

# V Ogólnopolska Konferencja Naukowa „Postępy w diagnostyce i leczeniu nowotworów neuroendokrynych”

27–28 kwietnia 2012, Katowice

## Streszczenia

### W1:

#### Neuroendocrine tumor G2 (NET G2) — case report

**Wanda Foltyn**

*Department of Endocrinology, Division of Pathophysiology and Endocrinology, Silesian Medical University, Katowice*

In January 2009, 60 years old woman had reported non-characteristic abdominal symptoms and weight lost. CT of the abdomen revealed enlarged liver with numerous metastases up to 60 mm, enlarged lymph nodes in the hilus of the liver and para-aortic nodes of up to 25mm. In search for the primary tumor, gastroscopy, colonoscopy, CT scanner of the chest, and USG TVS were done which did not show any pathological alterations. A thick-needle biopsy was made of the liver metastases – histopathological diagnosis: well differentiated neuroendocrine carcinoma, Ki67 13%. Somatostatin receptor scintigraphy (Tectreotyd 99mTc), showed an increased accumulation of tracer in the liver lesions and lymph nodes. In March 2009, the patient was admitted to the Oncology Department, where palliative chemotherapy was given (DPP+VP-16 — 4 courses, VP-16 — 2 courses and Paklitaxel+Doxorubicyna — 4 courses), without improvement. Since November 2009, a somatostatin analogue treatment of sustained effect has been applied. In CT of abdomen (December 2009) a pathologically enlarged pancreas tail was stated. The patient, with cachexia, was admitted to the Department of Endocrinology in Katowice in April 2010. On the basis of the clinical features and results of additional tests, a hormonal activity of the neuroendocrine carcinoma and multiple endocrine neoplasia (MEN) were excluded. However, a high concentration of chromogranin A was stated (above the limit of the standard curve after 20x dilution), increased concentration of AFP with correct functioning of the liver, and also abnormal empty-stomach glycemia and a pathological glucose overload curve. The 68Ga PET/CT test revealed numerous foci of increased receptor expression in the liver, two in the body and tail of pancreas and a few lymph nodes in the area of the pancreas head. Increased metabolism of glucose was also observed in these lesions in the 18FDG PET/CT test. On the basis of the obtained test results, the diagnosis was determined: highly differentiated neuroendocrine carcinoma with metastases to liver and lymph nodes in the hilus of the liver and the para-aortic area, most probably originating in the pancreas (NET G2 WHO 2010, Ki67-13%, IV degree of clinical advance). Diabetes type 2. Continuing the somatostatin analogue treatment of sustained effect, a radioisotope therapy was introduced. In the period from June 2010 till November 2011, six therapeutic activities 90Y DOTA TATE were given, resulting in a partial regression of the lesions in the pancreas and liver, visible in the control 68GaPET/CT (15.02.2012). At the moment, the patient is in a good general condition, with diabetes levelled with oral medicines, slight anaemia and leucopenia, correct functioning of kidneys and liver. She is on permanent somatostatin analogue treatment of sustained effect. In the case of disease progression, targeted therapy (everolimus, sunitinib) should be taken into consideration.

### W2:

#### Management of patients with NET-G2

**Alicja Hubalewska-Dydejczyk**

*Chair and Department of Endocrinology, Jagiellonian University, Medical College, Krakow*

The lecture will discuss diagnostic and therapeutic procedures in NET-G2 depending on their location and disease severity. The principles of therapeutic interventions in NET-G2 will be presented with respect to tumour localization and the result of histopathology, including surgical intervention at every stage of the disease, biotherapy, targeted radiotherapy, implementation of tyrosine kinase or mTOR inhibitors, and chemotherapy.

Neuroendocrine tumours of G2 are the largest group among all the NETs. Different imaging methods with radiological techniques such as CT/MRI, nuclear medicine procedures and endoscopies are used to find the primary focus of a disease and to stage the disease. PET/CT is an increasingly used diagnostic technique that allows assessment of the extent of the disease, qualification to the appropriate therapeutic intervention, assessment of the effectiveness of the therapy, and it can alter patient management. In many types of tumours, PET/CT is combined with other imaging examinations, especially with endoscopic techniques.

The choice of the therapy method of the NET-G2 is associated with the progression of disease. Surgery is generally proposed as the first method of treatment and in some cases it can be preceded by neoadjuvant therapy: targeted radionuclide therapy or chemotherapy. Specific pharmacological therapy and biotherapy with somatostatin analogue (exceptionally interferon) are used to control the symptoms of the disease. Palliative treatment is mainly divided into systemic therapy with PRRT, molecular therapy and chemotherapy, and local liver ablative therapy including radiofrequency ablation, laser-induced thermotherapy, selective hepatic arterial embolization, selective arterial radionuclide therapy or chemoembolization. To find the optimal form of palliative therapy, the general state of the patient, extent of the disease, positive result of scintigraphy with labeled ss analogue (SPECT/PET/CT), concomitant symptoms characteristic of each type of NET, the results of laboratory tests and response to earlier forms of therapy used, should be taken under consideration.

### W3:

#### Treatment with radiolabelled somatostatin analogues PRRT in neuroendocrine tumors — PRO

**Jolanta Kunikowska, Leszek Królicki**

*Nuclear Medicine Department Warsaw Medical University, Warsaw*

Treatment with radiolabelled somatostatin analogues is used in Poland since 2004. Currently there are no randomized trials on PRRT. Progression free survival (PFS) and overall survival (OS) for PRRT are longer than in chemotherapy and new therapies. There

are 25-36 months and 22-40 months for 90Y DOTATOC, 33 months and 46 months for 177Lu DOTATATE, 29.4 months and OS not reached for 90Y/177Lu DOTATATE; respectively. For chemotherapy (doxorubicin Streptozocyna + 5 FU) 18 months and 37 months, Temozolomide 14.0 months and 35 months. For new therapy option Everolimus PFS 11.0 months, Sunitinib PFS 11.4 months. Partial and complete remission PR/CR are observed in 8-33% patients treated with 90Y DOTATOC, 36-46% 177Lu DOTATATE, 20% 90Y/177Lu DOTATATE; in chemotherapy 39%, Everolimus 5% and 9% of sunitinib patients. Hematological toxicity grade 3 and 4 after PRRT was observed in 5% of patients, after chemotherapy in 23%. Reported in previous studies kidney damage, now is less common (1-3.5% 90Y DOTATOC, 0.5-1% 177Lu DOTATATE, 0% 90Y/177Lu DOTATATE). Increased creatinine and proteinuria occurs in 20-70% of patients treated with chemotherapy, grade 3 and 4 toxicity in 25% are revealed. In the case of Everolimus treatment increase creatinine level in 50% and sunitinib in 70% of patients is observed. Conclusions: PRRT is well tolerated by patients with improving the quality of life. Longer PFS and OS than other therapies and rare side effects are observed.

#### W4: Pancreatic neuroendocrine tumour — case report and expert discussion

**Violetta Rosiek**

*Division of Endocrinology, Department of Pathophysiology and Endocrinology, Silesian Medical University, Katowice, Poland*

A clinical case of a 45-year-old woman with metastatic pancreatic neuroendocrine neoplasms, who has had, since 2005, a lasting splenic vein thrombosis with splenomegaly and enlargement of the pancreatic tail. The first computed tomography of the abdomen, performed in May 2005, revealed a heterogeneous nodular poorly limited lesion of about 6 cm in the area of hilus lienis coming from the pancreatic tail with concomitant splenic vein thrombosis and collateral circulation. In July 2005, aspiration biopsy of the pancreas was performed under CT control, but in the cytological smear test no tumor cells were found. Three months later, due to symptomatic cholelithiasis, the patient underwent cholecystectomy with simultaneous intraoperative biopsy of the pancreatic tumor. The cytological image of the material taken from the biopsy aroused suspicion of cancer. However, the patient was still only under observation. In December 2005, a subsequent abdominal CT confirmed the pathological lesions as described above. For 3 years the patient remained in good general condition without any treatment decisions (twice diagnosed at a ward of internal diseases). In July 2009, the patient was referred for surgical treatment for the first time, during which a total resection of the spleen was performed, the tumor of the hilus lienis area was removed and aspiration biopsy of the pancreatic tail was done again. The histopathological diagnosis of the tumor was a metastatic neuroendocrine neoplasm, with a Ki67 < 1%. Next, the patient received chemotherapy (08.2009-02.2010) — 6 courses of Gemzar (Gemcitabine) with 5-FLU. The abdominal CT, after chemotherapy ended in March 2010, still showed a visible tumor on the tail of the pancreas, increased mesenteric lymph nodes, and new hypodense focuses of right liver lobe appeared. A subsequent abdominal CT in May 2010 revealed a further progression of the neoplastic lesions (segmental infiltration of the stomach, two tumors of the pancreas, a metastatic focus in the liver, enlarged lymph nodes in the abdomen). In June 2010, the patient was admitted to Department of Endocrinology in Katowice. The pathological consultation of the preparations provided by the patient confirmed the diagnosis

of pancreatic neuroendocrine neoplasm with infiltration of the greater curvature of the stomach and liver, mesenteric and periaortal lymph nodes metastases (NET G1 according to WHO, T4N1M1, Ki-67 < 1%). The evaluated concentrations of hormones and NET markers (serotonin, chromogranin A, and 5-hydroxyindoleacetic acid in two daily urine collection) were within normal limits. The receptor scintigraphy confirmed progression of the disease (metastatic neuroendocrine process), with numerous lesions of increased expression of receptors in the stomach, liver, pancreas, periaortal lymph nodes and sacrum. In August 2010, the patient began treatment with a somatostatin analogue (Somatulin Autogel 90 mg), which is administered until now. After a surgical consultation the patient was again qualified for surgery, during which the pancreatic tail with the tumor and liver tumors were excised (18/10/2010). In May 2011, receptor scintigraphy (68Ga-DOTA-TATE PET/CT) was done again, after which a radionuclide therapy was started. To date, the patient has received 4 doses of somatostatin analogues with Yttrium chloride (90Y) with good tolerance of the treatment. At the end of the radionuclide therapy we plan to do hormonal and imaging control examinations.

**Conclusion:** The patient is an example of late diagnosed neuroendocrine tumor of the pancreas at an advanced (metastatic) stage. Despite the enlarged tail of the pancreas and splenic vein thrombosis with splenomegaly since 2005 an effective attempt to explain the cause of the disease and implementation of an adequate treatment was not made.

#### W5: Results of histopathological examination and decision on further treatment in patient with neuroendocrine tumour of the stomach — case report

**Anna Sowa-Staszczak**

*Chair and Department of Endocrinology, Medical College, Jagiellonian University, Krakow*

**Introduction:** The decision on the further treatment of the patient with neuroendocrine tumour of the stomach is made on the base of the result of histopathological examination. In case of low-differentiated tumours (NET G3) decision on the surgical treatment is usually obvious. However in case of neuroendocrine tumours of intermediate degree of histopathological advancement doubts might occur.

**Case report:** 33 years old patient without symptoms underwent gastroscopy in March 2011 due to family history of stomach cancer. Two polyps of the stomach fund were excised. On histopathological examination neuroendocrine tumour was found. On immunohistochemical examination positive reaction to chromogranin and synaptophysin was revealed. Ki-67 expression was positive in 30% of the cells (NET G3). Patient did not accede for the surgery. She was then consulted in two other Centres in Poland and one Center abroad, where the histopathological diagnosis was verified. The diagnosis of neuroendocrine tumour of the stomach remained unaltered. But Ki-67 differed between Centres and ranged from 3 to 20%, what has changed the classification to NET G2 according to WHO 2010. But the last Center, where the patient was consulted, also advised surgical treatment. Patient was then reported to the Department of Surgery, where gastroscopy revealed another new neoplastic lesion in the stomach. Patient acceded for the surgery.

**Conclusions:** Above case report shows possible difficulties in the treatment of patients with neuroendocrine tumours of the stomach of intermediate degree of histopathological advancement.

## Streszczenia plakatów

### P1.

#### Diagnostic and therapeutic dilemmas in case of pancreatic neuroendocrine tumours of uncertain clinical prognosis — case report

*Anna Sowa-Staszczak, Agnieszka Stefańska,  
Maciej Kołodziej, Monika Tomaszuk,  
Alicja Hubalewska-Dydejczyk*

*Chair and Department of Endocrinology, Medical College, Jagiellonian University, Krakow*

**Introduction:** Pancreatic neuroendocrine tumours, despite development of diagnostic and therapeutic possibilities in this group of tumours, remain still a clinical challenge.

**Case report:** 30 years old woman after cholecystectomy performed in 2007. MRI performed in November 2008 due to abdominal pain revealed tumour of the pancreatic head — 35 x 42 x 32 mm. In May 2009 patient underwent excision of the pancreas. On histopathological examination neuroendocrine tumour NET G2 with Ki67 16% was found. Treatment with long acting somatostatin analogue was started. CT performed in October 2009 revealed lesion in the 7th hepatic segment — lesion was verified prior to the surgery as hemangioma. There was no pathological uptake visible in SRS performed in August and then in December 2009. The size of the lesion in the liver was stable on usg performed in February 2010. However usg examination in June 2010 showed additional three lesions in the liver. The progression of the liver changes was confirmed with CT. PET/CT Ga68-DOTA-TATE revealed increased expression of the receptors in the hepatic lesions. Patient did not accede for the surgery and was qualified to the radioisotope therapy with Y90-DOTA-TATE. PET/CT performed two months after therapy revealed two additional hepatic changes. Patient was suggested again to undergo surgery. The complete excision of the hepatic metastases was performed.

**Conclusions:** Above case report shows the necessity of rigorous follow-up of the patients with pancreatic neuroendocrine tumours of intermediate degree of histopathological advancement with uncertain clinical prognosis.

### P2.

#### The long-term complications of isotope treatment of neuroendocrine tumors

*Barbara Michalik, Tomasz Olczyk, Kornelia Hasse-Lazar,  
Beata Jurecka-Lubieniecka, Daria Handkiewicz-Junak*  
*Department of Nuclear Medicine and Endocrine Oncology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch*

**Introduction:** Although radiopeptide therapy of neuroendocrine neoplasm is an effective treatment, delayed kidney toxicity remains a major concern. The aim of our study was to evaluate frequency and intensity of late radiation kidneys' toxicity in patients treated with radiolabelled somatostatin analogues.

**Material and methods:** 81 patients (49 men, 32 women) aged 19-77 years (mean 56) treated from August 2004 to August 2010, who were observed at least 1 year after radiopeptide treatment, were included into the study. Patients were treated with somatostatin analogues labelled either with 90Y (90Y-DOTATATE) in 4 courses

every 3 months or since 2007 with 90Y-DOTATATE every 6 weeks with a lutetium boost (177Lu-DOTATATE). The cumulative activity of 90Y and 177Lu was respectively 150–370 mCi and 150–200 mCi. Only patients without nephritic contraindications to radiopeptide treatment were included. Amino acids infusion was used to decrease radiation.

**Results:** During follow-up no increase in creatinine concentration was noted in (46,92%) of patients. In 13,58% the elevated creatinine concentration did not exceed 130  $\mu\text{mol/L}$ , in 27,16% was within the range of 130–350  $\mu\text{mol/L}$ , and in 6 out of 10 patients with creatinine above 350  $\mu\text{mol/L}$  were referred to dialysis. Increase in creatinine concentration was observed about 3 (1–4,5) years after therapy.

**Conclusions:** Therapy with radiolabelled somatostatin analogues is an safety option in treatment of advanced neuroendocrine neoplasm. However, as 5–10% of treated patients develop substantial renal toxicity, further study on renal protection are necessary.

### P3.

#### Morphological changes in neuroendocrine cancers metastases after radiopeptide therapy — radiological evaluation

*Daria Handkiewicz-Junak, Józef Szczasny, M. Kaszuba,  
Kornelia Hasse-Lazar, Tomasz Olczyk, Joanna Roskosz,  
Jolanta Krajewska, Barbara Jarzab*  
*Maria Skłodowska Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch*

**Introduction:** Expression of somatostatin receptors in neuroendocrine neoplasm (NEN) allows for peptide receptor radionuclide therapy (PRRT) with somatostatin analogues. Disease remission or stabilization is observed in majority of patients, yet little is known about evolution of NEN metastases after PRRT. The aim of this retrospective study was to evaluate morphological changes of liver NEN metastases as assessed in radiological examinations.

**Material and methods:** 35 patients, treated with radiolabelled DOTATATE and followed-up for > 2 years were evaluated. 30 (86%) patients were treated with four 90Y-DOTATATE treatments repeated every 12 weeks, 5 patients were treated with four 90Y-DOTATATE and one cycle of 177LU-DOTATATE at 6 week intervals. Radiological examinations (CT or MRI) were repeated at 4-6 month intervals.

**Results:** 32 (91%) patients suffered from liver metastases, in 20 (54%) they had also extrahepatic metastases. There was a direct correlation between number of liver metastases and their diameter. After RPPT there was a decreases in: (1) tumor contrast enhancement, (2) number of solid metastases. During the follow-up 15 (43%) of patients suffered from disease progression with median PFS of 50 months. 6/15 (40%) of the patients progressed both in liver and extrahepatic sites, 5/15 (33%) progressed in liver and 4/15 (27%) patients suffered from extrahepatic progression only. 8/11 (73%) of liver progressions was due to diagnosis of new metastases.

**Conclusions:** Radiological evaluation of metastases morphology after RPPT suggest degenerative changes. Most of the disease progression after the treatment is due to the growth of new liver metastases.

**P4.****Data from the Neuroendocrine Tumors Register, Chair and Department of Endocrinology, Cracow**

*Ewelina Baczyńska<sup>1</sup>, Anna Sowa-Staszczak<sup>2</sup>, Aleksandra Gilis-Januszewska<sup>1</sup>, Małgorzata Trofimiuk-Müldner<sup>1</sup>, Agnieszka Stefańska<sup>2</sup>, Maciej Kołodziej<sup>2</sup>, Alicja Hubalewska-Dydejczyk<sup>1</sup>, Dorota Pach<sup>1</sup>*

<sup>1</sup>Chair and Department of Endocrinology, Jagiellonian University, Medical College, Krakow,

<sup>2</sup>Nuclear Medicine Unit, Chair and Department of Endocrinology, Jagiellonian University, Medical College, Krakow

**Introduction:** Gastroenteropancreatic neuroendocrine tumors (GEP-NET) are still diagnosed too rarely, often in the stage of neoplastic spread, several years after the first symptoms. Symptoms of GEP-NET are varied, creating a diagnostic problem for physicians of all specialties.

**Material and methods:** We investigated patients from the Department of Endocrinology Register, with neuroendocrine tumors diagnosed between 1987 and 2011. A retrospective analysis of data, with assessment of location, tumor type according to WHO classification (reclassification of diagnoses from WHO 2000 to WHO 2010 in preparation) and the most common symptoms of GEP-NET was done.

**Results:** The register contains 378 patients with neuroendocrine tumors. 85% of them are GEP-NET, of which 55.5% are women. The average age of GEP-NET diagnosis is 52 years  $\pm$  16. Most tumors (51%) belong to group 1. according to WHO 2000 (constituting in rectum, appendix and stomach 92%, 83% and 61% of cases, respectively). The most common location of GEP-NET is pancreas (31.5%), small intestine (17%) and stomach (16.5%), where mainly occur tumors group 2. according to WHO 2000 (small intestine-64%, pancreas-60% of cases). The most common symptoms are: chronic abdominal pain (36%), diarrhea (13%), fainting and loss of consciousness (11%). Asymptomatic course is observed in 13% of cases. Coexisting neoplasms are found in 9% of patients, among them 67% are malignant tumors.

**Conclusions:** The increasing number of GEP-NET is related probably to improved diagnostic methods. Further research is needed to select people at risk of GEP-NET occurrence and unify management in this group of patients.

**P5.****Type 3 Neuroendocrine Tumors of the Stomach**

*Aleksandra Gilis-Januszewska<sup>1</sup>, Ewelina Baczyńska<sup>1</sup>, Małgorzata Trofimiuk-Müldner<sup>1</sup>, Beata Piwonska-Solska<sup>1</sup>, Dorota Pach<sup>1</sup>, Krzysztof Krzemieniecki<sup>2</sup>, Alicja Hubalewska-Dydejczyk<sup>1</sup>*

<sup>1</sup>Chair and Department of Endocrinology, Jagiellonian University, Medical College, Krakow

<sup>2</sup>Chair and Department of Oncology, Jagiellonian University, Medical College, Krakow

**Introduction:** Type 3 gastric neuroendocrine tumors (NETV) are rare subtypes of NETV with poor prognosis, not fully understood biology and not well investigated diagnostic and therapeutic procedures. The aim of the study was to analyze tumor biology, clinical course and the outcome of differentiated treatment in patients with type 3 neuroendocrine tumors of the stomach.

**Material and methods:** A prospective follow up of 5 patients with type 3 NETV treated in our institution was undertaken

**Results:** We investigated and followed up for 11 years 5 patients with histopathologically confirmed type 3 NETV. The diagnosis and gastric resection (total 3/5, partial 2/5, palliative 1/5) was performed 3-12 month after first tumor related symptoms presentation 5/5. The solitary tumors 5/5, were from 20 to 90 mm in diameter, located in fundus 4/5 and in cardia 1/5, infiltration beyond submucosa occurred in all cases. Metastases to regional lymph nodes were present in 5/5 cases during surgery, liver and distant (peritoneum, retroperitoneal space) metastases occurred in 4/5 in 0-11 month from diagnosis/gastrectomy. Chemotherapy was given in 3/5 in 2-6 month from diagnosis/gastrectomy. 1 patient was treated with 90Y in 6 month after diagnosis. 3/5 patients died in 8-18 month from diagnosis/gastrectomy. 2/5 patients are alive in 20-38 month from diagnosis/gastrectomy, 1/5 patient is free of disease in 38 month from diagnosis/gastrectomy.

**Conclusions:** The increasing number of type 3 NETV related probably to improved diagnostic methods and their poor prognosis require more profound investigation of the tumor biology and improvement of the treatment procedures

**P6.****Atypical presentation of type 1 gastric neuroendocrine tumor should increase our awareness**

*Aleksandra Gilis-Januszewska, Ewelina Baczyńska, Małgorzata Trofimiuk-Müldner, Beata Piwonska-Solska, Dorota Pach, Alicja Hubalewska-Dydejczyk*  
Chair and Department of Endocrinology, Jagiellonian University, Medical College, Krakow

**Introduction:** Among 3 types of gastric neuroendocrine tumors (GEPNETV) type 1 is most common. In this type occur atrophic gastritis, achlorhydria and deficiency of intrinsic factor, resulting in G cell hyperplasia, hypergastrinaemia. Endoscopy reveals multiple and polypoid lesions (< 1-2 cm) in the corpus. Five-year survival in these patients is not different from survival in the selected age-group population. Type 1 GEPNETV metastasizes rare (2-5% of cases).

The aim of our study was to present atypical type 1 GEPNETV.

**Case report:** In the Department of Endocrinology we follow up 41 cases of GEPNETV, among them 30 of type 1. M.S., 33-aged male, in 2008 due to anemia and epigastric pain had gastroscopy. It revealed 3 wide-based polypoid lesions bigger than typical lesions (15-30 mm in diameter). In biopsy there was highly-differentiated neuroendocrine tumor expressing chromogranin. Ki-67 index < 1%. In addition, atrophic gastritis was found. In abdomen CT, scintigraphy with somatostatin analogues (SRS) no specific changes were found. Patient refused surgery and for 1 year was lost for follow up. In next gastroscopy in 2010 there were 3 polypoid lesions up to 30 mm in diameter, with similar biopsy to former examination. In 2011 total gastrectomy was performed. Histopathology revealed neuroendocrine cancer with metastases to local lymph nodes. In postoperative SRS no uptake of tracer was found, patient is treated with somatostatin long acting analogue.

**Conclusions:** Atypical presentation of type 1 GEPNETV should increase our awareness. If endoscopic removal is not possible partial or total gastrectomy should be considered.

**P7.**  
**Neuroendocrine tumors in children and young adolescents — analysis of own material from Institute of Oncology in Gliwice**

*Sylvia Szpak-Ulczok, Jolanta Krajewska, Daria Handkiewicz-Junak, Kornelia Hasse-Lazar, Beata Jurecka-Lubieniecka, Ewa Paliczka-Cieślak, Barbara Jarząb*  
 Department of Nuclear Medicine and Endocrine Oncology, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch

26 children and young adolescents (range 13–25) with neuroendocrine neoplasms (NENs), among them 3 with MEN1 syndrome were consulted in Institute of Oncology in Gliwice during the recent 5 years. Mostly appendix NENs were diagnosed (n = 11) and complete remission achieved after surgical treatment. Only in one girl with appendix NEN (Ki-67 5%), radically operated, lymph node and peritoneum metastases were observed. There were 5 subjects with lung carcinoid — radical surgery led to complete remission in all of them, even in one case with atypical carcinoid with lymph node metastases. Well differentiated pancreatic NENs were diagnosed in other 5 patients, among them 2 insulinomas, one VIPoma and 2 non-secreting pancreatic NENs. Insulinomas were multifocal tumors. One patient was successfully treated only with the operation, whereas in the second subject with hormonally active liver metastases, waiting for liver transplantation, glycemia was normalized thanks to long-acting somatostatin analogue therapy. In one case with ACTH secreting malignant thymus NEN with lymph node and lung metastases progressive disease was confirmed despite of 3 different chemotherapy schemes administered. Treatment with metyrapone and somatostatin analogue led to good clinical symptoms control. In 3 other patients the origin of NEN was unknown. In one of them with liver metastases complete remission was achieved after 90-Y DOTATATE therapy. However, in the second 20-year old subject with poorly differentiated NEN with lung, liver and bones metastases the disease progressed in spite of chemotherapy and radio-isotope treatment. The presented NEN cases in young subjects illustrated diversified course of the disease depending on the origin, histopathological grade and hormonal activity.

**P9.**  
**Treatment with anti-angiogenic tyrosine kinase inhibitor sunitinib for metastatic pancreatic neuroendocrine tumors of GEP-NET G2 — a case report**

*Ewa Wachuła<sup>1</sup>, Wojciech Rogowski<sup>1,3</sup>, Jarosław Ćwikła<sup>2,3</sup>*

<sup>1</sup>Department of Chemotherapy at the Ministry of Internal Affairs and Administration's Hospital and Warmińsko-Mazurskie Oncology Centre, Olsztyn

<sup>2</sup>Nuclear Medicine Laboratory at the Ministry of Internal Affairs and Administration's Central Research Hospital, Warsaw

<sup>3</sup>Faculty of Medical Sciences of the University of Warmia and Masuria, Olsztyn

**Introduction:** Pancreatic neuroendocrine tumors (PNETs) are rare and generally resistant to systemic treatment. Most of them present metastases at the time of diagnosis, which limits the survival. Thus effectiveness of therapeutic methods used in PNETs is limited and is still unsatisfactory. The use of molecularly targeted therapy sunitinib, blocking several tyrosine kinase receptors e.g: PDGFR-alpha, PDGFR-beta, VEGFR1, 2, 3, KIT and others, seems to be quite an attractive and promising therapeutic modal-

ity. We present our experience from the Oncological Centre in Olsztyn. Case report: 32-year-old female, in good performance status (WHO-0), obese, periodically presenting hypoglycemia, underwent radical resection large retroperitoneal tumor (130 mm) located in the pancreas area in 2002. Histopathological diagnosis revealed: The islet tumor of the pancreas, insuloma malignum, Chromogranin (+), Synaptophysin (+) pT3N0 (2002). Reassessment according to the current classification of 2010 showed: neuroendocrine tumor group 2 WHO (Well differentiated endocrine tumor), Ki-67 3-3.5%. In May 2005, signs as secretory symptoms like diarrhea and pain in the epigastrium appeared. The abdominal MRI showed disease progression. There were multiple metastases in the liver and local recurrence. The somatostatin receptor scintigraphy (SRS) with 99m Tc HYNIC-TOC (590 MBq) SPECT showed active uptake in the liver and in the tumor bed. Patient received 6 cycles of chemotherapy with streptozocine + 5-fluorouracil, which resulted in a partial response to treatment and pain relief. Due to persistent secretory symptoms, long-acting somatostatin analogues therapy was applied, initially lanreotide (Somatuline Autogel ® 60 mg sc), which was replaced after 3 months by octreotide (Sandostatin LAR ® 20 mg sc) because of intolerance of lanreotide. There was no signs of progression during the follow up until February 2008, when the abdominal MRI showed disease recurrence. The patient underwent "hot" analogues therapy (PRRT-peptide receptor radionuclide therapy) — Y-90 DOTATATE, resulting in CR: complete remission of local recurrence and PR: partial remission of the liver metastases, and in a clinical benefit such as resolution of the symptoms. Up to November 2011 treatment with "cold" somatostatin analogues was applied. In subsequent control visits, the abdominal MRI 22.11.2011 — revealed progression of lesions in the liver and lymph node metastases 66 mm to 18 mm in the abdominal cavity. Radiological progression was also accompanied by biochemical progression: an increase in chromogranin from 39 to 245 ug/L (10,8-47,5 ug/L) was observed. The patient presented moderate intensity of abdominal discomfort : abdominal pain CTC\* grade 1 and the appearance of diarrhea CTC grade 1. Targeted therapy with Sunitinib (Sutent ®) was started. From 12.12.2011 till 06.03.2012 patient received three cycles of treatment with sunitinib (Sutent ®) at a dose of 37.5 mg orally, every 28 days. Toxicity evaluation of treatment: After 10 days of treatment the patient started to comply of gastrointestinal complications such as: heartburn-CTC grade 2, nausea and vomiting-CTC grade 2, a strong burning sensation in the esophagus during the feeding of any substance whether liquid or constants CTC grade 2. This reaction was accompanied by patient's anxiety. Physical examination showed: dry mouth with mucositis-CTC grade 2, and epigastric tenderness during palpation. An endoscopy (gastroscopy) showed reddening of the gastric mucosa (erythematous gastropathy) and hiatal hernia. Urease test were negative. Patient was prescribed the following treatments: the proton pump inhibitors (IPP40 mg 1 x 1 tablet in the morning), H2-blocker (40 mg Famogast 1 x 1 tablet at night) and the derivative phosphatidylolepine (Essentiale forte 3 x 2 tablets). Treatment with sunitinib was stopped for 7 days. Psychological support was applied. All symptoms resolved and, patient continued treatment at full dose: Sunitinib 37.5 mg tablet daily. At the beginning of the 3rd cycle, patient reported burning and painful lesions of the thumbs of both hands (hand-foot syndrome/palmar-plantar erythrodysesthesia CTC grade 2. Doxycyclinum 100 mg for 7 days orally was prescribed, resulting in resolution of skin changes within a few days. No delay in treatment with sunitinib were ordered. The third cycle are given in full dose of sunitinib at 37.5 mg. When it was finished patient appeared again the complications such as:

asthenia — CTC grade 2, the more intensity of palmar-plantar erythrodysesthesia in the new of sites, painful lesions on the skin of hands and feet — CTC grade 2, depigmentation of the hair of the head including eyebrows and eyelashes. Sunitinib therapy was stopped until the symptoms disappear. The reduction in dose to 25 mg at the beginning on next cycle was planned.

\*Toxicity assessed according to the criteria of three versions of NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events v 3.0). Response to treatment evaluation: abdominal MRI performed after 3 cycles of treatment with sunitinib showed - stabilization (SD according to RECIST criteria). 10% decreasing of liver lesions and stabilization of nodal changes in the retroperitoneal space were obtained

\*\*RECIST — the scale of assessment of response, Response Evaluation Criteria in Solid Tumors v 1.0. Clinical profits: relief of diarrheal symptoms and abdominal pain. Conclusions: Treatment with targeted tyrosine kinase inhibitor sunitinib malate for metastatic neuroendocrine tumors of the pancreas, appears to be alternative therapeutic option with a different toxicity profile than chemotherapy and than radionuclide therapy.

#### P10.

### Typical lung carcinoid causes ACTH-Dependent Cushing's Syndrome accompanied by primary hyperparathyroidism — a case study

*Magdalena Londzin-Olesik, Wanda Foltyn, Violetta Rosiek, Anna Zemczak, Janusz Strzelczyk, Beata Kos-Kudła*

*Endocrinology Clinic, Chair of Pathophysiology and Endocrinology, Medical University of Silesia, Katowice*

The case of an 82-year-old patient diagnosed, in October 2011, with Cushing's syndrome on the basis of classic phenotypical characteristics of hyporcortisolemia accompanied by complications of recently diagnosed diabetes and unstable hypertension. Hormonal tests have confirmed the diagnosis — ACTH-Dependent Cushing's Syndrome. An MRI scan of the pituitary gland was taken to identify the cause of the syndrome, ruling out the central form of the syndrome. To identify the ectopic source of ACTH secretion, the patient was given a CT scan of the chest. A hamartoma of the lower lobe of the left lung was identified. Subsequent MRI scans in February and October 2011 did not reveal any change of the diameter of the tumour (16 mm). To confirm the ectopic source of ACTH secretion, a thin-needle biopsy of the lung tumour was performed in the patient, which allowed for diagnosing *highly differentiated neuroendocrine tumour*. Hormonal tests performed at the Endocrinology Clinic confirmed ectopic ACTH syndrome, with correct concentrations of *neuroendocrine tumour markers*. Diagnostic tests were performed to identify possible coexistence of MEN syndromes. The tests revealed coexistence of primary *hyperparathyroidism with confirmed presence of adenoma of the lower left parathyroid gland in a scintigraphic test (MIBI-Tc-99m)*.

The patient was given a  $^{18}\text{F}$ -FDG PET/CT test, which did not reveal any focuses of increased glucose metabolism, and a scintigraphic test of somostatin receptors (with the use of  $^{68}\text{Ga}$  PET/CT) did not reveal increased accumulation of radiotracer in the region of the lung tumour (no expression of the somostatin receptors).

After pharmacological preparation, the patient was referred for thoracic surgery. A histopathological examination of the lung

tumour confirmed the existence of typical lung carcinoid. After the surgery, all the symptoms of hyporcortisolemia disappeared. Currently, in therapeutic management of the patient, operative treatment of symptomatic hyperparathyroidism is being considered and the patient will be observed after radical treatment of the *neuroendocrine lung tumour*.

#### P11.

### Neuroendocrine tumor of unknown primary origin of metastatic to the liver and central nervous system

*Agnieszka Haczek-Kluczevska<sup>1</sup>, Violetta Rosiek<sup>1</sup>, Anna Zemczak<sup>1</sup>, Wanda Foltyn<sup>1</sup>, Jolanta Kunikowska<sup>2</sup>, Beata Kos-Kudła<sup>1</sup>*

<sup>1</sup>*Department of Endocrinology, Division of Pathophysiology and Endocrinology, Silesian Medical University, Katowice*

<sup>2</sup>*Department of Nuclear Medicine, Warsaw Medical University, Warsaw*

**Introduction:** The occurrence of brain metastases in neuroendocrine tumors is estimated by various authors to 1.5–5%. In the case of primary tumor in the pancreas, the risk of brain metastases is < 2%. NET primary tumor localization in the lungs is associated with higher risk of brain metastases. MR is the most sensitive imaging method for brain metastases in both single and multiple.

**Case report:** A 71-year-old patient in whom the diagnosis of neuroendocrine tumor (NET G2, Ki-67 — 15%) on the basis of core biopsy material changes in the liver of a metastatic, incidentally detected during abdominal CT. Due to the presence of focal lesion in the pancreatic corpus size 7 mm foods came to suspect that this may be the primary focus. The patient was admitted to the Endocrinology Clinic in Katowice to broaden diagnostic. Rated hormones and biogenic amines were within the reference range, showed only elevated Chromogranin A. The coexistence of MEN syndrome were excluded. As done somatostatin receptor scintigraphy (PET / CT with  $^{68}\text{Ga}$ -DOTA-TATE), describes changes in the liver hypodense showing no expression of the receptor and the presence of changes in the left temporal lobe and in cerebellar tentorium. Therefore recommended  $^{18}\text{F}$  FDG PET/CT, which revealed changes in the liver increased with intensified metabolism of  $^{18}\text{F}$  FDG and sclerotic focus in the body of L2 vertebra. The patient was referred for EUS examination, stating on the border of pancreatic body and tail hypoechoic structure - to differentiate between GEP and echodense cyst of the pancreas. MRI of the head with contrast revealed a number of metastatic lesions in the cerebellar hemispheres in the brain stem, the occipital, temporal and frontal and examination MRI aim on pituitary had only confirmed the pituitary macroadenoma. In the absence of somatostatin receptor expression and increased  $^{18}\text{F}$  FDG metabolism in metastases to the liver patient was referred for systemic chemotherapy and radiotherapy of the CNS, getting stabilization of illness and improvement in the clinical state.

**Conclusions:** NET are often recognized in the stage of appearance of metastases. In spite of rare appearing of metastatic to central nervous system in NEN, at the majority of sick persons in the IV stage of the progress of illness it is necessary to consider the MRI of the head performance, in order to plan the most effective treatment.