ONCOLOGY

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ON THE COMPLEXITIES OF INTERPRETATION OF RARE NEUROENDOCRINE TUMORS IN CHILDREN

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Amongst 305 patients with EC-cellular morbid growth of gastrointestinal tract, 21(6,8%) have been diagnosed with pancreas carcinoids.There are certain difficulties, associated with diagnostics and treatment of neuroendocrinal oncomas in this focalization. One of the clinical observations exemplifies difficulties of verification pancreas carcinoids and deficiencies of medical assistance arrangements, even when conducted by specialised medical services. It is demonstrated that laboratory equipment-aided examination methods in the pancreas carcinoids diagnostics are applied in a format of general examination concepts, same as used for abdominal cavity illnesses. Pancreas carcinoid post-operational therapy selection is made without taking into account specificity of clinical presentations of illness, relevant morphological research data or EC-cellular morbid growth dynamics prognosis. By use of data, obtained from domestic and international publications sources, possible ways of improvement of medical assistance quality in cases of pancreas carcinoids are being given consideration in regards with both the organisational and technical aspects (of this problem).

Keywords: carcinoids, pancreas

Среди 305 больных с Ec-клеточными новообразованиями желудочно-кишечного тракта (ЖКТ) карциноиды (Крц) поджелудочной железы (ПЖ) выявлены у 21(6,8%) пациента. Диагностика и лечение нейроэндокринных опухолей (НЭО) данной локализации представляет определенные трудности. На примере одного из клинических наблюдений продемонстрированы трудности верификации Крц ПЖ, несовершенство организации мероприятий при оказании медицинской помощи даже в условиях специализированных учреждений. Показано, что лабораторно-инструментальные методы исследования при диагностике Крц ПЖ применяются в формате самых общих принципов обследования пациентов с заболеваниями органов брюшной полости. Выбор средств послеоперационной терапии при карциноидах ПЖ осуществляется без учета специфики клинических проявлений, данных специальных морфологических исследований и прогноза течения Ec-клеточных новообразований. С учетом полученных данных и сведений отечественных и зарубежных источников литературы обсуждены возможные пути (организационные и технологические) улучшения качества оказания медицинской помощи при Крц ПЖ.

Ключевые слова: карциноиды, поджелудочная железа

Introduction

Finding answers to questions related to medical care for patients with neuroendocrine disorders, continues to be one of the urgent tasks of surgical endocrinology. Among the neuroendocrine diseases of the gastrointestinal (GI) tract carcinoid found in 55% of cases were detected in 4,2 cases per 100 000 thousand of the population [4,6]. In the majority of cases, EC-cell tumors of the digestive tract are localized in a thin (25%), direct (14%) of the intestines, as well as in the appendix (12%) [9]. In the structure of serotonin-producing carcinoid tumors of the pancreas (Krc Ps) is less than 1% of cases [3]. Diagnosis of pancreatic RRC presents special difficulties. The sources of foreign literature from 1966 to 1995, presents the total 29 cases of serotonin-producing tumors of the pancreas, and in the world, according to statistics published information on 150 observations of this type of tumor [1-3]. Despite the development and implementation in practice of modern special techniques for verification Krc Ps remain certain problems [7]. First of all, this is due to the lack of specific clinical manifestations of so-called «carcinoid» syndrome, lack of awareness of physicians about it, the rarity of the use and interpretation of ambiguous data of laboratory and instrumental methods of examination of patients with carcinoid tumors [4,5,9,10].

Verification of neuroendocrine tumors (NET), paired with the need to perform surgery [8]. However, the final diagnosis of pancreatic Krc, 76% of cases already detected signs of metastasis. In this regard, the 5-year survival rate of patients with pancreatic KRC as a whole is not more than 34% [4], which is slightly higher than for adenocarcinoma of the pancreas, where the rate of 5-year survival rate is less than 5%. Conducting a specific pathogenetic treatment slightly increases the time duration of life of patients with inoperable pancreatic RRC, but does not prevent cases of deaths [10].

In the algorithm, providing medical care to patients with pancreatic Krc one of the key elements is to perform morphological studies using immunohistochemical techniques [1]. However, prostate biopsy prior to surgery now, even when using advanced minimally invasive technology, is not always possible.

A small number of publications devoted to cases of Krc Ps induces a focused data analysis on the causes of difficult verification of this type of NET and the results of treating patients with this pathology.

Materials and methods

Analyzed data on 305 patients with serotonin-producing tumors of the digestive tract, to be screened and treated in the period from 1954 to 2010. in a number of health care facilities (HCF) in St. Petersburg. Among them, Krc pancreas were found in 21 cases. The results of the examination and treatment patients were assessed clinically, both directly and in the late period of observation for patients. On the example of one of the clinical observations analyzed the difficulties of verification cases Krc Ps and medical care to such patients, even in specialized medical institutions.

Results

Among observed patients with serotonin-producing tumors of the gastrointestinal tract cases of carcinoid tumors of the pancreas was 6.8%. A small number of clinical observations Krc Ps requires detailed evaluation of each such case to improve the quality of medical care. As an example of the complexity of interpreting clinical data and results of special investigations for verification RRC RV, as well as difficulties in choosing the optimal treatment strategy of patients with this disease, we present the following clinical observation.

Patient G., a resident of St. Petersburg, from 8 years old (1993) observed a neurologist due to episodes of dizziness and headaches in the morning and repeated syncope. After the echo of electroencephalography (EEG, Echo) revealed signs of intracranial hypertension. Was under observation and was treated with a diagnosis of «Vegetative dystonia with a predominance of vago insular system. Syncope (orthostatic collapse)». Within 5 years of patient care provided to a physician clinic in the community.

With 13 years of age the patient began to bother recurrent abdominal pain (without clear localization), frequent loose stools that pediatricians who observed this patient, was associated with gastroduodenitis, reflux esophagitis, asthenic-neurotic syndrome. By ultrasound (USG) abdomen revealed pancreatic tumor size 3×3 cm. At the same age the patient for urgent indications was admitted in one of the children's city hospital in St. Petersburg with suspected acute appendicitis. In a survey of surgical pathology of abdominal organs was not identified. However, ultrasound abdomen confirmed the presence there neoplasms with clear margins in the tail of the pancreas, liver echogenicity above. Suspected pancreatic insulinoma. When computed tomography (CT) study of abdominal organs, including pancreas, signs of volume growths were not observed. Identified structural changes in the pancreas in the form of increasing the density in the tail, smoothing body contours. To clarify the nature of structural changes in the pancreas and exclusion of neuroendocrine tumors (insuloma) the magnetic resonance imaging (MRI) and angiography. It was found that in projection body of pancreas located thin-walled circular formation with a diameter of 35 mm associated with pancreatic duct (Fig.1). The hypothesis was that the patient has pancreatic body cyst. Angiography revealed that the blood supply to the normal pancreas, prostate flat contours. In the area of the gate in the spleen parenchymal phase with angiography, defined circular avascular neoplasm with clear margins. Based on the results of the research of patients exposed to the diagnosis of pancreatic cyst.

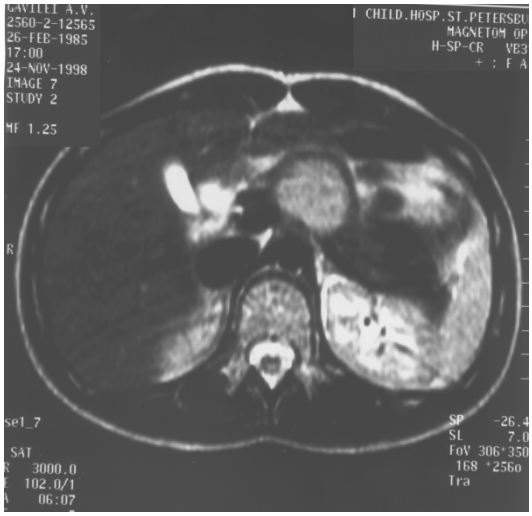

Figure 1. MRI patient G. (1998). Neoplasm of the pancreas

Given the mixed results of instrumental studies, no violation of extra-and endocrine secretory function of the pancreas, performing surgery deemed inappropriate. A course of treatment Roncoleukin. Continued dynamic observation pediatrician. The patient was repeatedly hospitalized for a stationary surveys in specialized children's hospitals of St. Petersburg, where the conduct of laboratory and instrumental methods stated that the progression of the pancreas is not observed (Fig.2).

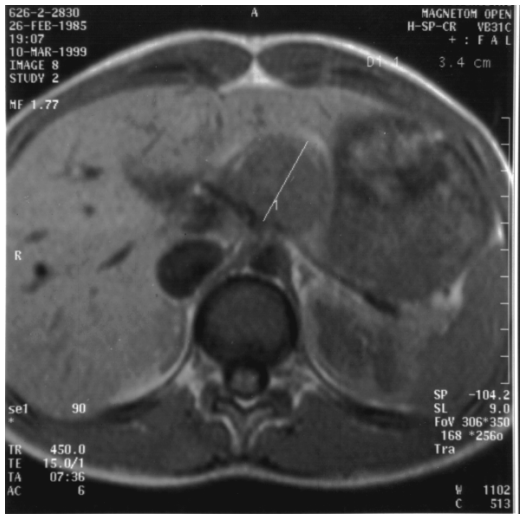

Figure 2. MRI patient G. (1999). Neoplasm of the pancreas (control study)

This patient was administered drugs improving cerebral blood flow (nootropil, piracetam, pikamilon). However, the patient continued to periodically harass nausea after eating fried foods, seizures consciousness disorders with palpitation. In connection with these disorders have repeatedly in the 15-year age of the patients examined by neurologists, and she carried out courses of conservative treatment. On the background of this therapy for several years, the loss of consciousness is not mentioned, however, remained periodic headaches and dizziness. With reference ultrasound Abdominal growths of the pancreas was not detected. Targeted dynamic observation of the patient ceased.

In 17 years of age of the patients examined by an endocrinologist. Given episodes of palpitations, headaches and fainting prevent pathology of thyroid gland (TG), pituitary and central nervous system (epilepsy). To the differential diagnosis of these diseases the patient performed the EEG, ultrasound of thyroid gland, radioimmunoassay blood test to measure levels of thyroid hormones of the thyroid gland, X-ray examination of sella. During the EEG revealed violations of brain activity with reduced functional status of the cortex in the frontal lobes. Focal and paroxysmal changes not observed. A thyroid ultrasound, diagnosed with a cyst in her left lobe. When control CT and MRI of the pancreas is ascertained the presence of a tumor (cyst? adenoma?) Sizes up to 5,3 cm. Given the lack of infiltrative growth of bulk process in the pancreas within a few years of observation (over 2 years new growth increased by 2,3 cm) suggested that the patient has a benign tumor of the pancreas without evidence of malignancy and hormone production. In order to exclude organic hyperinsulinism specifically assessed the blood glucose level. The level of sugar amounted to 3,8-6,4 mg/dL. Taking into account the patient's age (17 years), as well as the ambiguous interpretation of the data obtained by different specialists, considered appropriate dynamic observation surgeon and oncologist. The patient carried the conservative measures regarding the presence of tumor of the body with pancreatic cystic component, with no hormonal activity. Chronic gastroduodenitis. Syndrome vascular dystonia of mixed origin. Irregular menstruation (periods of 12,5 years, irregular to 16,5 years). Syncope (orthostatic).

Within two years of follow-up of the patient (from 17 to 19 years) clinically deteriorating state of health were noted. According to the reference MRI and CT studies have established that the available tumor in the body of the pancreas remains practically same size (5,4×4,2 cm) (Fig.3).

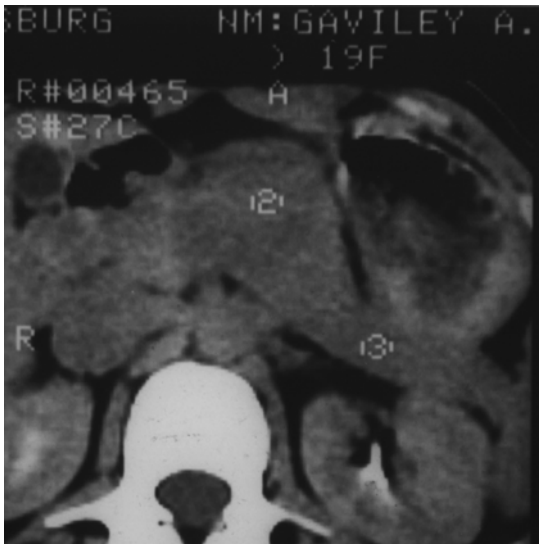

Figure 3. MRI prostate patient G.: pancreatic neoplasm dimensions 5,4×4,2 cm (2004)

In control studies the content of pituitary hormones and thyroid, as well as ultrasound of thyroid pathology was not revealed. Indicators of thyroid-stimulating hormone level of antibodies to thyroid-stimulating hormone, T4, prolactin radioimmunoassay during the blood tests were within normal limits. A survey of patient data for the violation of the endocrine organs and malignant neoplasms of the pancreas nature was not revealed. From surgery for pancreatic tumor decided to abstain.

Patient examinations were carried out by specialists every 6 months.

In 21 years of age the patient's condition worsened. It began to bother intense abdominal pain, frequent episodes of dizziness, there were moments of consciousness disorders. At the age of 22 years, the patient consult a specialized clinic in Moscow. Confirmed the diagnosis of neoplasms of the pancreas (Fig.4). Proposed operation. Performed subtotal resection of pancreatic tumors in her size 10×12×10 cm, located in the body and tail of the pancreas. The histological study of the drug (10.12.2007) — carcinoid of the pancreas. Diagnosis is confirmed by results of morphological (immunohistochemical) study. According to histological structure and phenotype of tumor cells was a cystic solid-pseudo-papillar tumor of the pancreas with uncertain malignant potential.

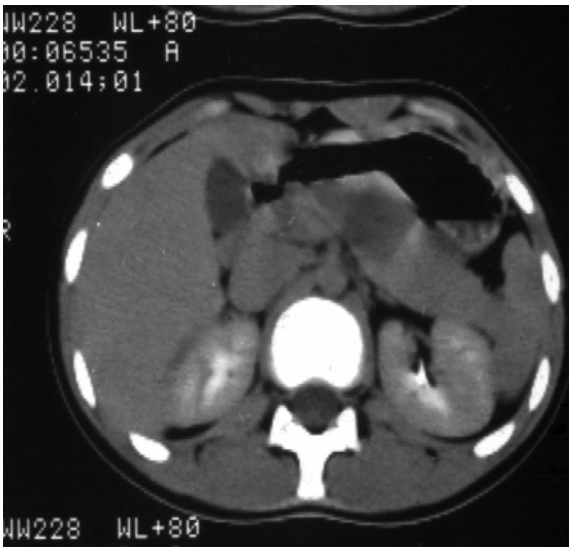

Figure 4. MRI prostate patient G.: neoplasm of the pancreas size 10×12 cm (2007)

Chemotherapy was not performed. Keeping a diet and nutrition, patients had an endocrinologist with regular monitoring of blood levels of hormones.

2 months after the operation, with intense abdominal pain, according to emergency indications patient hospitalized in a hospital in St. Petersburg. According to the ultrasound and CT in the abdomen revealed fluid collection in the omental pouch with thick irregular walls and seizures. At the insistence of the patient's continued treatment in a hospital in Moscow, where she previously performed surgery. The examination diagnosed with pancreatic cyst. Holds its drainage. Postoperatively, pancreatic fistula was formed (Fig.5), which was eliminated by using antisecretory therapy.

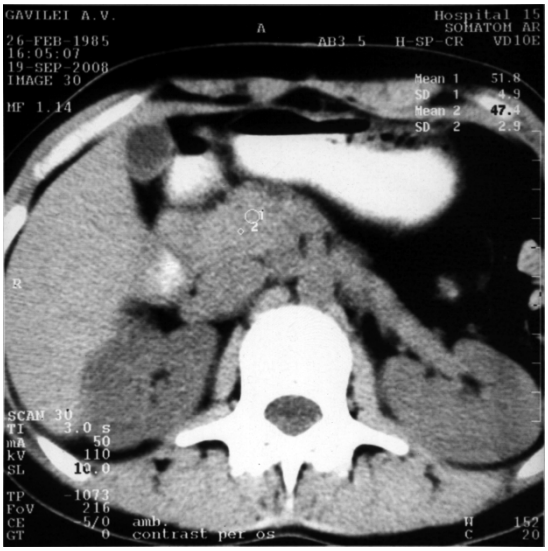

Figure 5. MRI of the pancreas patient G. Pancreas after surgery (2007)

3 months after surgery the patient is showing signs of excretory pancreatic insufficiency, in connection with which the patient received enzyme replacement therapy drugs, observed the diet, was long on a diet, there was a gastroenterologist and an endocrinologist, who evaluated the feasibility and effectiveness of monitoring blood glucose levels. Clinical signs of diabetes were noted.

Later, during the year, signs of secretory insufficiency of the pancreas in the patient increased. He was troubled by recurrent pain and swelling in the abdomen, frequent diarrhea. From the proposed hospital and survey (to address the issues of choice of modes of reception of enzyme preparations and their doses) the patient refused. Within 6 months of medical care are not addressed.

One year after surgery due to the need for regular re-examination of the line medical and social assessment (ITU) inspected the district physician. Symptoms of exocrine pancreatic insufficiency persisted. An appointment Creon to 1 (0,15 g) capsule 3 times a day. After passing through the ITU recognized invalid of the first group.

In 2009, medical care is not addressed. However, in March 2009 (1,5 years after surgery) inspected a neurologist at the episodes of vertigo with loss of consciousness. Identifying patient symptoms that resemble manifestations of the disease before surgery, probably indicates that maintaining a patient neuroendocrine pathology, etiology of which is not completely clear.

Discussion

Neuroendocrine tumors of the pancreas — a relatively rare pathology. Problems caused by the difficulty of interpreting the data, as well as difficulties in the selection of treatment of patients with pancreatic Krc generalists accessed by the patient, are understandable. Necessary experience in treating patients with this pathology have mainly specialists a few branches of surgical endocrinology. Not surprising therefore, the fact unreasonably prolonged examination patients with carcinoid of the pancreas.

On the example presented by clinical observation, it can be assumed, and a number of shortcomings in the organization providing patient care. Defect tactics can be considered as fact observing the patient for many years about the undoubted neoplasms of the pancreas, with its apparent increase in size (from 5 to 12 cm). During the follow health workers not been taken active steps to establish the nature and character of the tumor and not made an attempt to eliminate the pathological process in the pancreas. In health care the patient is seen not following the diagnostic algorithm pancreatic neuroendocrine tumors. In particular, the patient is not performed stress tests to assess the status of carbohydrate metabolism, radioimmunoassay studies of serotonin, insulin, pro-insulin, C-peptide, gastrin. Not performed selective angiography with an investigation of these hormones on the background of stimulation of calcium gluconate. Just as no attempt was made to scintigraphy, positron emission tomography — techniques that are required in the algorithm verification of neuroendocrine neoplasms of the pancreas. Against this background, again, no measures were taken to verify the final diagnosis of the pathological process. Participants in the diagnostic and treatment process were not initially considered particularly clinical carcinoid of the pancreas, characteristic of the pathology of the EU-cells -namely, the presence of recurrent abdominal pain, accompanied by relief chair. At the same time, the manifestations of hypoglycemia in the form of repeated (up to 15 times a day), fainting against hunger or due to carcinoid crises give rise to a unique interpretation of the nature of the disease, experts have been difficult to exclude the suspicion of organic hyperinsulinism.

Delay in surgical treatment of a patient whose data are analyzed in this publication, in the early stages of pancreatic carcinoid led to the progressive growth of tumors, progressive pathological effects on the body of biologically active substances (in particular — serotonin). Underestimating the resources of the regional health system and lack of information about the possibilities of medical institutions of St. Petersburg for treatment of of patients with similar pathology pancreas caused by the fact that the patient was forced to seek help own to a medical facility other city.

It is obvious that the earlier performance of surgery the patient G., in identifying the growth formation of the pancreas, could be accompanied by less traumatic in terms of operation — resection of the distal pancreas, which in modern conditions can also be performed laparoscopically. Under this option, surgical intervention could minimize the possibility of postoperative complications after resection of the pancreas, and notes in such cases, the violations of its exo- and endocrine functions.

Analysis of the data suggests that these constant medical check-up with the conduct of modern special studies were not given good reason to doubt the experts uniquely benign growths verified. Theoretically, the question of surgical intervention could be delivered already in the first months of monitoring the patient. However, it is obvious that the implementation of a major operation the patient in childhood, of course, would involve a high degree of development of dangerous complications. In particular, such an operation in a child could lead to severe diabetes with an unpredictable prognosis.

From the materials submitted by the observation that the issue of timeliness of diagnosis and treatment of patients pancreas Krc are controversial and still largely remained unanswered.

In general, according to leading experts, the quality of care a patient G., can not be considered adequately primarily due to delays in determining the indications for surgical treatment of the patient, in which an increase in neoplasms of pancreas in an amount not in doubt. When examining the quality of care in this case is obvious overspending of health resources. Repeated examinations of professional advice and direction of the patient to be examined in different medical institutions have led to the fact that for a patient no one has made a final decision, referring to each other's opinions and the incompleteness of the survey. Surgical treatment was performed late in the hospital another city.

Conclusion

The fate of of patients with pancreas neuroendocrine pathology depends on competent and consistent actions of professionals involved in clinical processes.

A detailed analysis of examination and treatment of patients in each clinical observation, we can promptly detect a carcinoid tumor of the pancreas and thus reduce the costs of treating this complex and controversial category of patients. Therapeutic and diagnostic measures are required to conduct direct treating physicians. However, control over the quality of care must exercise, and other specialists, including health and organizers who are responsible for monitoring the quality of care in hospitals. Proper control over the observance of the algorithm of care for patients with neuroendocrine tumors of pancreas can improve outcomes in patients with this pathology.

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