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## Pancreatic abscess: a modern look at an old problem

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**Abstract:** *analysis of morphological and etiologic characteristics and clinical features of pancreatic abscesses on the basis of previous publications. Theoretical analysis and generalization, classification, analysis of scientific and methodical literature. The analysis of the literature was carried out using electronic scientometric database Scopus, Web of Science, Ulrich's Periodicals, Google Scholar, PubMed, Medline. We analyzed literary sources published since 1909, using the keywords, such as: pancreatic abscess, abscess of pancreas. Articles published in professional English-language journals were included. Were analyzed publications dedicated to acute pancreatitis, chronic pancreatitis, infected pseudocysts as a cause of pancreatic abscess. We analyzed scientific works concerning benign and malignant tumors of pancreaticoduodenal area, scientific papers concerning fish bone penetration into the pancreas. Causes of pancreatic abscess development such as trauma of the pancreas, thrombosis of a.lienalis and pancreas divisum were described in the publication for the first time. Other scientific works are devoted to infectious agents, diagnosis and treatment of abscesses. Pancreatic abscess is the body's response to pancreatic infection that is characterized by specific morphological structure and heterospecific etiology. Pancreatic abscess is the transition state that combines acute destructive (acute infected necrotizing pancreatitis) and chronic degenerative (a chronic fibrotic-degenerative pancreatitis complicated by the pancreatic pseudocyst) pancreatitis. Pancreatic abscess can be considered as the marker of chronization of inflammatory and destructive pathological processes that need etiologic authentication and further treatment.*

**Keywords:** abdominal abscess, acute pancreatitis, chronic pancreatitis, pancreatic pseudocyst, chronic pancreatitis, pancreas

### Introduction

Pancreatic abscesses (PA) are attributed to nonspecific surgical abdominal infections, the main cause is purulent-destructive and degenerative diseases of the pancreas. PA is a polyethiological condition to the formation of which lead chronic (Ammann,1992; Gedam, 2017; Rodriguez, 2020) and acute pancreatitis (Fink, 1988; Rani, 2016; Reuken, 2018), the annual incidence of which ranges from 13 to 45 per 100,000 persons. (Hoilat & Katta, 2021). The other causes of PA are the following - penetration of duode-

nal ulcers, perforation of the posterior wall of the stomach into the bursa omentalis with subsequent penetration into the pancreas (An, K.Kim, J. S.Kim & J.I.Kim, 2007), splenic artery thrombosis (Lun, Jiang, Xin & Zhang, 2017), cystic degeneration and destruction of solid tumors - adenocarcinomas, Non-Hodgkin lymphomas and neuroendocrine tumors of pancreas (Greenberg, Bank & Stark, 1990). The causative agents of infection that often lead to the PA are Escherichia coli, Enterococcus, Klebsiella, Staphylococcus, Peptostreptococcus та Pseudomonas (Brook &

Frazier, 1996; Srikanth et al. 2002). Considering that the abscess is a morphological form of many pancreatic diseases, rather than a single nosology, identification of its cause is the first priority that will determine prognosis and treatment tactics.

### Aim

To analyze the characteristics of morphological, etiologic and clinical features of pancreatic abscesses on the basis of previous publications.

### Materials and methods

The analysis of the literature was carried out using electronic scientometric database Scopus, Web of Science, Ulrich's Periodicals, Google Scholar, PubMed, Medline. We analyzed literary sources published since 1909, using the keywords, such as: pancreatic abscess, abscess of pancreas. Articles published in professional English-language journals were included.

### Rewiew and discussion

Most scientific works were focused on acute pancreatitis as a cause of PA, but since the revision of Atlanta classification of acute pancreatitis in 2012, pancreatic abscesses have been excluded from the list of complications of acute pancreatitis (Colvin, Smith, Morgan & Porter, 2020). Local complications reflecting the evolution of necrotic pancreatitis are classified as acute pancreatic fluid collections (APFC), acute necrotic collections (ANC), acute pancreatic pseudocyst (PC) and walled-off necrosis (WON). As a result, in 2012 after the revision of the classification of acute pancreatitis, diagnosis or complication «pancreatic abscess» lost its clinical significance.

#### *Microbiological characteristics of pathogens of pancreatic abscess.*

A PA is an encapsulated accumulation of pus that has an intrapancreatic location. Approximately one-third of pancreatic abscesses are polymicrobial, caused mainly by enteric facultative microorganisms, the other two-thirds are predominantly gram-positive or gram-negative aerobes and anaerobes. To identify the most common causative agents of PA Brook & Frazier (1996) in the period from 1973 to 1988, based on modern aerobic and anaerobic bacteriological methodologies, investigated the types of agents that caused abscess in 46 patient cases. During the study Aerobic or facultative organisms were present in 17 specimens (37%), anaerobes were

present in 10 (22%), and mixed aerobic-anaerobic organisms were present in 19 (41%). The predominant aerobes were *E. coli*, *K. Pneumoniae* ra *S. aureus*. The predominant anaerobes were *Pep-tostreptococcus*, group B. *Fragilis*, *Clostridium*, *Prevotella*, *Veillonella* and *Fusobacterium*. In the literature were described the first reported cases of PA caused by *Bordetella bronchiseptica* (Matic & Bunce, 2015) and *Salmonella enteritidis* (Tai, Upadhyay, Jain & Goldstein, 2018). Hemanth, Guchait & Naithani (2015) performed a bacteriological analysis of the abscess content in a case of a 32-year-old woman and described the growth of *Candida tropicalis* and *Pseudomonas aeruginosa*. Gascun et al. (2007) described first reported case of PA caused by *Aeromonas hydrophila*. Reuken et al. (2018) performed a retrospective analysis of pathogen spectrum and outcome of infected pancreatic necrosis (WON) and pancreatic pseudocysts (PC) collecting data from 113 patients. Fungal infections, predominantly caused by *Candida* species, were identified in cases of 52 patients (46%). Patients with fungal pancreatic infections had a longer hospital stay (34 days vs 14 days,  $P < 0.001$  needed intensive treatment more often (55,8% vs 27,9%,  $P = 0,002$ ) and had a lower 365-day survival rate (78,4 [SE, 6,6%] vs 95,0 [SE, 2,0%],  $P = 0,035$ ), than in patients with bacterial etiology of pancreatic abscess. This analysis demonstrates the polymicrobial aerobic and anaerobic etiology of pancreatic abscess. In the literature were described several cases of pancreatic abscess due to hematogenous spread of infection. Tomás (2013) reported about infected nidus in a case of a 70-year-old woman, which had an odontogenic genesis and was visualised on CT as a PA and had an odontogenic flora (*Streptococcus anginosus*), obtained after bacteriological examination. Pethe et al. (2020) reported about odontogenic genesis of PA in a case of a 61-year-old male. Aspirate from the pancreatic cyst grew oral flora with *Actinomyces Odontolyticus* and *Rothia Dentocarioa*.

#### *Pancreatic tuberculosis as a factor in the development of pancreatic abscess.*

The incidence of pancreatic tuberculosis (PT) has increased worldwide in recent decades, accounting for 5% of all forms of tuberculosis. There are cases misdiagnosed as cystic neo-

plasms. The authors connect this to the diagnostic similarity and similar clinical picture of these diseases. Sometimes PT is complicated by PA, which is frequently observed in patients with immunodeficiency conditions (in HIV-positive patients, diabetic patients) (Chavadi, 2015; Maulahela, 2020). Panic, Maetzel, Bulajic, Radovanovic & Löhr (2020) analyzed cases of pancreatic TB published from 1978 to 2017. In a total of 121 cases a pancreatic abscesses were present in 12.1% of patients, localised mainly in the pancreatic head (59.0%) and less often in the body (18.2%), tail (13.4%) or neck (1.8%)

*Pancreatic abscess in acute pancreatitis.*

In 1988 Fink et al. (1988) analyzed 100 cases of PA treated in five different hospitals in Los Angeles, USA. All cases of pancreatic abscess followed episodes of pancreatitis: 56 cases occurred after the initial episode of pancreatitis, 12 after the second known attack of pancreatitis and 4 after the third attack. Only 48% of the patients reported fever in history, and only 23% had a temperature 38.3°C or above during hospital admission. 36% of patients had a normal serum amylase concentration on hospital admission, and in half of all cases the amylase concentration was two times less than the normal level. In the literature were described 12 cases of xanthogranulomatous pancreatitis (XGP), which is a mixed inflammatory process characterized by infiltration of lipid-laden foamy histiocytes and other inflammatory cells with marked fibrosis and destruction of the parenchyma organ. Xanthogranulomatous inflammation occurs in various organs such as skin, gastrointestinal tract, genitourinary system, soft tissues and lymph nodes. Okabayashi et al. (2007) described 2 cases of PA on a background of xanthogranulomatous pancreatitis.

*Infected pancreatic pseudocyst (PC).*

Pancreatic PC is an inflammatory lesion occurred on the background of acute or chronic pancreatitis. Since the revision of Atlanta classification of acute pancreatitis in 2012, pancreatic abscesses have been excluded from the list of complications of acute pancreatitis and was recommended to use the definition «pancreatic pseudocyst» which has similar characteristics to pancreatic abscess (pseudocapsule and presence of pus). According to Tan, Zhou, Cao & Zhang

(2018) pancreatic PC incidence range from 5 to 16% in cases of patients with acute pancreatitis, while 20–40% in cases of patients with chronic pancreatitis. The author also reported a correlation between infectious pancreonecrosis and the development of pancreatic pseudocyst (OR, 4.253; 95% CI, 3.574-7.339; p = 0.021) which has been infected and led to the formation of pancreatic abscess.

*Pancreatic abscess on the background of chronic pancreatitis.*

According to Khanna, Tiwary & Kumar (2012) pancreatic pseudocysts is most common to arise among patients with alcoholic chronic pancreatitis (from 70% to 78%). The second cause is idiopathic chronic pancreatitis (from 6% to 16%), followed by biliary pancreatitis (from 6% to 8%). Ammann et al. (1992) analyzed 336 patients with chronic pancreatitis, 10 (3%) developed an intra-abdominal abscess (6 pancreatic, 4 liver abscesses). The author reports, factors that cause abscess formation may be divided into two categories: general predisposing conditions and local factors related to pancreatic abscesses. Intra-abdominal abscesses were significantly more common in alcoholic CP (9 of 245; 3.7%) as compared with nonalcoholic CP (1 of 91; 1.1%). Splenectomy, diabetes mellitus (DM) and severe exocrine insufficiency may contribute to the development of pancreatic abscess. Among the local factors, the author includes pancreatojejunostomy, which was performed in 9 out of 10 patients. Rodríguez et al. (2020) also describe the clinical case of pancreatic abscess in a case of patient with chronic pancreatitis and decompensated DM due to excessive alcohol consumption for 5-months.

*Acute obstructive suppurative pancreatic ductitis (AOSPD).*

In the literature were described 14 studies (64 patients) concerning AOSPD, occurred on the background of chronic pancreatitis (Gedam, 2017; Wali, 2015) or as a complication of pancreatic cancer (Iwatsuka, 2018; Sheikh et al., 2020; Shimizuguchi et al., 2020). Gedam, Sadriwala & Bansod (2017) reported about the case of 33-year-old female with chronic pancreatitis, which on ultrasonography was hyper-echoic and atrophic pancreas with main pancreatic duct dilated up to 1

cm and 6mm calculus in the main pancreatic duct at the level of pancreatic head, that according to the author caused the development of AOSPD. Shimizuguchi et al. (2020) reported about 5 patients with pancreatic ductal adenocarcinoma (PDAC) and 1 patient with chronic myelogenous leukemia (CML), which were diagnosed AOSPD. In most cases each patient had fever and abdominal pain. Endoscopic retrograde cholangiopancreatography (ERCP) showed dilatation of the main pancreatic duct (MPD) and suppuration of the pancreatic duct. Pseudocysts, abscesses and pancreatic necrosis were excluded on abdominal CT. The authors link the occurrence of AOSPD with obstruction of the main pancreatic duct and retrograde infection from the gastrointestinal tract or biliary tract into the pancreas; bacteria produce serine protease, a kind of enzymes, and the enzyme can damage the tight junctions between pancreatic duct epithelial cells and allow leakage of pancreatic juice through protease-activated receptor 2 (PAR2). Sheikh et al. (2020) reported the development of acute obstructive purulent ductitis in a case of 71-year-old patient with pancreatic adenocarcinoma. In the literature were described 2 clinical cases of acute obstructive purulent ductitis as a complication of ERCPG (Isono, 2016; Wang, 2019). The authors attribute this to possible reflux of bacteria from the gastrointestinal tract or biliary tract into the pancreas; oversize stent, a swollen pancreas and insufficient sphincterotomy of the papilla during the first ERCP may have also aggravated outflow obstruction.

#### *Pancreatic Abscesses associated with Splenic artery Thrombosis.*

Lun, Jiang, Xin & Zhang (2017) described the case of a 65-year-old man, which was presented with acute total splenic infarct of distal part of the pancreas, complicated by the formation of an abscess due to Splenic artery Thrombosis. The authors related the development of an abscess to the anatomical feature of blood vessels. In this case, were detected no branches proximal to the thrombosed segment, which provoked ischemic necrosis of the tail of the pancreas with the subsequent development of an abscess.

#### *Pancreatic melioidosis.*

In the literature published 1 article devoted to the development of pancreatic abscess among pa-

tients with melioidosis. Intra-abdominal abscesses are a common manifestation of melioidosis, but the involvement of the pancreas is surprisingly rare and has not been registered before. Chong, Lim & Sharif(2010) described 4 clinical cases of pancreatic abscess on the background of melioidosis. Three patients had multifocal microabscesses and one had a large focal abscess. Acute and chronic pancreatitis were excluded on the basis of instrumental examination (abdominal CT). In favor of melioidosis were indicators such as general clinical manifestations, concomitant microabscessions of the liver and spleen, isolation of the pathogen *Pseudomonas pseudomallei* from blood and pus.

Among the rare causes of pancreatic abscess in the literature were described cases of penetration of duodenal ulcers into the pancreas, which was confirmed endoscopically (M. J.Kim, 2015). An et al. (2007) described a case of perforation of the posterior wall of the stomach into the pancreas by a fishbone. There are also isolated cases of pancreatic abscess, secondary to Non-Hodgkin's pancreatic lymphoma, gastrinoma and in case of patients with pancreatic adenocarcinoma (Greenberg et al. 1990).

#### *Diagnostics of pancreatic abscess.*

In order to diagnose and establish the cause of pancreatic abscesses should be used contrast-enhanced computed tomography (CT), which is the most universal method for assessment of pancreatic diseases. It has a high rate of diagnostic accuracy for determining the nature of both tumors and inflammatory disease (Mathew & Thomas, 2017). CT has a sensitivity of 90–100% for the diagnosis of a pseudocyst and fluid collections, transabdominal ultrasound (US) is 70–90% sensitive in detecting pancreatic pseudocyst or WOPN. The sensitivity and specificity of MRI, CT, and the US to detect solid debris within PFC are 100% and 100%, 25% and 100%, and 88% and 54%, respectively (Agalianos et al.2018; Umapathy et al. 2020). Endoscopic ultrasound can detect most of the cystic lesions even with size less than 2 cm, and it has 93–100% sensitivity and 92–98% specificity for differentiating pseudocyst from other fluid collections (Agalianos et al.2018). The pancreas can be visualized with ultrasound in 75–93% of patients (Dhaka et al. 2015).



### *Treatment of pancreatic abscess.*

Once the abscess is diagnosed, immediate combined antibacterial and, if possible, minimally invasive drainage should be performed. In recent years there are many results of successful surgical treatment of abdominal abscesses of various localizations, including the pancreas, by drainage under ultrasound or CT guidance (Jo, 2015; Lee, 2017; Rani, 2016; Yang, 2016). Shavrina et al. (2019) analyzed 103 clinical cases of percutaneous ultrasound-assisted drainage of intraperitoneal abscesses in the period from 2012 to 2017. According to the authors research, full recovery was observed in 101 (98%) out of 103 patients within 10-73 days. Drainage with ultrasound navigation is an effective independent way to treat abscesses. The method has demonstrated high efficiency, availability and safety, avoiding open surgical approach. Szakó et al. (2020) compared the results of endoscopic and percutaneous drainage of infected pseudocysts. Clinical success of endoscopic intervention was better than percutaneous drainage (OR = 3.36; 95% CI, 1.48, 7.63; p = 0.004). Also the recurrence rate was lower after endoscopic drainage (OR = 0.23; 95% CI 0.08, 0.66; p = 0.006). Open methods used in patients with necrotising pancreatitis. Van Brunschot et al. (2018) analyzed 1980 patients with necrotising pancreatitis, 1167 underwent open necrosectomy and 813 underwent minimally invasive surgical (n=467) or endoscopic (n=346) necrosectomy. There was a lower risk of death for minimally invasive surgical necrosectomy (OR, 0.53; 95% CI 0.34 to 0.84; p=0.006) and endoscopic necrosectomy (OR, 0.20; 95% CI 0.06 to 0.63; p=0.006). Endoscopic necrosectomy was associated with a lower risk of death than open necrosectomy in the high-risk group (3/40 vs 12/40; risk ratio, 0.27; 95% CI 0.08 to 0.88; p=0.03) and in the very high-risk group (12/57 vs 28/57; risk ratio, 0.43; 95% CI 0.24 to 0.77; p=0.005). Bang et al. (2019) didn't find significant difference in mortality (endoscopy 8.8% vs surgery 6.3%; P = .999), but complications rate was significantly higher in the surgery group ( $0.69 \pm 1.03$ ) compared with the endoscopy group ( $0.15 \pm 0.44$ ) (P = .007). Wang et al. (2019) compare laparoscopic approach or an open surgical procedure, percutaneous catheter drainage and endoscopic drainage.

Laparoscopic surgical approach associated with the shortest mean length of stay (P = 0.009), and it had the lowest total charge (P = 0.03). All three modalities have similar inpatient mortality (P = 0.28). The study also revealed that percutaneous drainage associated with more emergent admission (P < 0.001). Farias (2019) didn't find significant difference between treatment success rate (risk difference [RD] -0.09; 95% confidence interval [CI] [0.20,0.01]; P=.07) and recurrence (RD: 0.02; 95% CI [-0.04,0.07]; P=.58) between surgical and endoscopic treatment. Regarding time of hospitalization, the endoscopic group had better results (RD: -4.23; 95% CI [-5.18, -3.29]; P<.00001). When it comes to treatment cost, the endoscopic arm also had better outcomes (RD: -4.68; 95% CI [-5.43,-3.94]; P<.00001).

### **Conclusions**

1. Pancreatic abscess is the body's response to pancreatic infection that is characterized by specific morphological structure and heterospecific etiology.
2. Pancreatic abscess is the transition state that combines acute destructive (acute infected necrotizing pancreatitis) and chronic degenerative (a chronic fibrotic-degenerative pancreatitis complicated by the pancreatic pseudocyst) pancreatitis.
3. Pancreatic abscess can be considered as the marker of chronization of inflammatory and destructive pathological processes that need etiologic authentication and further treatment

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### **Conflicts of interest**

Authors have no conflict of interest to declare.

### **Consent to publication**

Its publication has been approved by all authors and patients.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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## Абсцеси підшлункової залози: сучасний погляд на «стару» проблему

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**Анотація:** на підставі попередніх публікацій у фахових джерелах проаналізувати характерні морфологічні, етіологічні та клінічні особливості перебігу абсцесів підшлункової залози. Теоретичний аналіз і узагальнення, систематизація, аналіз наукової та науково-методичної літератури. Проведено аналіз літератури, присвяченої дослідженню причин розвитку абсцесів підшлункової залози (ПЗ) з використанням електронних наукометричних баз даних Google Scholar, PubMed, Scopus, Web of Science та Medline. Проаналізовано літературні джерела, за ключовими словами - панкреатичний абсцес, абсцес підшлункової залози з 1909 року. Включено статті фахових англomовних видань. Проаналізовано публікації, присвячені гострому панкреатиту, хронічному панкреатиту, інфікованим псевдокістам як причині абсцесу підшлункової залози. Проаналізовано роботи присвячені доброякісним та злоякісним пухлинам панкреатодуоденальної зони, пенетрації підшлункової залози риб'ячою кісткою. Травма підшлункової залози, тромбоз *a.lienalis* та *pancreas divisum*, як причини розвитку абсцесу підшлункової залози, описані в літературі уперше. Інші роботи – інфекційними чинником, діагностиці та лікуванню абсцесів. Абсцес підшлункової залози є відповіддю організму на панкреатичну інфекцію, що характеризується специфічною морфологічною будовою та неспецифічною етіологією. Абсцес підшлункової залози є перехідним станом, що поєднує гострий деструктивний (гострий інфікований некротичний панкреатит) та хронічний дегенеративний (хронічний фіброзно-дегенеративний панкреатит ускладнений псевдокістою ПЗ) панкреатити. Абсцес підшлункової залози можна вважати маркером «хронізації» запального та деструктивного відносно сприятливого патологічного процесу, що потребує етіологічної ідентифікації та інтервенційного лікування.

**Ключові слова:** абсцес черевної порожнини, гострий панкреатит, хронічний панкреатит, псевдокіста підшлункової залози, підшлункова залоза



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