Diagnosing Disconnected Pancreatic Duct Syndrome: Many Disconnects, Few Answers

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In a subset of patients with severe acute pancreatitis (AP), central necrosis affecting the main pancreatic duct (MPD) may create a discontinuity between the left-sided pancreas and duodenum. Such an interruption in the setting of a viable upstream portion of the gland gives rise to the disconnected pancreatic duct syndrome (DPDS), which is generally regarded as a diagnostically and therapeutically challenging condition [1]. The clinical presentation of DPDS includes persistent external pancreatic fistula, recurrent pseudocyst, and/or obstructive recurrent acute or chronic pancreatitis of the upstream pancreatic parenchyma [1, 2]. Patients with the syndrome, reported in 30–50% cases of necrotizing pancreatitis (NP), are more likely to require hybrid therapeutic interventions, reintervention, rescue surgery, and/or longer hospital stay [2].

Although the available literature may imply a necessity to urgently address this pathology with active therapy, indications for invasive procedures remain unclear. The data addressing the natural history and conservative treatment are scarce, likely due to its underdiagnosis, misdiagnosis, as well as inadequate follow-up of patients who do not develop symptomatic DPDS after hospital discharge. It is unclear what percentage of patients with a disconnected duct are asymptomatic and/or resolve their syndrome without

intervention. Still, early diagnosis may reduce treatment delay in patients who would otherwise linger through a prolonged disease course.

With regard to the aforementioned, as the reported incidence rates vary across the literature, true figures remain unknown. Since available studies addressing the incidence of DPDS are relatively few, their results should be interpreted with caution. By requiring diagnostic confirmation, often by advanced modalities, in order to meet inclusion criteria, the true prevalence could be underestimated. Moreover, the general lack of clear distinction between DPDS and a clinically silent disconnection raises the question of whether the stated incidence reflects the occurrence of true DPDS.

The confusion in key concepts and terminology may also be a hindrance to progress. A disconnected duct is defined as a complete (circumferential) interruption of the duct integrity, whereas a disrupted duct may refer to a partial interruption [3]. The term disconnected pancreatic duct (DPD) describes an anatomical state in which the ductal continuity between viable pancreatic tissue and duodenum is interrupted. In contrast, DPDS is a clinical condition characterized by symptomatic production of pancreatic juice in an isolated pancreatic segment. It is important to differentiate them as they require different management decisions. In a study comparing complete and partial disruptions, patients with complete MDP interruption had higher incidence of recurrent/refractory fluid collections or recurrence of pancreatitis after initial treatment and higher frequency of surgical intervention [4]. Incomplete disruptions can be managed with transpapillary stenting, whereas a more complex approach is required in DPD [1, 5]. Furthermore, spontaneous healing may be anticipated with lesser degrees of ductal injury.

In current clinical practice, pancreatic duct disruptions or disconnections are not aggressively looked for in patients with NP as the entire focus of initial management is elsewhere, although the integrity of the MPD is an important contributor to long-term outcomes. Diagnosis of DPDS

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may be concurrent with that of NP or may be evident often months–years after resolution of necrotic collections [6]. Although some patients may also have a disconnected duct and be completely asymptomatic with their ductal discontinuity only visualized incidentally on imaging, universally accepted recommendations regarding the preferred method and timing in diagnosing a disrupted or disconnected pancreatic duct are currently lacking. The revised Atlanta classification mentions DPDS, or rather a disruption of the pancreatic duct, briefly in connection with necrotic collections or as a possible factor in the formation of pancreatic pseudocysts. In the section dedicated to walled-off necrosis (WON), it is stated that demonstration of the presence or absence of pancreatic ductal communication is not necessary in the classification of WON, although determination of such is of potential importance for further care [7]. Though the international multisociety International Association of the Pancreas/American Pancreatic Association guidelines published in 2013 are an outstanding source of data addressing the management of AP, systematic guidelines addressing the management of DPDS have not been formulated or implemented [8] although their update is underway, suitably with a section on DPDS. The current guidelines of the European Society of Gastrointestinal Endoscopy on the management of NP suggest performing imaging (preferably secretin-enhanced magnetic resonance cholangiopancreatography) of the MPD prior to stent removal after endoscopic drainage of WON, although this recommendation was indicated weak with very low-quality evidence [5].

Leaving aside clinical suspicion, the diagnosis of DPDS is fundamentally based on imaging methods. Several modalities may be employed including widely available contrast-enhanced computed tomography (CECT), along with endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasonography (EUS). To aid the diagnostic process, it is possible to measure amylase levels in the drain output in patients with percutaneously drained fluid collections, ascites, or pleural effusions. The radiodiagnostic features suggested to confidently recognize DPD have been the presence of viable pancreatic tissue upstream from the site of necrosis and extravasation or total cutoff of contrast material injected at pancreatography. Though the reference method for confirming the diagnosis has historically been ERCP, as an invasive procedure with a risk of complications, its indications are subject to strict criteria. Furthermore, it fails to show the upstream pancreatic duct and cannot differentiate between a high-grade stenosis and a disconnected duct [9]. In this respect, MRCP is far more appropriate. Although the prevalence of this method is increasing, it is still not routinely available at many institutions, especially its secretin variant (sMRCP). That being said, CECT remains the diagnostic pillar for assessing the severity of AP in all patients.

In the preceding context, there are not many studies on the diagnostic accuracy of imaging modalities for the detection of DPD. In this issue of *Digestive Diseases and Sciences*, Timmerhuis et al. [10] present a meticulous systematic review evaluating several diagnostic methods for diagnosing a disrupted or disconnected pancreatic duct in patients with moderate to severe AP. They included eight studies, evaluating five different diagnostic modalities in 142 patients. Abdominal CECT demonstrated the lowest sensitivity, ranging from 0 to 80%. A sensitivity of 100% was reported for EUS and ERCP. A sensitivity of 100% and a specificity of 50% were found for amylase measurements in drain fluid. The sensitivity for MRCP with or without secretin was 83%, both with a specificity of 100%. For a combined cohort of MRCP and sMRCP, a sensitivity of 92% was found, with authors' conclusion that MRCP/sMRCP should be recommended as the first-line diagnostic modality.

Strengths of this systematic review [10] include punctilious conception and execution. Granted, this is currently the only literature available, the number of relevant patients was relatively low, the majority of conclusions were built on one or two studies per modality, and only about half of the analyzed studies looked into the diagnostic accuracy as their target endpoint. Of note, the examined studies used ERCP or surgical confirmation as their reference standard, focusing solely on duct integrity and somewhat disregarding the presence or absence of gland enhancement upstream. Another drawback is that duct disruption and disconnection could not be distinguished in the systematic review. Nonetheless, the results of Timmerhuis et al. are without a doubt relevant for clinical practice and will be helpful to design new studies with improved methodology that are needed to ultimately define an algorithm for early and accurate detection of DPD.

Given the favorability of the available data, it is now tempting to proclaim sMRCP as the ideal instrument for diagnosing DPDS, though CECT unarguably deserves its place in the diagnostic algorithm and maybe a little more understanding before it falls out of favor, in particular since its operational characteristics in the detection of DPD simply have not been formally investigated, especially later in the disease course when obvious signs may be expected. Since imaging findings in NP evolve over time, DPD features may not be evident during the initial hospital course. This early imprecision is less relevant as the initial treatment is identical in all patients with severe AP regardless of MPD integrity. Available data show that although pertinent CECT features of DPD become evident in most patients by 2 weeks after the initial insult [9], DPDS was diagnosed at a median duration of 163 days (3–1095 days) after symptoms onset [9, 11].

Regarding CECT, Timmerhuis et al. [10] analyzed two studies with one demonstrating a sensitivity of 0% [9]. When examined in detail, it concerned CT images of 26 patients

Fig. 1 CECT showing unequivocal DPD (circled) 1 year after completed endoscopic transluminal necrosectomy, with transgastric double-pigtail stents remaining in place

with surgically confirmed DPD that were viewed retrospectively for features of DPD. Even though signs consistent with the diagnosis of DPD could be traced in all, not a single original report described DPD. Therefore, the most common reason for delayed or missed diagnosis is a lack of awareness and general unfamiliarity among treating physicians and radiologists. Virtually every imaging study has zero sensitivity when physicians involved are not familiar with the diagnosis.

Granted, CECT or any other imaging method may provide confusing results early in the evolution of severe NP. However, late in the course, and particularly after demarcation or debridement of pancreatic necrosis is complete, CECT often provides an obvious clue as to the presence of DPD (Fig. 1). The differentiation between early DPD and late DPD is not often made.

Although the DPDS is an underrecognized complication of NP, it may be the main long-term challenge in this patient population. CT imaging, in concert with appropriate clinical and laboratory data, is still the mainstay of assessing the severity and prognosis for all patients with severe AP, and it should be the means of diagnosing DPD whenever possible. If there is subsequent ambiguity about the diagnosis, advanced modalities may be used. Last but not least, symptomatology of the condition is necessary and is to be regarded essential when making the diagnosis.

Compliance with Ethical Standards

Conflict of interest All authors declare no conflicts of interest relevant to this article.

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