours. Non-secretory tumours are the other group. They do not secrete active substances and do not manifest with associated clinical syndromes. Neuroendocrine tumours situated in the chest area originate from the foregut. They are revealed within the lungs and thymus mainly, rarely in other localisations (ectopic parathyroid glands, posterior mediastinum). The histopathological classification of bronchial neuroendocrine tumours is also complicated and was evolving for years. The latest World Health Organization Classification of Lung Neoplasm do not discern a separate category for neuroendocrine tumours of lung. Tumours with neuroendocrine activity are considered in the general definition of lung cancers of endothelial origin (11). Neuroendocrine tumours of lungs include four types of neoplasms: SCLC- small cell carcinoma, typical carcinoid, atypical carcinoid and LCNEC -large cell neuroendocrine carcinoma (tab. 2). Moreover, single or fine multiple nodular changes consisting of small foci of neuroendocrine cells proliferation are defined as carcinoid tumourlets, also considered as small carcinoids (2, 12, 13).

Carcinoids – carcinoid typicum / carcinoid atypicum

Carcinoids are the most common neuroendocrine neoplasms and amount up to 56-86% of all neoplasms originating from the APUD cells. About 70-85% of carcinoids is situated in the alimentary tract, 10-20% in lungs, other possible localisations are: thymus, kidney, ovary, prostate, skin. It is estimated that bronchial carcinoids constitute 2-5% of primary lung cancers (2, 14-17). Bronchial carcinoids are distinguished into 2 subtypes considering histopathological characteristics and clinical course: more benign typical carcinoids, up to 80-90% and more malignant atypical carcinoids, 10-20% of cases (15, 18, 19, 20). These neoplasms develop mainly in the 3th and 4th decade of life and occur a little more frequently in men than in women. Patients with carcinoids are usually younger than patients with other primary lung cancer (21, 22). Most lung carcinoids tend to locate centrally, almost 70% of neoplasms develop within main and lobar bronchi, the remaining 30% of is situated peripherally (23).

Statistical data show that, for unknown reasons, carcinoids tend to locate peripherally, in the middle lobe of the right lung (16, 24). Neoplasms of central localisation are generally typical carcinoids. It obviously effects the earlier clinical manifestation caused by bronchial obturation and local inflammation symptoms in the form of cough attacks, haemoptysis, recurrent pneumonia with atelectasis and dyspnoea (16, 20, 25). In patients with peripheral carcinoids the disease is mainly symptomless and the tumour is revealed, often accidentally, in the routine radiological examination of the chest.
Therefore, the atypical carcinoids are detected in patients about 10 years older than in case of centrally located typical carcinoids. Moreover, these tumours are more frequently associated with tobacco smoking (26). The course is symptomless in nearly 50% of patients with carcinoids. In 9% of cases the tumour is detected accidentally in sections removed in procedures performed for other reasons or on autopsy. From the morphological point of view, the carcinoids show the image of a well-bordered, cohesive, vascularized, yellowish tumour.

Centrally situated carcinoids have the average diameter of 3.5 centimetres (from 0.5 to 10 centimetres) and are usually bigger than peripheral carcinoids (average 2.4). The atypical carcinoids are usually bigger in size than typical carcinoids. In atypical carcinoids a greater tendency to bleedings and local necrosis of tumour is also observed. Correlation of carcinoid and multiple peripheral tumours of carcinoid tumourlet type is commonly known (15, 18, 20, 27). Metastases to the local lymph nodes occur more often in atypical carcinoids (30-50%), nevertheless, it can not be a criterion of differentiation of carcinoids. They are diagnosed in almost 5-20% of cases of typical carcinoids. Distant metastases may affect organs such as: skin, ovary, breast, eye bulb (24).

Among neuroendocrine syndromes, related with the secretion of bioactive hormones and parahormones into circulatory system, the most significant are: carcinoid syndrome, Cushing’s syndrome and acromegaly. The carcinoid syndrome occurs in 2-7% of patients and in most cases (86%) coexists with metastases to the liver (16). It is vital for diagnostics and monitoring of treatment to assay a concentration of metabolite of serotonin conversion- 5-hydroxyindolacetic acid in urine. Manifestation of Cushing’s syndrome may be present in case of a bronchial carcinoid with ectopic production of ACTH and/or GHRH (growth hormone releasing hormone) (28). Circumstantially, bronchial carcinoid is diagnosed in patients with multiple endocrine neoplasia type I (MEN I) (29). Classic radiological imaging is still crucial for the diagnosis of carcinoids, as well as other lung tumours. A radiogram may reveal nonspecific round shadow in case of peripheral tumour. In patients with central tumour, the radiological manifestations of atelectasis and segment or lobar pneumonia are predominant in the area of the bronchus affected by the tumour.

Computer tomography of chest or multiscan spiral CT and endoscopic ultrasonography are the most contributory to assess the local advancement. Diagnostic preopertaive use of FDG-PET (positron emission tomography with 18F-fluorodeoxyglucose) gives new possibilities. Functional scyntygraphic examinations...
(radioisotopic) predominantly with the use of somatostatin analogs (SRS, somatostatin receptor scintigraphy) labeled with $^{111}$In or $^{99m}$Tc and less frequently with the use of biogenic amine analogs labeled with $^{123}$I, $^{131}$I MIBG (metaiodobenzylguanidine).

Sensitivity of radioisotopic test in NET examinations is high and amounts 65-100% in certain tumours. What is crucial, it also enables diagnostics of pathologies of area inaccessible for CT (30-33). The diagnosis of the histological type of the neoplasm in the preoperative period may be established only basing on the analysis of cytological samples taken during the thin-needle transthoracic aspiration biopsy of peripherally located tumours. In case of centrally situated tumours, there is a possibility to obtain samples for histological examination directly from the tumour or through the bronchial wall. One of the most important examinations that contribute to determination of the histological type of tumour is bronchofiberoscopy. A characteristic image of a well vascularised tumour of violet and bluish colour and smooth contour, bleeding easily after touching, may be observed with bronchoscopy (15, 16, 34).

In case of insufficiency of the methods mentioned, establishing a diagnosis is based on examination of lung samples and lymph nodes collected during videothoracoscopy, VATS (video assisted thoracic surgery), mediastinoscopy or thoracotomy with intrasurgery examination.

The treatment of choice for bronchial carcinoid is a radical resection according to the procedures applied for non-microcellular lung cancer. The extent of resection depends on the location and type of tumour. Typical carcinoids are resected non-radically if possible. The lobectomy is the most frequent procedure, segmentotomy is far less common. The mediastinal lymph nodes should be resected in every case (lymph node sampling) (16, 19, 25).

In peripheral typical carcinoids the non-anatomical resection (marginal, wedge) is thought to be extensive enough. Nonetheless, considering the risk of recurrence and metastases, the anatomical resection is recommended. In case of typical carcinoid situated in the ostium of the right upper lobar bronchus it is possible to perform a sleeve resection. In rare cases a pneumonectomy may be necessary. It is not advised to resect carcinoids with endoscopic techniques, except for the palliative treatment. The intrabronchial carcinoids usually expand outside the bronchial lumen, which is the reason why endoscopic resection is almost always non total (25, 34).

The resection of the tumour affected lung lobe and lymph nodes is recommended in cases of more aggressive atypical carcinoids. Wedge resection as a treatment for atypical carcinoid is reserved exceptionally, as in different types of lung cancer, for patients with serious risk factors and slight breathing reserves measured with the spirometric examination. In patients with clinical manifestation of carcinoid syndrome, where a radical surgical treatment is impossible, even a partial resection of tumour tissue or metastatic foci may reduce the symptoms essentially (35). In the treatment for metastatic foci the embolisation of tumour supplying vessels is also performed (25). Bronchial carcinoids are resistant to radiotherapy. Only cases of local recurrence of neoplasm or metastatic foci are indications for radiotherapy. It was proved that radiotherapy reduces pain in case of osseus metastases (25, 34). Indications for chemotherapy in patients with locally recurrent or metastatic carcinoids are not clearly defined. Considering the resemblance of atypical carcinoid and microcellular cancer, it is thought that similar methods of treatment may be employed. 5 year survival in surgically treated patients with typical carcinoid amounts to more than 90%-95%, in case of atypical carcinoids is estimated for about 50%-70% (24).

Large cell neuroendocrine carcinoma (combined large cell neuroendocrine carcinoma)

Large cell neuroendocrine carcinoma (LCENC), a type of large cell carcinoma, was described for the first time in 1991 by Travis et al. who classified it as a neuroendocrine tumour due to the resemblance of its clinical and pathological characteristics with other neoplasms of this group (35). It is defined as a well differentiated tumour showing neuroendocrine features, which morphologically is between the atypical carcinoid and small cell lung cancer. Apart from its principal pulmonary location it occurs seldom in other regions of the chest, mainly in the mediastinum (35, 36, 37). Morphologically, the large cell carcinoma consists of cells with clear cytoplasm and
Neuroendocrine tumours of the chest area

big nucleus, which contains large nucleolus. The neuroendocrine form is distinguished on the basis of features such as: trabecular growth, formation of rosettes and palisade systems as well as the expression of the neuroendocrine markers (12, 19, 35). The neuroendocrine features demonstrated with light microscopy should be verified with immunohistochemical tests and electron microscopy. In this tumour, there are positive readings NSE (100%), chromogranin (80%), synaptophysin (40%), Leu-7 (70%), CEA (100%) and cytokeratin (100%). The aneuploidy flow cytometry result is observed in 75% of cases. This result is similar to the small cell carcinoma and also considerably higher than in atypical carcinoid. As far as molecular biology is concerned, according to the latest reports, the mutation of P53 protein is present in large cell neuroendocrine carcinoma and small cell carcinoma, while not in carcinoids (27, 35, 38, 39).

Large cell neuroendocrine carcinoma is identified in about 2, 9% of primary lung neoplasms resected surgically and 19% of resected neuroendocrine tumours. About 12% of all types of large cell carcinomas was the neuroendocrine type (13, 40, 41).

The average age of patients diagnosed with this tumour is 64 years, males are affected more often than females. The majority of patients (nearly 60%) are the long term smokers. According to the literature data, the cases of ectopic hormone secretion have not been observed so far in these tumours (35). The description of only one case of tumour with the secretion of α-fetoprotein (AFP) is known (42).

LCNEC may locate both centrally and peripherally, spreading to the pleura and the structure of chest wall. The tumour may reach the size of 1,5 to 10 cm (average about 3 cm). It is described as a cohesive, non-encapsuled tumour in the colour of yellow, white or light brown, often with the area of vast necrosis and hemorrhagic changes. In about 24% of cases this tumour may be accompanied by pleural exudation (43). The diagnosis of this neoplasm is based on the same rules as in case of other primary lung cancers. For the most part, CT is used in the diagnosis of the stage of local advance, however, PET may provide significant data. As far as the invasive examinations are considered, the bronchofiberoscopy, transbronchial ultrasonography, mediastinoscopy and, if indicated, videothoracoscopy are performed.

In the evaluation of the histopathological type of the tumour, the preoperative diagnosis is inclined to determine if the tumour is the small cell carcinoma or the non-small cell carcinoma, basing on the procedures such as: thin-needle aspiration biopsy, bronchofiberoscopy with the section of the bronchial tree, analysis of the material obtained on mediastinoscopy or videothoracoscopy. In this stage of diagnosis it is difficult to ascertain the presence of LCNEC. Nonetheless, the diagnosis of the non-small cell type of tumour is sufficient to classify to a procedure, in which at least lobectomy or larger anatomical lung resection with mediastinal lymphadenectomy should be performed. The neuroendocrine characteristics of the tumour is generally confirmed by the histopathological examination of the postoperative sections, accompanied by the specific immunohistochemical tests, which determine the further method of complementary treatment.

From the biological point of view, LCNEC is characterised by high degree of malignancy and poor prognosis. Paci et al. state that LCNEC, even in early stages, has worse prognosis than other non-small cell lung carcinomas. It is estimated that 5-year survival rate does not exceed 21-30% (44).

Aggressive clinical course, early metastitic abilities and poor prognosis cause that LCNEC is more similar to small cell carcinoma in its biology, however, to the contrary, it does not react well to chemo- and radiotherapy (19, 35). It is thought that the treatment should be surgical in case of tumours with such a possibility. In locally advanced, non-radically removed tumours, there are indications for radiotherapy. After surgical treatment, the adjuvant chemotherapy is recommended due to the aggressive character of the tumour. The patients with an advanced disease should be qualified to aggressive multidrug chemotherapy.

Small cell carcinoma

Small cell carcinoma amounts to about 20-25% of all primary lung cancers. This neoplasm is highly correlated with tobacco smoking and exposure to the ionizing radiation. It belongs to the group of anaplastic malignant neoplasms originating from epithelial cells of the bronchial tree with characteristic cytological features. It is composed of small cells with scarce cytoplasm and primitive nucleus
with fine-grained chromatin, without nucleolus. High mitotic index and forming of extensive areas of necrosis are characteristic for this neoplasm. It is a tumour of fast growth, high rate of doubling of tumour mass and high aggressiveness. In the beginning, it usually proliferates submucously, constricts bronchial lumen from the outside and may expand polyously to the interior. It also gives early distant hematogenous metastases, most frequently to the liver, skeletal system, brain, marrow, suprarenal glands and local lymph nodes. In nearly 60-70% of patients there is a general pathology developed at the moment of establishing the diagnosis (45), it is correlated with poor results of surgical treatment. A crucial feature of the microcellular cancer, differing from other types of lung cancer is relatively high susceptibility to cytostatic drug treatment and ionizing radiation, which is the standard of contemporary therapy of this tumour (46, 47). This tumour occurs significantly more often in men. The average age of patients with such a neoplasm is above 60 years.

In almost 90% of cases the microcellular cancer develops perihilarly in major bronchi, rapidly affecting mediastinal lymph nodes and the surrounding organs of thoracic cavity (23, 34, 35, 47, 48).

The diagnostics includes the same methods as in other lung tumours. It is performed on purpose to establish the histological diagnosis and advancement level of the disease. Immunohistochemistry is an important method that complementes the diagnostics of the microcellular cancer. Due to the fact that the tumour shows neuroendocrine differentiation, many markers used in diagnostics of various neuroendocrine tumours are also used in the immunohistochemical tests. The most commonly used are: chromogranin A, synaptophysin, NSE, Leu-7. Positive immunohistochemical reaction was observed respectively: with chromogranin (47-60% of cases), NSE (33-60%), Leu-7 (24-40%) and with synaptophysin from 5% to 19% (11). In microcellular carcinoma positive reactions with EMA and cytokeratin are also detected, although a positive expression of the latter is not found in all cases. At the time of establishing a diagnosis, patients usually have a disseminated pathology, with primary tumour, micrometastases and affected lymph nodes, which disqualifies from the surgical treatment. Due to the susceptibility of microcellular cancer to multicomponent chemotherapy and ionizing radiation, these methods are the basic treatment in contemporary therapy of microcellular cancer. The tumour in LD stadium (limited disease) is treated with multidrug therapy combined with radiotherapy. ED (extended disease) staged neoplasm is treated with chemotherapy only. In part of patients palliative radiotherapy is performed to soothe some of disease symptoms (12, 34, 46, 47).

The average survival of patients without treatment is 3 months. In treated patients, in LD form it is about 15 months on average, in case of disseminated ED is under 8 months. In former group, 2 years survival rate amounts to 25%, whereas in latter decreases to only 2-3% (12, 34, 46, 47). In part of microcellular carcinoma cases, combined small cell carcinoma is observed. It is the reason of serious diagnostic difficulties and usually worse prognosis for the patients with the diagnosis of only one component of the tumour, which determines the treatment adequate to the certain histological type of tumour. It is usually a tumour consisting of microcellular and non-microcellular cancer texture, for the most part of planoepithelial cancer, adenocarcinoma or large cell carcinoma (49).

Neuroendocrine tumours of mediastinum – thymus neuroendocrine tumors

Tumours of the anterior mediastinum are rarely observed. They include: carcinoid of thymus, parathyroid tumour, microcellular cancer and large cell neuroendocrine cancer. As far as histological structure, clinical course, diagnostics and prognosis are considered, the characteristics of two latter tumours is similar to the previously discussed microcellular and large cell cancer of lung.

Carcinoid is the most frequent neuroendocrine tumour of thymus, it may cause 2% to 4% of all tumours of anterior mediastinum and less than 1% of human body carcinoids (50, 51). Thymic carcinoid was confused with thymoma for many years, before the classification of neuroendocrine tumours had been created. Thymic carcinoids are diagnosed in various age groups. It is estimated that average age of patient with such a tumour is 40 to 50 years. In men it is diagnosed three times more frequently than in women (52).
This tumour may manifest clinically in four ways: 1) as a tumour diagnosed accidentally in a routine radiological examination, 2) in relation to the compression symptoms caused by tumour affecting organs of thoracic cavity, 3) rarely observed symptoms of endocrinopathy, 4) due to the symptomatic metastases in different organs (eg. brain, liver, lungs, bones etc.) (52). It is a potentially malignant tumour, with local invasiveness and metastatic potenncy. Thymic carcinoid is more aggressive than carcinoid of a different localisation. Duh et al. reports that the course is aggressive in 80% of cases whereas in lung carcinoid only in 26% (51). Valli states that carcinoid with mediastinal localisation always presents more malignant course and is adequate to atypical lung carcinoid (52). It is estimated that, at the time of the diagnosis, about 20-30% of patients suffers from distant metastases (54, 55). Nearly one fourth of neuroendocrine thymic tumours is functionally active and manifests with adequate hormonal syndromes such as Cushing’s syndrome. In about 8% of cases they may be a part of multiple endocrine neoplasia type I predominantly (56, 58). From the morphological point of view, thymic carcinoid is a vast pathological mass in the anterior medias tinum, often encapsulated, with the invasion of surrounding organs in advanced tumours. In two third of cases local and distant metastases are observed, mainly in the liver, bones, lymph nodes and central nervous system (58).

Significant part of thymic carcinoids (30%) at an early stage does not manifest with clinical symptoms, which is the reason for the accidental diagnosis with X-ray or computer tomography. Symptoms resulting from the compression of surrounding structures manifest in the following period. In thymic cancers, local symptoms manifest more frequently because of the aggressive course and affection of the adjoining organs. Local symptoms manifest with: shortness of breath, cough, pain in chest, superior vena cava syndrome, palsy of diaphragmatic or recurrent laryngeal nerve.

Paraneoplastic syndrome in form of: erythroid hipoplasia, aplastic anaemia, gammaglobulin deficiency are extremely rare. Cases of the coexistance of thymic carcinoid and myasthenic syndrome have not been reported in the literature (59, 60).

Treatment. Radical resection, if possible, is the best way of treatment. Radiotherapy and chemotherapy are applied in case of tumours of local invasiveness, with minimum effect. Prognosis is poor and hard to predict in these tumours. In retrospective studies by Tiffet’s et al. no correlation between the histological characteristics and prognosis was noted (61).

Neuroendocrine tumours of the anterior mediastinum include also parathyroid adenomas of such a location, which are benign in most cases. Single or multiple ectopic parathyroids are often situated in the mediastinum. It is estimated that almost 5-20% of pathologically changed parathyroids (adenomas) develop within mediastinum, 80% of which is located in the anterior mediastinum (62, 63). Accessory parathyroids are situated mainly in the space under lower edges of thyroid and below, in the anatomical area of mediastinum. They are usually located in upper lobes of thymus or are immersed in the adipous tissue below the lower edges of thyroid. In part of cases multiple adenomas develop, which seriously complicates their intrasurgical detection (64). Mediastinal location of parathyroids is the effect of their disturbed migration in the embryonic period. It mainly concerns the lower parathyroids, which migrate downward to the mediastinum. Parathyroid gland situated above the thyroid and evolving from upper thyroidis (undescended parathyroids) also occur. From the histological aspect, almost only adenomas or parathyroid hiperplasia are diagnosed, in only about 0, 5% to 2% of cases it is the primary parathyroid cancer (63, 64). In patients with primary hyperparathyroidism, an ectopic production of parathormone within pathologically changed mediastinal parathyroid is observed in 11-25% of cases (62, 64).

Symptoms: Local symptoms of mediastinal parathyroid adenoma often do not manifest because of the small size of the tumour. In clinical picture, the general symptoms resulting from the disbalance of calcium metabolism such as: osteitis fibrosa cystica, nephrolithiasis and urolithiasis, neuromuscular disorders, pathological fractures, hypercalcemic crisis are predominant. High calcium level and the exceeded standard level of parathormone (PTH) are characteristic for biochemical tests. Morphologically, the mediastinal parathyroid adenomas are usually spherical, well-encapsuled, and do not exceed 3 centimeters in diameter. They are difficult to diagnose with CT if smaller than 1 centimeter. Magnetic resonance or
PET may provide essential data in such a case. It is thought that the disbalance of calcium metabolism and elevated PTH level revealed in laboratory tests are indications for the imaging diagnostics for parathyroid adenomas. The scintigraphy with labeled radioisotope of technetium $^{99m}$Tc-MIBI is a commonly performed examination. The other modern examination is single proton emission computed tomography (SPECT), which enables the three dimensional imaging of location of enlarged thyroid. Nowadays, less common are the invasive examinations: angiography, digital subtraction angiography (low sensitivity <36%), catheterization of jugular veins, brachiocephalic, internal thoracic, vertebral with a fine catheter 5-6 French with assessment of concentration of i-PTH (sensitivity even > 86%) (62, 63, 64).

Treatment: In case of primary hyperthyroidismus caused by parathyroid adenoma or hyperplasia of an ectopic mediastinal parathyroid gland recovery is provided by surgical treatment. Resection of mediastinal parathyroid adenoma is usually performed via neck access or partial upper sternotomy. Median sternotomy may be necessary in case of tumours with high local advancement. Cases of parathyroid adenomas are increasingly often resected via videothoracoscopic access (65). Intrasurgical tube for detection of ionizing radiation may be used to localise small adenomas or diseminated ectopic patologies. In patients qualified for surgery, for 2-3 hours before the surgery a small dose of radiopharmaceutic is administered (80-100 MBq), usually $^{99m}$Tc-MIBI, which enables localisation of parathyroid gland with manual gamma camera. Results of surgical treatment are usually satisfying. Non-radical resection of tumour or missed fine, multiple parathyroid adenomas, may effect in recurrence of the disease.

Neuroendocrine tumours of posterior mediastinum

Paraganglioma and neuroblastoma, which are classified as endocrine tumours, are localised in the area of posterior mediastinum.

Paraganglioma

Paraganglioma originates from primary neural crest that later is also the origin of sympathetic ganglions situated along the spinal cord and suprarenal glands. It is a well differentiated, usually benign tumour. It affects mainly young patients and is revealed in the 2nd or the 3rd decade. It is located in posterior mediastinum, connected with bodies of the vertebrae. The tumours consists of lobes and are covered by fibrous capsula (66, 67). Clinical course is usually asymptomatic. A group of patients may show symptoms of labile hypertension and flushing as an effect of tumour production of catecholamines. In children and young patients the chronic diarrhoea syndrome is observed (68). After surgical resection of tumour the hormonal symptoms withdraw. In case of tumours of considerable size, patients complain of non-specific pain in chest and symptoms resulting from compression of major vessels and bronchial tree. Diagnostics of paraganglioma-type tumours is difficult, especially in the asymptomatic period. At that time they may be revealed on classical radiological examination, computer tomography or magnetic resonance performed for other reasons. Surgical treatment is the treatment of choice. Despite the benign character of the tumour, it may be locally aggressive because of compression on mediastinal structures and possibility to proliferate into intervertebral foramina and compression on the spinal cord.

Neuroblastoma

Neuroblastoma is a highly aggressive tumour with early local and distant metastatic potency. It affects mainly children, 95% of patients is under 5 years old. This pathology is unknown in adults. Considering the morphological aspects, it is a spheric tumour situated in the posterior mediastinum, with continuity with the vertebral spine, non-encapsuled, with foci of necrosis, haemorrhage and cystic degeneration. The tumour may cause local destructive changes of skeletal system (69, 70, 71, 72). In about two third of children with neuroblastoma the symptoms related with distant metastases are present: pain, neurological defects, Horner's syndrome, ataxia, respiratory insufficiency. Neuroblastoma, as well as ganglioneuroblastoma, may produce and secrete catecholamines and vasoactive substances to the circulatory system. It may manifest with flushing, hypertension and diarr-
Neuroendocrine tumours of the chest area

rhoea. In laboratory tests of urine the metabolites of catecholamine desintegration may be observed, which is contributory to establishing the diagnosis. Imaging of such tumours is based on computer tomography, magnetic resonance and scintigraphy enabling to reveal metastases to the skeletal system. On the X-ray imaging almost 80% of tumours show the features of calcification. The treatment depends on the stage of the disease (fig. 2) (73). In patients with 1st stage of the disease advancement the surgical treatment is advised, which gives good results. Patients with IIrd and IIIrd stage of the disease are offered a resective cytoreduction complemented with chemotherapy and adjuvant radiotherapy. In IVth stage of disease the role of treatment is controversial. Nonetheless, delayed surgical treatment after an introductory chemo and radiotherapy may improve the results of the treatment. Combination of targeted isotopic therapy using labeled radiopharmaceutics with chemotherapy may improve results of the treatment.

Pheochromocytoma

In the posterior mediastinum, because of the close contact with exo-peritoneal space, there are sporadic cases of pheochromocytoma. After confirming the diagnosis, localisation of tumour and appropriate preparation minimising the risk of hormonal crisis the patient is qualified for surgical treatment. It usually gives positive results and effects in few complications (69, 70).

Summary

Neuroendocrine tumours situated in the anatomical chest area, despite common origin and neuroendocrine activity showed in histopathological studies and specific immunohistochemical tests, are characterised by a great variety of elements such as: location of the tumour, clinical manifestation, biological progression, diagnostic difficulties, susceptibility to different methods of treatment and prognosis. Therefore, they need an individual diagnostic attitude and treatment enabled by specific and modern techniques provided by specialised centres.

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