

PANCREATIC CANCER DIAGNOSIS OVERCOMING BIAS AND ERRORS (CASE SERIES)

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Abstract

Diagnosing malignant pancreatic neoplasms presents a challenging task fraught with the possibility of diagnostic errors due to similarities with other pathologies such as pancreatitis, neuroendocrine tumors, and cystic formations. The key diagnostic method is contrast-enhanced multi-detector computed tomography, yet even this method has certain limitations that may affect diagnostic accuracy. Through the analysis of clinical cases, typical errors accompanied by visual characteristics that can be misleading in differential diagnosis have been identified. Hypodensity and tissue structure alterations, changes in ducts, or mass effect may be common features of both cancer and pancreatitis. Comparing visual signs with the clinical picture and employing additional methods aids in reaching a more precise diagnosis. It is important to note that rare pathologies such as serous oligocystic adenoma and intraductal papillary mucinous neoplasm may also pose additional challenges for accurate diagnosis due to their unusual characteristics on computed tomography scans. The conclusions of the study underscore the importance of a multimodal approach to diagnosing malignant pancreatic neoplasms, including the use of various imaging methods to ensure an accurate diagnosis and the selection of the most appropriate treatment strategy.

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Ұйқы безінің қатерлі ісігінің диагностикасы біржақтылық пен қателерді жеңу (жағдайлар сериясы)

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АҚ, Алматы, Қазақстан

Тұжырым

Ұйқы безінің қатерлі ісіктерін диагностикалау күрделі, ол панкреатит, нейроэндокринді ісіктер және кистоздық түзілімдер сияқты басқа патологиялармен ұқсас болғандықтан диагностикалық қателер жиі кездеседі. Негізгі диагностикалық әдіс - көп кесінділі контрастты компьютерлік томография, бірақ бұл әдіс диагноздың дәлдігіне әсер ететін шектеулерге ие. Клиникалық жағдайларды талдау кезінде, дифференциалды диагностикада көрнекі сипаттамалармен қатар жүретін типтік қателер анықталды. Гиподенсивтілік және тін құрылымының өзгеруі, түтіктердің өзгеруі немесе масс- әсер ісіктің де, панкреатиттің де ортақ белгілері болуы мүмкін. Визуалды белгілерді клиникалық көрініспен және қосымша әдістермен салыстыру дәлірек

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диагноз қоюға көмектеседі. Серозды олигоцистальқ аденома және интрадукталды шырышты-папиллярлы ісік сияқты сирек патологиялар компьютерлік томография сканерлеуіндегі ерекше сипаттамаларына байланысты дұрыс диагноз қоюға қосымша қиындықтар тудыруы мүмкін екенін атап өткен жөн. Зерттеу нәтижелері дәл диагнозды қамтамасыз ету және ең қолайлы емдеу стратегиясын таңдау үшін әртүрлі бейнелеу әдістерін қолданумен қоса, ұйқы безінің қатерлі ісіктер диагностикасында мультимодальды тәсілдің маңыздылығын көрсетеді.

Диагностика рака поджелудочной железы: преодоление погрешностей и ошибок (серия случаев)

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Ключевые слова:

Протоковая Аденокарцинома
Поджелудочной Железы,
Инвазивный Внутрпротоковый
Папиллярный Муцинозный Рак,
Нейроэндокринная Опухоль,
Компьютерная Томография,
Поджелудочная Железа

Аннотация

Диагностика злокачественных новообразований поджелудочной железы представляет собой сложную задачу, обремененную возможностью диагностических ошибок из-за сходства с другими патологиями, такими как панкреатит, нейроэндокринные опухоли и кистозные образования. Ключевым методом диагностики является мультиспиральная компьютерная томография с контрастным усилением, однако и этот метод имеет определенные ограничения, которые могут сказаться на точности диагностики. В ходе анализа клинических случаев были выявлены типичные ошибки, сопровождающиеся визуальными характеристиками, которые могут ввести в заблуждение при дифференциальной диагностике. Гиподенсивность и изменение структуры ткани, изменения в протоках или масс-эффект могут быть общими признаками как рака, так и панкреатита. Сопоставление визуальных признаков с клинической картиной и дополнительными методами помогает поставить более точный диагноз. Редкие патологии, такие как серозно-олигокистозная аденома и внутрпротоковая слизисто-папиллярная опухоль, могут также представлять собой дополнительные сложности для правильной диагностики из-за их необычных характеристик на сканах компьютерной томографии. Выводы исследования подчеркивают важность мультимодального подхода к диагностике злокачественных новообразований поджелудочной железы, включая использование различных визуализационных методов для обеспечения точного диагноза и выбора наиболее подходящей тактики лечения.

Introduction

Every year, over 1100 new cases of pancreatic cancer are registered in Kazakhstan, leading to the death of approximately 800 patients. The disease affects elderly men and women equally; however, the high mortality rate is due to late diagnosis at stages when surgical intervention is no longer possible. Surgical resection is the primary treatment method that can improve the five-year survival rate up to

30% if the disease is detected early. Nevertheless, most cases are discovered at an inoperable stage, highlighting the critical importance of timely diagnosis. Multislice computed tomography (MSCT) is a key diagnostic method, providing high accuracy and sensitivity in determining the stage of the disease. This not only facilitates precise staging and prediction of tumor resectability but is also crucial for planning treatment strategies.¹

The aim of this study is to analyze common diagnostic errors in pancreatic cancer (MSCT) and to differentiate it from other pathologies such as pancreatitis, neuroendocrine tumors, and cystic formations. The work focuses on identifying and thoroughly examining these errors to improve diagnostic approaches. Modern imaging methods combined with histological analysis offer opportunities for accurate differentiation of pancreatic cancer from other diseases, which is critical for selecting the optimal treatment strategy.

Materials and Methods

In this retrospective study, clinical and histological data from 301 patients diagnosed with pancreatic cancer between 2018 and 2022 were analyzed. Among these, 4 cases with the most challenging diagnostic scenarios were selected. The diagnostic evaluation was conducted in the Department of Radiology at the National Scientific Center of Surgery named after A.N. Syzganov, using multislice computed tomography (MSCT-160 Canon Aquilion). The studies were performed with slice thicknesses of 0.8 cm and the administration of the contrast agent Iopromide 370, with the dosage calculated based on the patient's body weight at a ratio of 1 kg x 1.22 ml of contrast agent.

Histological verification of diagnoses was based on materials obtained through cytobiopsies or surgical interventions. The processing of histological samples was carried out in the pathology department of the same center.

The study was approved by the ethics committee of the National Scientific Center of Surgery named after A.N. Syzganov. All participants provided informed consent for the processing and use of their medical data within the framework of this research project.

Case presentation

Patient 1, 32 years old

Complaints upon admission: Jaundice of the sclera and skin, abdominal pain and heaviness, and general weakness. Biochemical blood analysis: ALT - 36.90 U/L; AST - 33.50 U/L; Total Bilirubin - 40.20 μ mol/L.

Ultrasound examination of the abdominal organs (US AB): Ultrasound findings suggest biliary hypertension. An irregular area in the projection of the major duodenal papilla (MDP) may correspond to a neoplasm.

CT of the abdomen with bolus contrast enhancement (CT AB with CE): The Wirsung duct is visualized throughout its entire length and is dilated up to 3 mm. In the MDP projection, circular thickening of the duodenal mucosa is noted, with an area of mucosal thickening adjacent to the head of the pancreas and the common bile duct (CBD), approximately 3.9 x 2.6 cm in size. Lymph nodes in the portahepatis, peripancreatic, and para-aortic regions are enlarged up to 3.0 cm. Conclusion of CT AB with CE: The CT findings are more consistent with an MDP neoplasm. Para-aortic adenopathy. Resident physicians' description: No differences from the primary conclusion.

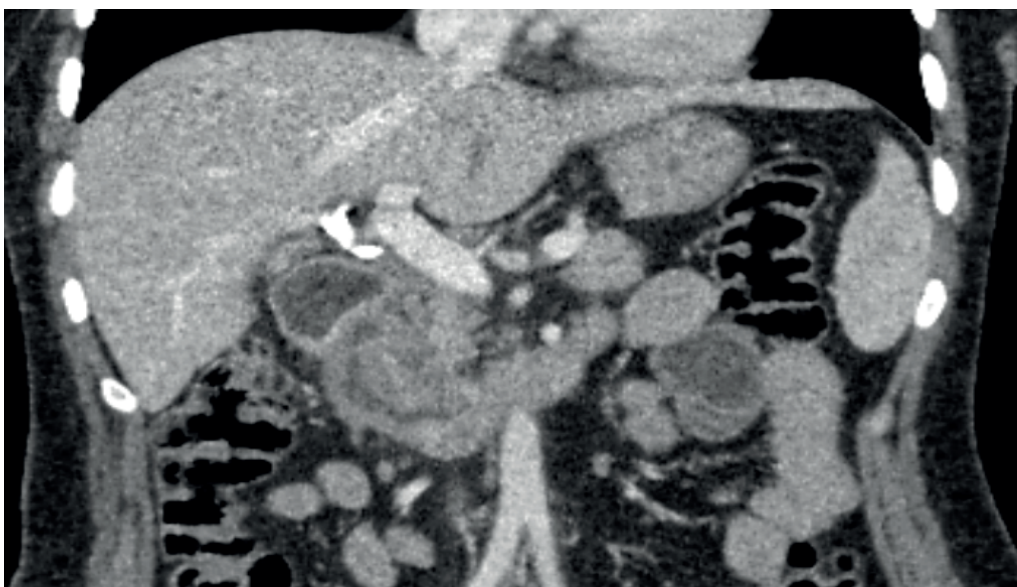


Figure 1.
Circular thickening of the duodenal mucosa in the MDP projection.

Figure 2.
Affected area adjacent to the
head of the pancreas.

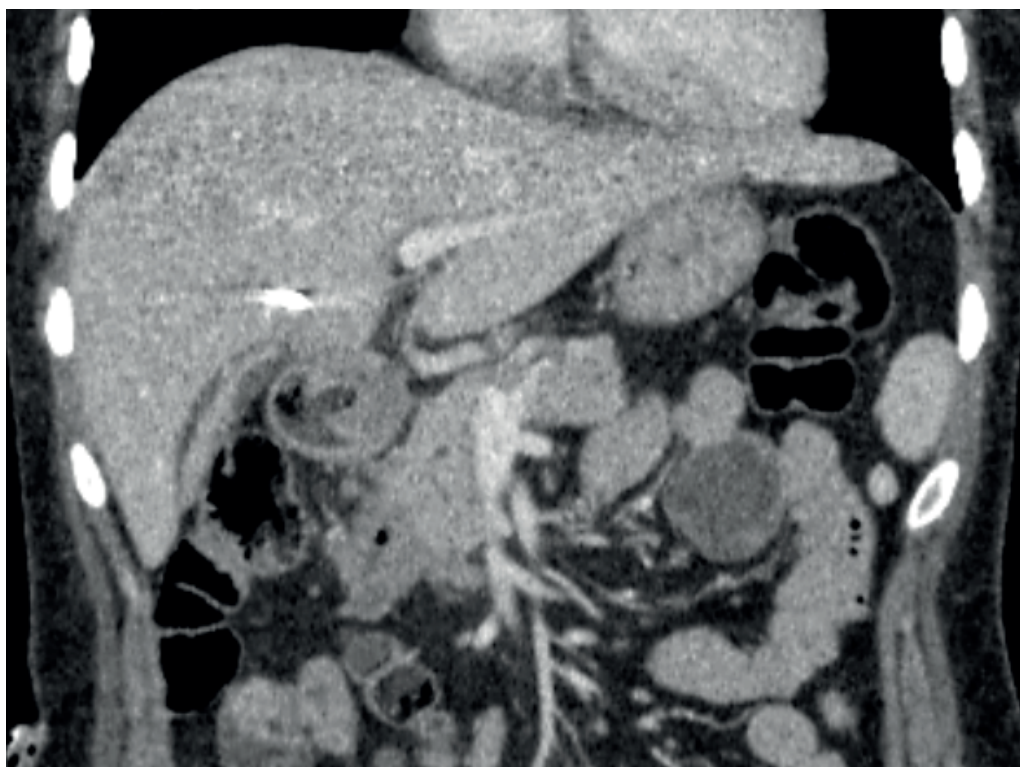
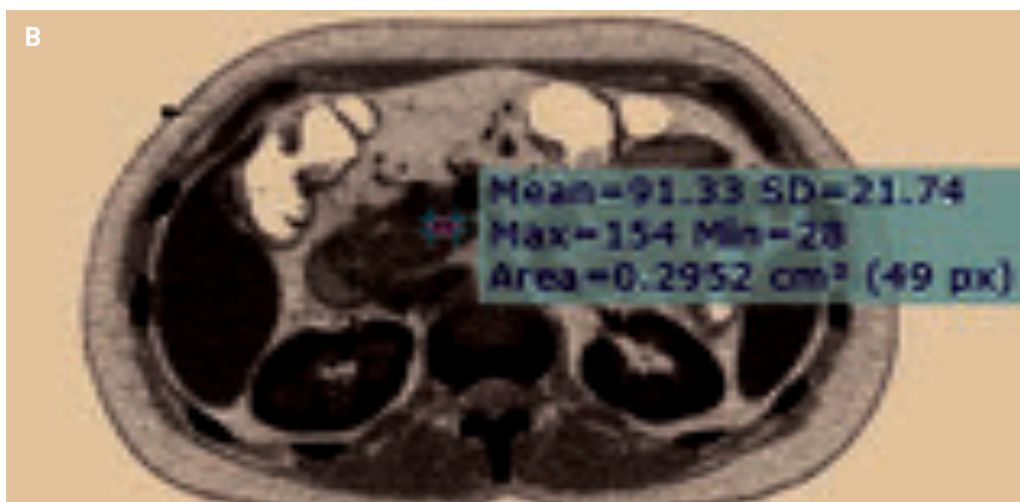
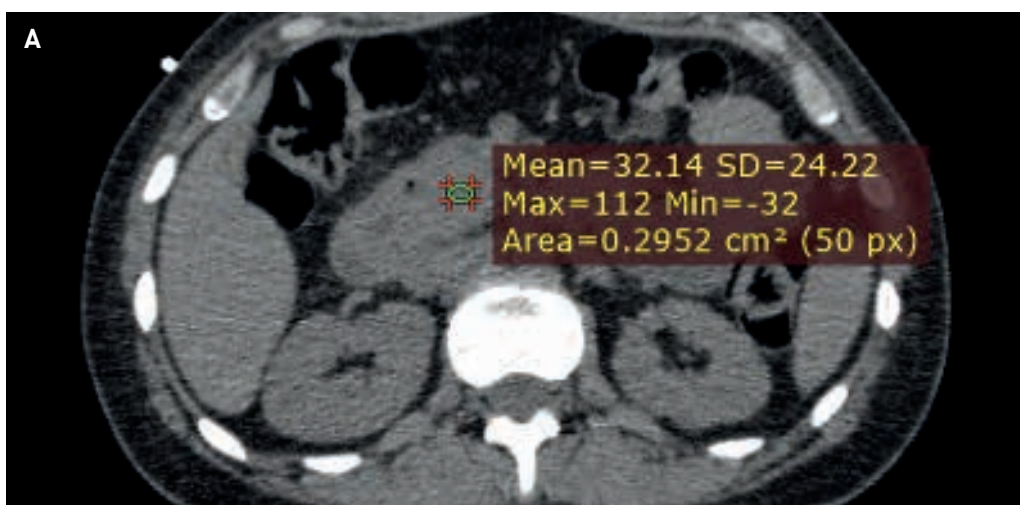


Figure 3 A, B.
Does not show signs of delayed
contrast accumulation



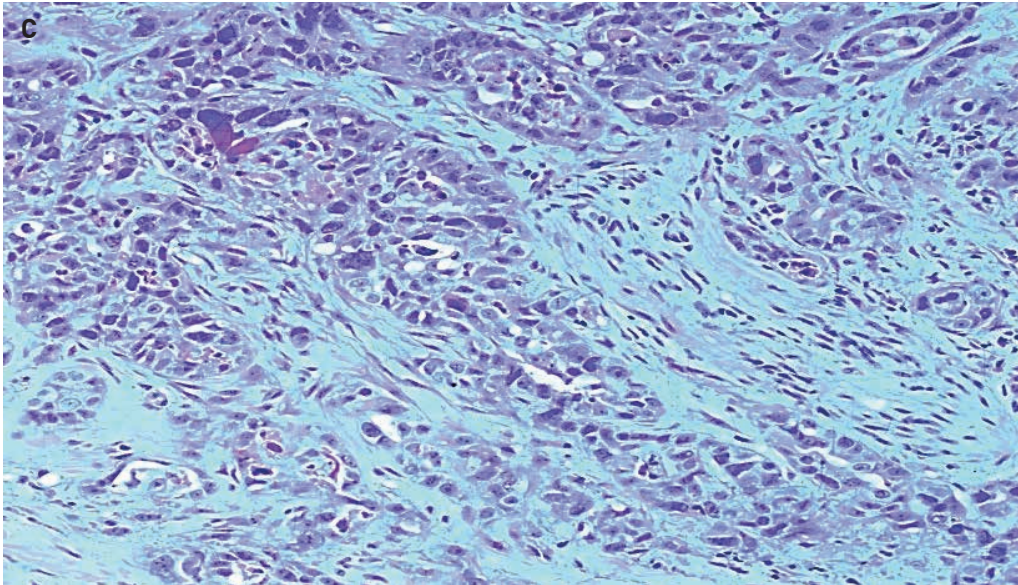
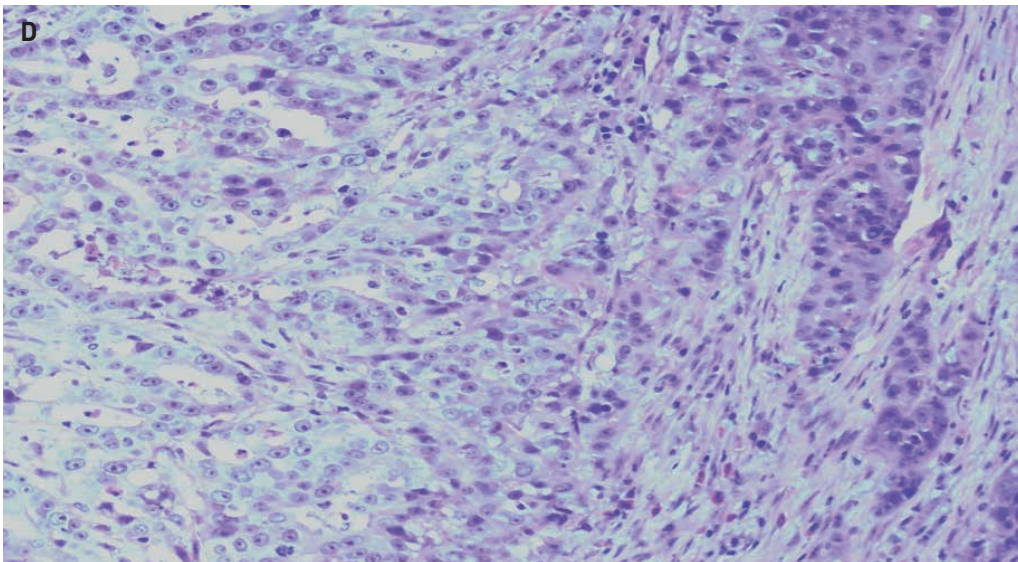


Figure 3 C, D.
The preparations contain fragments of a tumor of the head of the pancreas with a tumor of solid-tubular structure, made up of rounded cells with eosinophilic cytoplasm, high nuclear-cytoplasmic ratio, polymorphic vesicular nuclei with large nucleoli. Proliferative activity is up to 8 mitotic figures (including atypical mitoses) per 10 fields of vision at a magnification of x400. Tumor complexes are immersed in desmoplastic stroma, infiltrated with neutrophils and lymphocytes. Stained with HE. UV x200



Patient 2, 57 years old

Complaints upon admission: Episodes of pain in the right hypochondrium and epigastrium of a girdling nature, general weakness, fatigue, and a weight loss of 14 kg over the past year. Biochemical blood analysis: ALT - 15.40 U/L; AST - 22.50 U/L; Total Bilirubin - 8.40 μ mol/L.

CT of the abdomen with bolus contrast enhancement (CT AB with CE): In the projection of the pancreas body, a mass with well-defined, irregular contours and heterogeneous structure is noted, intensely and heterogeneously

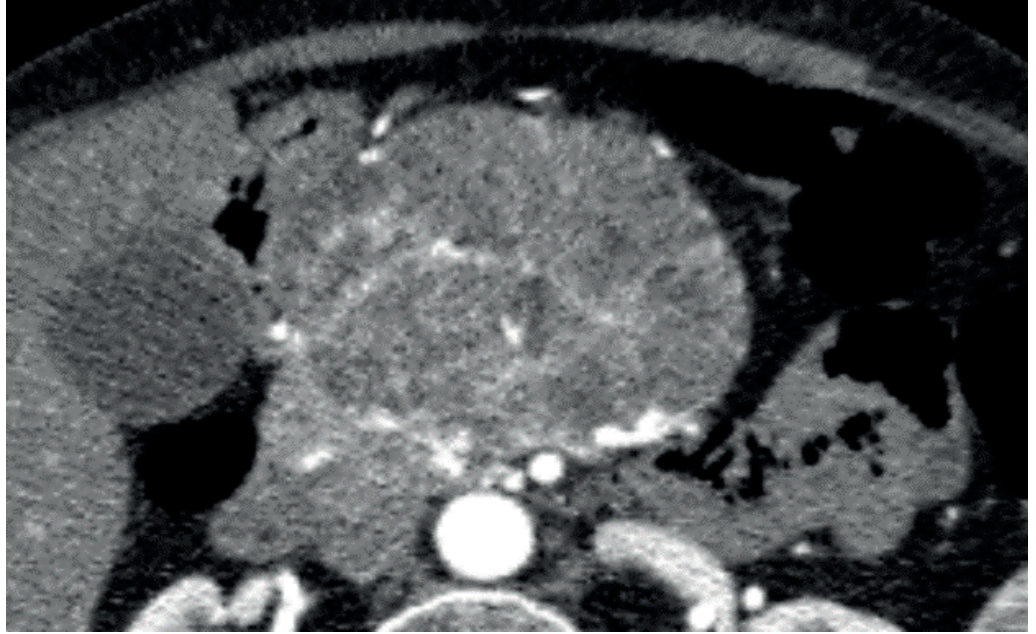
accumulating contrast medium, measuring 8.4 x 8.1 cm, with vessels within its structure. The pancreatic duct is slightly dilated. Enlarged peripancreatic and para-aortic lymph nodes up to 1.6 cm are observed (Figure 4).

endocrine tumor of the pancreas body with secondary adrenal involvement. Para-aortic and peripancreatic adenopathy.

Resident physicians' description: No differences from the primary conclusion. Histological conclusion: Serous oligocystic adenoma of the pancreas.

Figure 4.

In the projection of the pancreas body, a mass with well-defined, irregular contours and heterogeneous structure, intensely and heterogeneously accumulating contrast.



Conclusion of CT AB with CE: The CT findings may correspond to a neuroendocrine tumor of the pancreas body with secondary adrenal involvement. Para-aortic and peripancreatic adenopathy.

Resident physicians' description: No differences from the primary conclusion. Histological conclusion: Serous oligocystic adenoma of the pancreas.

Patient 3, 66 years old

Complaints upon admission: Pain in the epigastric region and retrosternal area, vomiting, weight loss of 10 kg over 2 weeks, general weakness. Biochemical blood analysis: ALT - 17.3 U/L; AST - 100.80 U/L; Total Bilirubin - 51.5 μ mol/L.

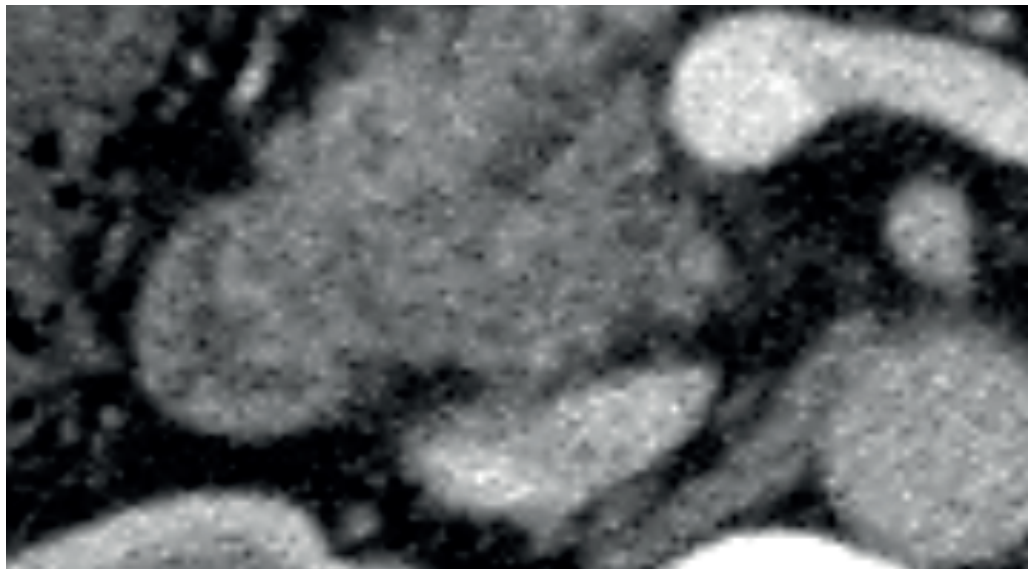
Conclusion of abdominal ultrasound (US AB): Diffuse changes in liver tissue

consistent with hepatitis. Calcification in the right lobe of the liver. Splenomegaly.

CT of the abdomen with bolus contrast enhancement (CT AB with CE): In the projection of the pancreas head, a mass with indistinct contours and tissue density is noted, measuring 4.0 x 3.8 cm, with slight contrast enhancement after administration. The mass involves the duodenum (DU), gastroduodenal artery (GDA), and the wall of the portal vein (PV) (about 30%). The superior mesenteric vein (SMV) is not involved. The pancreatic duct is dilated up to 5 mm. Enlarged lymph nodes in the peripancreatic and para-aortic regions up to 1.7 cm (Figure 5,6).

Figure 5.

In the projection of the pancreas head, a mass with indistinct contours and tissue density, with slight contrast enhancement after administration.



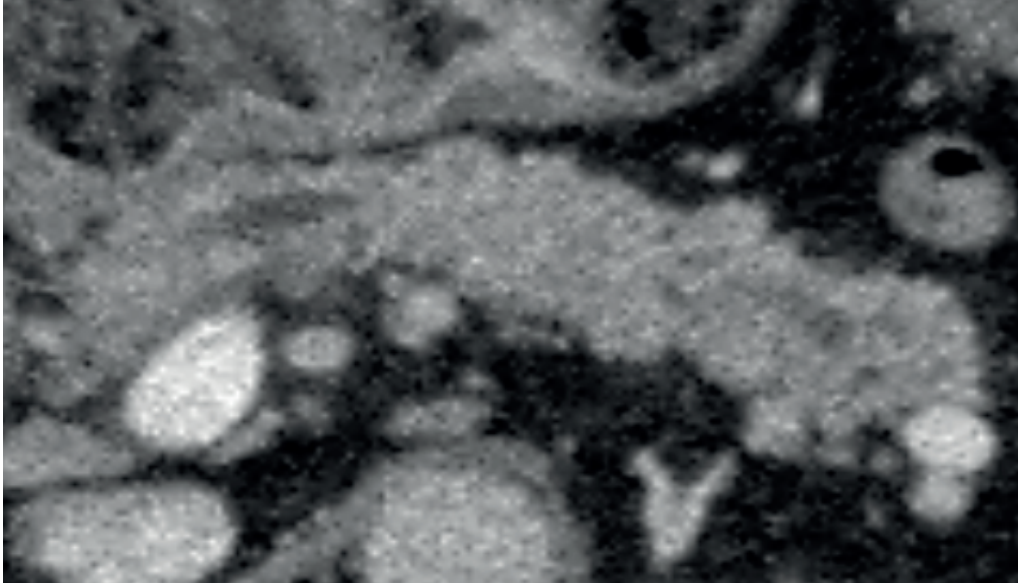


Figure 6.
The pancreatic duct is dilated
up to 5 mm.

Conclusion of CT AB with CE: The mass in the projection of the pancreas head is more consistent with adenocarcinoma involving the DU, PV, and GDA. Pancreatic duct dilatation (Virungaectasia). Para-aortic and peripancreatic adenopathy.

Resident physicians' description: No differences from the primary conclusion. Histological conclusion: In durative calculous pancreatitis of the head with foci of inflammatory exacerbation.

Patient 4, 63 years old

Complaints upon admission: Pain in the epigastric region, general weakness. Biochemical blood analysis: ALT - 41 U/L; AST - 31 U/L; Total Bilirubin - 7.6

μmol/L.

Conclusion of abdominal ultrasound (US AB): Moderate choledochectasia. A mass in the retroperitoneal space, likely originating from the uncinate process or head of the pancreas.

CT of the abdomen with bolus contrast enhancement (CT AB with CE): Hypodense mass along the posterior contour of the pancreas head, irregular in shape with unevenly thickened walls and parietal inclusions, measuring 5.8 x 4.7 x 3.8 cm. The mass shows intense contrast enhancement of the walls, displaces the pancreas head anteriorly, and intimately abuts and compresses the common bile duct and right adrenal gland (Figure 7).

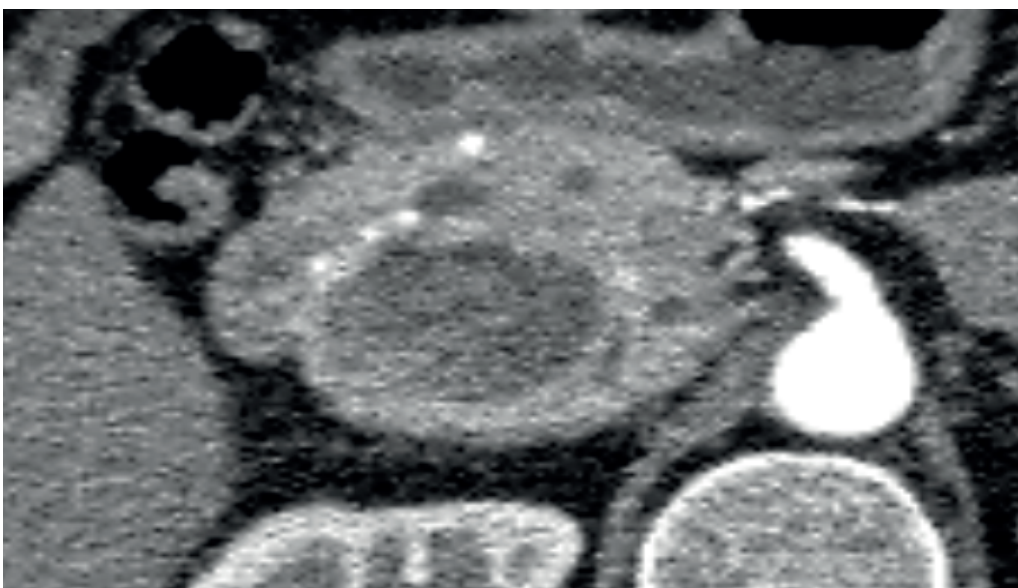


Figure 7.
Hypodense mass along the
posterior contour of the pan-
creas head, irregular in shape
with unevenly thickened walls
and parietal inclusions.

Conclusion: A mass in the right retroperitoneal space, with a differential diagnosis of neuroendocrine tumor (NET) and gastrointestinal stromal tumor (GIST). Moderate biliary hypertension.

Resident physicians' description: No differences from the primary conclusion. Histological conclusion: Intraductal papillary mucinous neoplasm (IPMN) of the pancreas associated with invasive carcinoma.

Discussion

Patient 1, 32 years old

The clinical presentation of ampullary cancer often mimics that of pancreatic cancer. Definitive surgical intervention is crucial for accurate histological diagnosis.² The Whipple procedure is the standard surgical treatment for both adenocarcinoma and ampullary cancer.² Despite the misdiagnosis not altering the treatment strategy, it is important to identify the key features that might have been overlooked or misinterpreted, leading to diagnostic errors. In Figures 1 and 2, the thickening of the mucosa in the duodenum with an area of thickening in both the mucosal and submucosal layers, closely abutting the head of the pancreas and the common bile duct, is evident.

The location of the neoplasm in this case does not allow the radiologist to clearly differentiate the primary growth. Due to the predominant localization of most of the neoplasm in the area of the distal bile duct system (DBDS), preference was given to this etiology. This demonstrates the limitation of the CT imaging technique. Pancreatic adenocarcinoma can involve neighboring tissues without showing radiological signs in the primary zone, as observed in this case. This phenomenon indicates the limitations of the CT diagnostic method and the necessity of using a comprehensive approach in evaluating such cases.

Patient 2, 57 years old

Upon analysis of the CT scans of the patient in the projection of the pancreatic body, a large-sized formation with clear contours and heterogeneous structure was identified, which intensely and heterogeneously accumulated contrast material. Such characteristics often indicate the presence of a neuroendocrine tumor (NET), which typically manifests

as a well-vascularized, hyperdense nodule with intense contrast enhancement in the arterial phase.³

However, histological examination revealed that the true pathology in this case was serous oligocystic adenoma (SOA) of the pancreas. Despite SOA being considered a rare pathology and traditionally not included in the main differential diagnosis, this does not exempt the radiologist from the responsibility of thorough consideration of all possible diagnoses.⁴ The rarity of the disease necessitates special attention to detail when analyzing diagnostic images to avoid missing key features that may indicate such unusual conditions. This case underscores the importance of a comprehensive approach to diagnostics, where every possible diagnosis should be carefully considered, even if rare, to ensure the best treatment plan and avoid potential diagnostic errors.

Patient 3, 66 years old

Ductal changes: Malignant neoplasms as well as chronic pancreatitis can induce alterations in pancreatic ducts. However, in pancreatitis, ductal changes are typically less uniform and may be accompanied by calcifications, which are not characteristic of cancerous tumors. In the examined scans, however, calcifications within the duct content were not identified.

Upon analysis of the CT scans of this patient, the physician and resident identified slight contrast material (CM) accumulation and washout in the region of the pancreatic head, which was interpreted as a possible adenocarcinoma.⁵ However, histological examination refuted this diagnosis, revealing patterns characteristic of focal indurated calcific pancreatitis with inflammatory foci.

Key visual features contributing to the diagnostic error:

1. Hypodensity and tissue structure alteration: Both adenocarcinoma and pancreatitis can lead to similar tissue density changes. In pancreatitis, this is often associated with fibrosis and calcifications, which may be mistakenly interpreted as tumorous alterations.

Localized thickening or mass effect: Chronic inflammation associated with pancreatitis can cause tissue thickening, mimicking the mass effect typical of ad-

enocarcinoma. This complicates differentiation based solely on CT data without histological confirmation.

This case underscores the complexity of diagnosing pancreatic diseases, particularly when similar visual signs are present on CT scans. Even with histological examination, differentiating indurativecalculous pancreatitis from adenocarcinoma remains one of the most challenging tasks in clinical practice. This case highlights the necessity of a comprehensive approach, involving not only imaging methods but also thorough examination for accurate diagnosis.

Patient 4, 63 years old

Upon analysis of the CT scans of the patient in the projection of the pancreatic head, a formation with clear, irregular contours and heterogeneous structure was identified, intensively and heterogeneously accumulating contrast material. These characteristics often indicate a neuroendocrine tumor (NET), which typically presents as a well-vascularized, hyperdense nodule with pronounced contrast enhancement in the arterial phase. However, histological examination revealed that the true pathology was an intraductal papillary mucinous neoplasm (IPMN) of the pancreas associated with invasive carcinoma.⁶

IPMN may resemble a cystic variant of NET, leading to a diagnostic error. Typically, IPMN presents as a round, single- or multi-cystic formation with septations, often with a larger cystic component and without a wide contrast-enhancing rim. In this case, these features were not clearly evident on the CT scans, complicating accurate diagnosis.⁷

This error underscores the importance of careful interpretation of CT data and consideration of all possible pathologies. The treatment approach for NET differs from that for IPMN and pancreatic adenocarcinoma: NET requires a specialized approach, while IPMN and adenocarcinoma necessitate resection

and aggressive treatment.⁸

Thus, a comprehensive approach, involving various imaging studies, is necessary for accurate diagnosis and selection of the optimal treatment strategy.

Limitations: one-center conducted study

Conclusion

In conclusion, diagnosing pancreatic tumors remains challenging for physicians due to their similarity to other diseases, as well as the presence of rare pathologies that may appear similar to more common tumors on imaging studies. Histological examination remains a necessary step for accurate diagnosis.

It is important to note that even with the use of modern imaging methods, such as contrast-enhanced computed tomography, diagnostic errors are possible. A comprehensive approach is necessary, incorporating various imaging techniques as well as histological examinations, for precise diagnosis and selection of the optimal treatment strategy for patients with pancreatic tumors.

The conclusion highlights that diagnosing pancreatic tumor remains challenging. Therefore, diagnosing different pancreatic tumors remains complex, necessitating a comprehensive approach that integrates diverse imaging modalities and histological examinations for accurate diagnosis and treatment planning.

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