Діагностика та хірургічне лікування нейроендокринної інсулінпродукуючої пухлини підшлункової залози із застосуванням генетичного дослідження

О. І. Литвин, Н. С. Джаран, С. О. Мотельчук, А. В. Малик

Національний інститут хірургії та трансплантології імені О. О. Шалімова НАМН України, м. Київ

Diagnosis and surgical treatment of neuroendocrine insulin-producing tumor of the pancreas using genetic testing

O. I. Lytvyn, N. S. Dzharan, C. O. Motelchuk, A. V. Malyk

Shalimov National Institute of Surgery and Transplantology, Kyiv

Neuroendocrine tumors (NET) occur with a frequency of up to 4% among all pancreatic tumors (pancreas). NET pancreas are divided into functioning (hormonally active) and non-functioning (hormonally inadequate). Most NETs are "inactive" but have malignant potential. Among the "active" NET most often occurs insulin-producing tumor - insulinoma. The clinical picture of NET is usually "blurred", the symptoms appear in the later stages, when the size of the tumor is too large and there are metastases to nearby organs and lymph nodes. The molecular pathogenesis of NET remains unknown. In recent decades, the random diagnosis of tumors has increased significantly due to the widespread use of advanced imaging techniques. Accurate diagnosis requires endocrine examination, imaging, histological data, and a detailed genetic history. A multidisciplinary approach to treatment, including surgical removal, locoregional and systemic therapy, is a popular and effective method. Here is a clinical observation.

Patient G., born in 1983, applied to the Shalimov National Institute of Surgery and Transplantology for medical help with severe symptoms of hyperinsulinism and hypoglycemia,

which is characteristic of NET (insulinoma). Insulinoma was diagnosed in accordance with current clinical guidelines and histopathologically confirmed. Previously, the diagnosis was established using the following six clear criteria: fixed blood glucose level ≤ 2.2 mmol / l; concomitant insulin levels ≥ 66 μ O / l (≥ 36 mmol / l); peptide levels ≥ 200 mmol / l; proinsulin levels ≥ 5 mmol; levels of β -hydroxybutyrate, 7 2.7 mmol / l; no sulfonylureas (metabolites) in plasma and / or urine. The patient had a burdened hereditary history, the third cousin had previously been diagnosed with insulinoma pancreas, surgical treatment was performed, the diagnosis was histologically confirmed. The genetic test revealed the MAFA gene, the Insulimatos and diabetes mellitus phenotype, in which affected individuals in the family have either hyperinsulinemic hypoglycemia secondary to NET pancreas or a non-insulin-dependent form of diabetes.

Positron emission tomography / computed tomography (PET / CT) of the abdominal cavity with intravenous contrast (Fig. 1) and magnetic resonance imaging (MRI) of the abdominal cavity were performed to confirm the presence of the tumor and determine its location. An ASVS test for the diagnosis of insulin-producing tumor pancreas was also performed in the preoperative period, according to which (Fig. 2) the localization of the tumor was determined, which in turn allowed to find it quickly and efficiently during surgery. According to research, insulin-producing tumor was localized in the head of the pancreas.

The patient underwent surgical treatment in volume - enucleation of NET (insulinoma) of the pancreas head (Fig. 3). During the operation, the material was sent for histological examination, which confirmed the NET pancreas. On the 1st postoperative day, biochemical examination of drainage secretions did not reveal pancreas amylase, which is associated with the use of a synthetic analogue of somatostatin - octreotide. Biochemical study on the 5th day revealed a small amount of the enzyme pancreas. On the 10th day, the patient was discharged from the hospital without hypoglycemia, at the time of discharge, the average glucose level was 5.5 mmol / liter. Final histopathological examina-

Fig. 1.
PET/CT. The formation is visualized in the software head.

Fig. 2.
Changes in insulin levels according to the ASVS test in a patient with insulin-producing tumor located in the head of the pancreas, as evidenced by an increase in insulin levels after stimulation of calcium by gluconate of the superior mesenteric artery (SMA) and gastric-duodenal artery (GDA); SA - splenic artery; OHA - own hepatic artery.

tion: neuroendocrine microadenoma of the pancreas (size 0.3×0.2 cm). In the surrounding pancreas tissue, there are signs of disorganization of the islets of Langerhans, as well as microfoci of neuroendocrine hyperplasia up to 100 µm, which is associated with familial insulinomatosis with a mutation in the MAFA p.Ser64Phe gene.

NET pancreas are rare malignancies characterized by slow growth and a tendency to metastasize. The heterogeneity of NET is striking: their course can be characterized by debilitating hormonal syndromes, diffuse metastases in the liver or be asymptomatic when tumors are detected by chance. CT of the abdominal cavity has a sensitivity to determine the location of tumors 73 - 96%, subject to certain rules of the procedure, such as performing sections of 1.25 mm and multiphase imaging. MRI should be used to determine the location of the tumor. NET pancreas demonstrate low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. As with CT, the size directly depends on the sensitivity. The overall sensitivity of MRI

Fig. 3.
Removed neuroendocrine insulin-producing tumor (insulinoma) of the pancreas.

to detect NET is 80 - 90% of NET pancreas are non-functional, stable in size. Tumors smaller than 2 cm should be observed, those that do not meet these criteria require resection. Standard resections include pancreatoduodenectomy for tumors of the head and central or distal pancreatotomy for tumors of the body and tail pancreas. Enucleation is an option for certain tumors smaller than 2 cm that do not connect to the pancreatic duct. In addition to routine screening methods in the event of suspected NET, it is also important to conduct genetic testing in relatives and to examine and treat as needed in the early stages of tumor development.

Funding. No source of funding has been received for this work.

Authors' contribution. All authors made the same contribution to this article.

Competing interests. The authors have no conflict of interest.

Consent for publication. All authors approved the paper to be published.

Received: 14.11.2020