NEW IN THE CLASSIFICATION OF PANCREATIC EPITHELIAL TUMORS (WHO, 2019, 5TH EDITION)

Grinberg V.B., Enin E.A.
«A.N. Syzganov National Scientific Center for Surgery» JSC, Almaty, Kazakhstan

Abstract

Most of the classification of pancreatic epithelial tumors in the 5th edition remains unchanged from the previous edition. In the new classification, precancerous lesions are classified according to two levels of dysplasia. Intraductal papillary tumors and intraductal papillary tumors associated with invasive carcinoma are separated from the other subtypes. Some changes have occurred in the TNM classification.

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Grinberg V.B.
orcid.org/0000-0002-6827-3721
Enin E.A.
orcid.org/0000-0001-9450-0599

Corresponding author.
Grinberg V.B. - *pathologist, pathologist department of JSC "A.N. Syzganov National Scientific Center of Surgery», Almaty, Kazakhstan*
E-mail: grin_vlad@mail.ru

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Ұйқы безінің эпителий ісіктерінің жіктелуіндегі жаңа өзгерістер (ДДҰ, 2019, 5-ші басылым)

Гринберг В.Б., Енин Е.А.
«А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ,
Алматы қ., Қазақстан

Аңдатпа

5-ші басылымдағы ұйқы безінің эпителий ісіктерінің жіктелуінің көп бөлігі алдыңғы басылыммен салыстырғанда өзгеріссіз қалды. Жаңа классификацияда ісік алды зақымданулар дисплазияның екі деңгейіне бөлінеді. Инвазиялық карцинома мен байланысты интрадуктальды онкоцитарлық папиллярлық ісіктер және интрадуктальды онкоцитарлық папиллярлық ісіктер басқа кіші түрлерден ерекшеленеді.TNM классификациясында кейбір өзгерістер болды.

Хат алысатын автор.
Гринберг В.Б. *– м.ғ.к., А.Н. Сызғанов атындағы Ұлттық ғылыми хирургия орталығы» АҚ, патологанатомиялық бөлімі, патологоанатом, Алматы қ., Қазақстан*
E-mail: grin_vlad@mail.ru

Түйінсөздер: *жіктелуі, эпителий ісіктері, ұйқы безі*

Новое в классификации эпителиальных опухолей поджелудочной железы (ВОЗ, 2019, 5-е издание)

Гринберг В.Б., Енин Е.А.
АО «Национальный научный центр хирургии им. А.Н. Сызганова»,
г. Алматы, Казахстан

Аннотация

Большая часть классификации эпителиальных опухолей поджелудочной железы в 5-м издании остаётся неизменной по сравнению с предыдущим изданием. В новой классификации предраковые поражения, классифицируются по двум уровням дисплазии. Внутрипротоковые онкоцитарные папиллярные опухоли и внутрипротоковые онкоцитарные папиллярные опухоли, ассоциированная с инвазивной карциномой отделены от других подтипов. Некоторые изменения произошли в классификации TNM.

Автор для корреспонденции.
Гринберг В.Б. *– врач-патологоанатом, патологоанатомического отделения, АО «Национальный научный центр хирургии им. А.Н. Сызганова», г. Алматы, Казахстан*
E-mail: grin_vlad@mail.ru

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Introduction

Since the release of the 4th edition of the WHO classification of digestive tumors in 2010, there have been important developments in the understanding of their etiology and pathogenesis, taking into account their molecular phenotype and histological characteristics. In April 2019, the International Agency for Research on Cancer (IARC) working group on digestive system tumors met in Lyon. As a result, the classification of tumors was revised and published in 2019 as part of the WHO Classification of Tumors series, 5th edition [1].

Most of the classification of pancreatic neoplasms in the 5th edition remains unchanged compared to the previous edition (Table 1). The classification includes epithelial tumors, with their division into benign tumors and precancerous lesions, and, malignant tumors. Besides, the whole spectrum of pancreatic neuroendocrine neoplasms, previously presented in WHO classification of endocrine tumors, is included in this classification. Mesenchymal tumors and lymphomas are presented as separate chapters. Another feature of the new classification is the presence of ICD-11 classification codes and a separate chapter devoted to genetic tumor syndromes of the gastrointestinal tract [1, 2, 3].

Table 1.
New classification of epithelial tumors of the pancreas (5th edition)

ICD-O code	Name
Benign epithelial tumours and precursors	
8441/0	Serous cystadenoma NOS** subgroup: Macrocystic (oligocystic) serous cystadenoma Solid serous adenoma Von Hippel-Lindau syndrome-associated serous cystic neoplasm Mixed serous-neuroendocrine neoplasm
8148/0	Glandular intraepithelial neoplasia, low grade
8148/2	Glandular intraepithelial neoplasia, high grade
8453/0	Intraductal papillary mucinous neoplasm with low-grade dysplasia
8453/2	Intraductal papillary mucinous neoplasm with high-grade dysplasia
8453/3	Intraductal papillary mucinous neoplasm with associated invasive carcinoma
8455/2*	Intraductal oncocytic papillary neoplasm NOS**
8455/3*	Intraductal oncocytic papillary neoplasm with associated invasive carcinoma
8503/2	Intraductal tubulopapillary neoplasm
8503/3	Intraductal papillary neoplasm with associated invasive carcinoma
8470/0	Mucinous cystic neoplasm with low-grade dysplasia
8470/2	Mucinous cystic neoplasm with high-grade dysplasia
8470/3	Mucinous cystic neoplasm with associated invasive carcinoma
Malignant epithelial tumours	
8441/3	Serous cystadenocarcinoma NOS**
8500/3	Duct adenocarcinoma NOS**
8480/3	Colloid carcinoma (Mucinous non-cystic cancer)
8490/3	Poorly cohesive carcinoma
8490/3	Signet-ring cell carcinoma
8510/3	Medullary carcinoma NOS**
8560/3	Adenosquamous carcinoma
8576/3	Hepatoid carcinoma
8014/3	Large cell carcinoma with rhabdoid phenotype
8020/3	Carcinoma, undifferentiated (anaplastic carcinoma) NOS**
8035/3	Undifferentiated carcinoma with osteoclast-like giant cells
8550/3	Acinar cell carcinoma
8551/3	Acinar cell cystadenocarcinoma
8154/3	Mixed acinar-neuroendocrine carcinoma
8154/3	Mixed acinar-endocrine-ductal carcinoma
8552/3	Mixed acinar-ductal carcinoma
8971/3	Pancreatoblastoma
8452/3	Solid pseudopapillary neoplasm of the pancreas subgroup: Solid pseudopapillary neoplasm with high-grade carcinoma

Note:
** - new codes for ICD-O as approved by the IARC/WHO Committee at the April 2019 meeting.;*
***NOS – not otherwise specified.*

The new classification classifies precancerous lesions, including pancreatic intraepithelial neoplasia, intraductal papillary mucinous tumors, and mucinous cystic tumors, into two levels of dysplasia (low and high grade) based on the highest degree of dysplasia detected, rather than the three-level system (low or medium and high grade) used in the 4th edition of the WHO classification. This change in classification was recommended at the 2014 Baltimore Consensus Meeting [4].

Intraductal oncocytic papillary tumors and intraductal oncocytic papillary tumors associated with invasive carcinoma are now separated from other subtypes of intraductal papillary mucinous neoplasms based on their distinctive genomic and morphological features. These tumors were first described in 1996 by Adsay et al, and the previous classification referred to them as the oncocytic type of intraductal papillary mucinous neoplasm. Their incidence is 4.5% of intraductal pancreatic neoplasms; they also occur in the bile ducts. 70% occur in the head of the pancreas, and 10% involve the entire gland. Macroscopically, these tumors are characterized as cystic masses with loose papillary or exophytic nodules, often within the main pancreatic duct, average size 4.5 cm. Microscopic structure shows multicameral or unicameral cysts containing complex and branched papillae with delicate fibrovascular stroma, papillae lined by several layers of tumor cells with bulk granular oncocytic cytoplasm and prominent large eccentric nuclei. Cribriform structures and intraluminal mucin formation are not rare. Papillae may fuse and form a continuous growth. Invasive carcinoma occurs in approximately 30% of cases. True invasion manifests differently: small infiltrative tubules, mucinous and dense nests of oncocytic cells. Abrupt transition from normal epithelium to oncocytic epithelium in the same duct contributes to pseudoinvasion [5].

The previously existing acinar cell cystadenoma (8551/0), has recently been recognized as a non-tumor pathology and given the name “acinar-cystic transformation of the pancreas” [6].

Some changes have occurred in the TNM classification.

The T1 category is divided into subcategories T1a, T1b, and T1c based on tumor size.

Categories T2 and T3 are based on the size of the invasive component of the tumors. Spread of neoplasms outside the pancreas is no longer considered.

Category T4 corresponds to arterial involvement of the tumor. The concept of “resectability” has been removed from the definition of this category.

TX - No primary tumor can be evaluated;

T0 - No signs of a primary tumor;

Tis - Cancer in situ. This category includes high grade pancreatic intraepithelial neoplasia (PanIN-3), intraductal papillary mucinous tumor with severe dysplasia, intraductal tubulopapillary tumor with severe dysplasia, mucinous cystic tumor with severe dysplasia;

T1 - Tumors not exceeding 2 cm in the greatest dimension;

T1a - Tumors up to 0.5 cm in greatest dimension;

T1b - Tumors greater than 0.5 cm and not greater than 1 cm in greatest dimension;

T1c - Tumors 1-2 cm in the greatest dimension;

T2 - Tumors greater than 2 cm and not greater than 4 cm in greatest dimension;

T3 - Tumors more than 4 cm in greatest dimension;

T4 - Tumors involving the cranial trunk, superior mesenteric artery, and/or common hepatic artery, regardless of size.

The pancreas is braided by a dense lymphatic network, so the lymph nodes in the parapancreatic tissues must be examined for accurate staging. When resecting tumors of the head and isthmus of the pancreas, the lymph nodes and tissue are removed along the common bile duct, common hepatic artery, portal vein, posterior and anterior pancreaticoduodenal arcades, and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery. Regional lymph nodes for tumors of the body and tail of the pancreas include lymph nodes located along the common hepatic artery, the splenic artery, and in the area of the spleen portal. Affection of other groups of lymph nodes is regarded as distant metastases [7,8,9].

Pathomorphological stage is established after surgical intervention, which usually is pancreato-duodenal resection, distal pancreatic resection or pancreatectomy with removal of regional lymph nodes. In the preparation after pancreatoduodenal resection it is necessary to evaluate bile ducts, pancreatic parenchyma, hook-shaped process, proximal (along the duodenum or stomach) and distal (along the duodenum) resection edges. The pancreatic resection margin is also called the pancreatic ductal, pancreatic isthmus, or distal pancreatic resection margin. Most cases of local tumor recurrence are observed in the pancreatic bed in the area of the edge of resection along the hook process [7,8,9].

It has been demonstrated in numerous studies that lymph node involvement, both by direct tumor invasion and by metastasis, is associated with an unfavorable disease outcome. Thus, it is important to identify and ooze the maximum number of regional lymph nodes in the surgical material. Given the survival data and the number of lymph nodes that can actually be obtained from the operative material, it is recommended to evaluate a minimum of 12 lymph nodes to accurately determine the N0 category. Recent studies have shown that the total number of lymph nodes affected and/or the ratio of lymph nodes involved to those examined (lymph node ratio - LNR) also serve as prognostic factors. Moreover, the total number of lymph nodes affected is superior to the LNR in informative value, as has been demonstrated in studies that have evaluated a sufficient number of lymph nodes. Thus, to date, the N category in pancreatic cancer, as in tumors of other parts of the GI tract, is determined by the number of lymph nodes involved. Although different thresholds have been used in studies based on available data, the following have been introduced into the current staging system: no lymph node metastases, 1-3 affected lymph nodes, 4 affected lymph nodes or more. Separating regional lymph nodes according to anatomic criteria

was not required. However, separately sent lymph nodes should be examined according to labeling. Peritoneal carcinomatosis (even if limited to the omental sac area) and tumor cells in peritoneal flushes allow M1 to be established [7,8,9].

Conclusion

The pancreatic epithelial tumor classifications in the 2019 5th edition remain largely unchanged from the 2010 4th edition. The changes affect precancerous lesions, which are now classified according to two levels of dysplasia. Intraductal oncocytic papillary tumors and intraductal oncocytic papillary tumors associated with invasive carcinoma are separated from the other subtypes. Some changes have occurred in the TNM classification.

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