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The morphologic evolution of necrotic pancreatic fluid collections and their management. Asymptomatic: delay, defer and don't panic!

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Pancreatic necrosis is a serious complication of acute pancreatitis (AP) that occurs in 10-20% of patients. It is a local complication involving pancreatic parenchyma, surrounding soft tissue and possibly extending to adjacent organs. Societal guidelines acknowledge pancreatic necrosis to be a marker for severity, associated with greater length of hospitalization, need for invasive interventions, mortality, and elevated risk for readmission following discharge when contrasted to patients with interstitial pancreatitis [1,2]. Pancreatic necrosis is associated with fluid collections. The revised Atlanta Classification distinguishes fluid collections in the setting of AP into two categories: collections that occur in the setting of interstitial pancreatitis or in the setting of pancreatic necrosis. Collections found in the setting of pancreatic necrosis are further categorized based on their maturity. Acute necrotic collections (ANC) are found within the first month following acute necrotizing pancreatitis and generally lack organization/coherent architecture. These collections progressively develop a well-defined wall, i.e. walled-off necrosis (WON) [3].

The amount of solid debris contained with ANC and WON varies. The revised Atlanta classification recommends that the term pseudocyst (PC) stringently be avoided for collections that contain any degree of solid, necrotic material. The degree to which the presence of solid debris establishes a pancreatic/peri-pancreatic fluid collection to be necrotic in origin is by no means reliable. One study evaluating CT findings in a cohort of patients managed with endoscopic therapy for fluid collections in the setting of AP reported CT evidence of solid debris to be more frequent in those ultimately diagnosed with WON. However, only 45% of patients with established WON had identifiable solid debris on CT scan imaging [4]. MRI and EUS may be more effective modalities for identifying a complex collection in the setting of pancreatic necrosis, possibly not without limitations as well [5-8].

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Importantly, beyond the limitations of imaging, very little is known about the natural history of fluid collections in the setting of necrotizing pancreatitis in the absence of intervention. Smaller collections (<4 cm) in the absence of pancreatic duct disruption are more likely to resolve; however, the available literature does not clearly delineate which fluid collections are in the setting of pancreatic necrosis [8-10].

Rana *et al* in this issue of *Annals of Gastroenterology* offer to us an intriguing assessment of the natural history of ANC and WON in the form of a prospective cohort study [11]. The authors enrolled patients with persistent fluid collections at 6 weeks on non-invasive imaging following necrotizing pancreatitis in a program of serial EUS surveillance at 6 week, 3 and 6 month intervals. Forty-seven patients were initially enrolled with the majority of them having radiographic evidence of extensive pancreatic injury (87% with >30% pancreatic gland necrosis) and all having evidence of pancreatic fluid collections at a 6-week interval.

Collections at the time of first (6-week) EUS assessment were large (median 10 cm) and the majority of patients (87%) had solid debris. Of interest, the authors documented a heterogeneous group of outcomes for patients that were followed longitudinally. First, of the 47 patients, 5 (11%) had complete resolution of their collections without intervention over 6 months. Eleven (23%) patients ultimately required endoscopic drainage presumably for attributing symptoms. Finally, in those patients with persistent collections that returned for repeat EUS exams throughout the duration of the study, the size of the collections decreased and solid debris was present in less than 50% at 6-month surveillance interval.

A substantial proportion of the study cohort (22 patients, 47%) did not return for all surveillance EUS exams, which is a limitation of the study. Also, details of the indications for those patients that underwent endoscopic intervention are missing. However, in spite of these limitations one may draw helpful conclusions from this study.

First, this study clearly supports what we are all beginning to realize about necrotizing acute pancreatitis. Such patients represent a heterogeneous group with respect to short and long term outcomes. It is clear that a substantial number of patients in this cohort required an invasive intervention for persistent, symptomatic collections (11, 23%). The majority of the endoscopic interventions were performed within the 6- to 18-week interval (7/11). However, a large proportion of the overall cohort (14, 30%) did not require an intervention at 6 months, with the majority of these collections having either resolved, diminished in size, or fully liquefied. While

it is difficult to make any assumptions on the 22 patients that were lost to follow up over 6 months, we can conclude that at least 60% of the cohort did not require an intervention at the 3-month interval imaging, with the collections in this subgroup of the cohort becoming liquefied and/or diminishing in diameter. This data certainly supports the fact that solid, necrotic debris within WON is dynamic, often liquefies and is potentially resorbed with time.

Second, these findings may have some import for medical decision making with reference to management of these patients. Our impression is that they further reinforce a strategy of watching and delaying when it comes to invasive interventions such as endoscopic drainage and/or necrosectomy; especially in the absence of debilitating symptoms. It is now well established that a delay and a minimally invasive approach in patients with WON translates to fewer complications and better outcomes [12-14]. With the knowledge from this study that an intervention can be either averted or delayed beyond 6 months in a significant proportion of patients with WON, we feel all that more confident with this conservative strategy. Additionally, based on large endoscopic series with varying median time intervals from sentinel AP to intervention, allotting these collections ample time to liquefy and mature may be associated with a greater likelihood of technical, recurrence-free success and possibly even lower procedure burden. However, more prospective research is needed to substantiate this theory [15-17].

Overall, this study, in spite of its limitations, adds to our understanding of the natural history of pancreatic fluid collections in the setting of acute necrotizing pancreatitis. A substantial proportion of ANC and WON will liquefy, diminish in size, and possibly even resolve spontaneously, though the exact proportion remains to be established. This study offers a convincing argument that there is a subset of patients with necrotic peripancreatic/pancreatic fluid collections that do not require intervention in spite of extensive pancreatic parenchymal injury. It also promotes the strategy of expectant management and radiographic surveillance, deferring early invasive interventions in the absence of debilitating symptoms or infection.

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