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Natural course of asymptomatic walled off pancreatic necrosis

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ABSTRACT

Introduction: There is paucity of data on natural course of asymptomatic walled off necrosis (WON).
Objective: To study the natural course as well as outcome of conservative management in patients with asymptomatic WON.
Methods: Retrospective analysis of prospectively maintained data base of patients with asymptomatic WON presenting to us 4–6 weeks after an episode of acute necrotising pancreatitis (ANP).
Results: Forty three patients (37 M; mean age: 38.2 ± 10.4 years) with asymptomatic WON were studied. The size of WON ranged from 5 to 16 cm (mean 8.2 ± 2.2 cm). The site of WON was head, body and tail in 5 (11%), 34 (79%) and 4 (10%) patients respectively. Thirty of 43 patients (70%) patients did not have any complications during the expectant management period of 3 weeks–32 months with 13 (30%) patients having spontaneous resolution within 6.2 ± 3.4 months. Thirteen (30%) patients became symptomatic or developed complication within 3.2 ± 1.3 months. These were refractory pain (n = 7), infection (n = 4), spontaneous rupture into gastrointestinal tract (n = 5; stomach in 3, duodenum in 1 and colon in 1 patient respectively) and bleeding from splenic artery pseudoaneursym in 1 patient.
Conclusions: Majority of patients with asymptomatic WON have an uneventful clinical course. However, one third patients will develop symptoms/complications requiring interventional treatment.

1. Introduction

Acute pancreatitis (AP) is a disease of varying severity and can be associated with life threatening local and systemic complications [1,2]. Pancreatic necrosis is one of the important determinants of prognosis in AP and its presence is usually associated with protracted and complicated clinical course [1]. Acute necrotizing pancreatitis (ANP) usually leads on to development of pancreatic fluid collections (PFCs) that can be symptomatic or cause various life threatening complications. These fluid collections were previously labelled as acute fluid collections in the early phase of illness when they were not enclosed by a well formed wall and the walled off collections in the delayed phase of illness were labelled as pseudocysts. However, better understanding of pathogenesis and course of disease led on to revision of the Atlanta Classification by the Acute Pancreatitis Classification Working Group [1]. In this new classification a PFC's following AP were classified into four categories with important differentiating criteria being presence or absence of enclosing wall and the content being liquid only or mixed with solid necrotic debris [1].

The walled off PFC following ANP with solid necrotic content is labelled as walled off necrosis (WON). WON may be symptomatic with abdominal pain, early satiety, fever, jaundice or gastric outlet obstruction or may remain asymptomatic. Symptomatic WON is an indication for intervention which may be endoscopic, radiological or surgical [2]. However, there is no consensus on management of asymptomatic WON and current guidelines recommend conservative treatment regardless of size of WON and etiology of AP [3,4]. The conservative management is associated with risk of life threatening complications like infection, bleeding and rupture of PFC. Also, these guidelines are usually based upon expert opinion and there is scant data to support expectant management of asymptomatic WON. The natural history of asymptomatic WON has not been adequately studied and available studies are few, retrospective with small sample size, short follow up and heterogeneous study population [5–8]. Moreover, consequences of long-term expectant management of patients with asymptomatic WON has not been studied. Therefore, we conducted a retrospective analysis of prospectively maintained data base of patients with asymptomatic WON seen in our unit over last three years with an aim to study their natural course as well as outcome of conservative management.

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2. Patients and methods

This retrospective study was based on prospectively collected data of all consecutive patients more than 18 years of age with asymptomatic WON seen in our unit, a pancreatology unit in a large tertiary care hospital in north India, over last three years (2014–17). All enrolled patients had been earlier diagnosed with ANP based on revised Atlanta classification and had subsequently developed asymptomatic WON [1]. The study protocol was approved by the institutional ethics committee.

Patients with well documented WON on imaging [computed tomography (CT)/Magnetic resonance imaging (MRI)/Endoscopic ultrasound (EUS)] were enrolled in the study. WON was defined as an encapsulated collection of fluid and solid necrotic debris that developed following ANP. The diagnosis of WON was made if all the following conditions were met:

1. Documented evidence of diagnosis of ANP earlier with contrast enhanced CT (CECT) documenting pancreatic/peri-pancreatic necrosis.
2. Encapsulated collection with solid necrotic component as depicted by relative hyperdense content within the hypodense collection on CECT or internal heterogeneity on T2 weighted MRI images or echogenic content on EUS. The presence of necrotic debris was confirmed by the presence of echogenic material on trans-abdominal ultrasound.

With an aim to study natural history of WON from the time of its presumed formation, patients of asymptomatic WON presenting within 4–6 weeks of an attack of ANP were included. Patients presenting >6 weeks after an attack of ANP, having symptomatic WON, pseudocyst, WON not clearly visualized on trans-abdominal ultrasound and patients not on regular follow up were excluded.

The clinical findings and laboratory investigations were retrieved from the data base. The details of imaging findings especially size of WON in longest dimension as well as its location were also retrieved. These patients were regularly followed up in outpatient clinic every three monthly. On follow up, a detailed clinical assessment as well as trans-abdominal ultrasound was done. The size of WON in its longest dimension was measured and recorded. In the event of occurrence of new symptoms or complications, imaging and interventions were done at the discretion of treating clinician. The patients were followed up till spontaneous clinical recovery with resolution of WON, need for intervention or mortality.

3. Results

During the study period, 163 patients with WON were seen in our unit. Since ours is a tertiary care referral hospital and patients were referred to us at different phases of illness, they presented to us at 4 weeks–6 months after an attack of ANP. Of these 163 patients, 120 were excluded (53 patients presenting >6 weeks after an attack of ANP, 52 patients having symptomatic WON, 5 patients having pseudocyst, WON not clearly visualized on ultrasound abdomen in 6 patients and 4 patients lost to follow up). After exclusion, 43 patients (37 males; mean age: 38.2 ± 10.4 years) with asymptomatic WON were studied. The etiology of ANP was alcohol in 28 (65%), gall stones in 7 (16%), hypertriglyceridemia in 1 (2%) and idiopathic in 7 (16%) patients. Nine (21%) patients had 2 or more WON whereas 34 (79%) patients had single WON. The size of WON in longest dimension ranged from 5 to 16 cm (mean: 8.2 ± 2.2 cm). The WON were located adjacent to head of pancreas in 5 (11%)

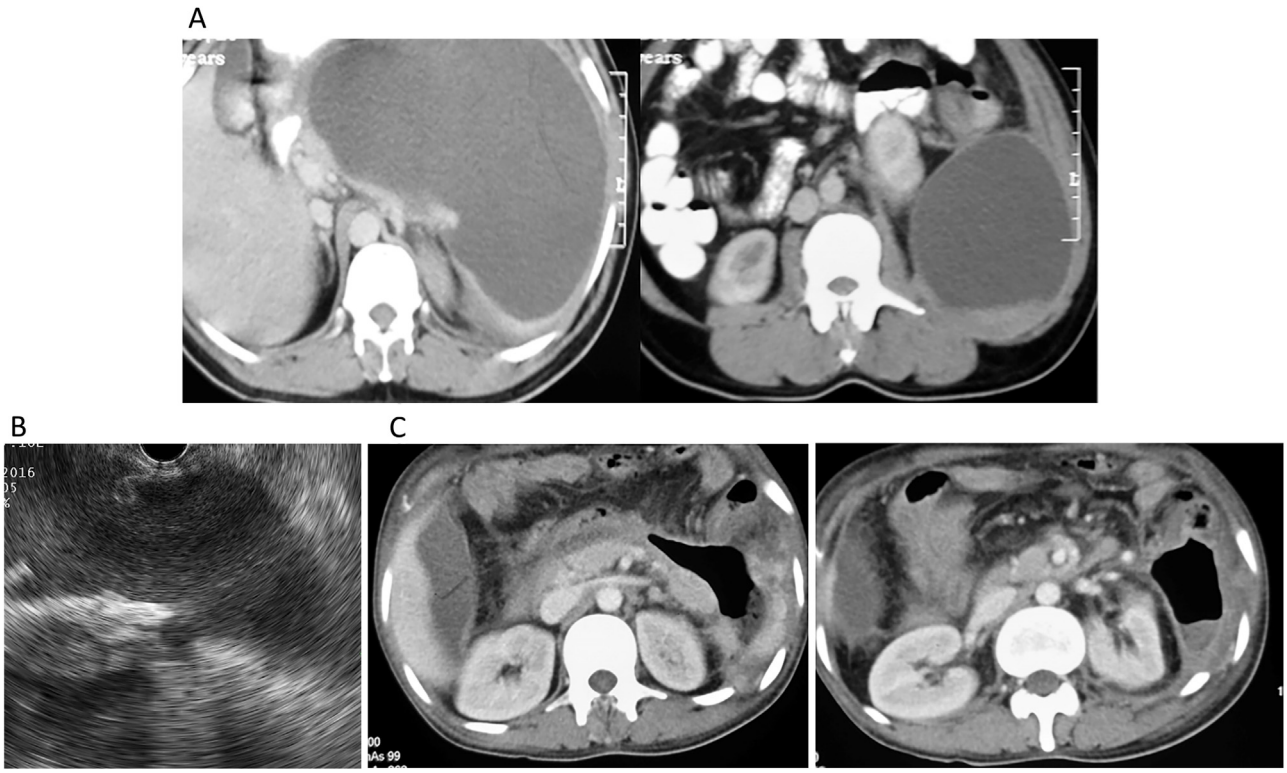

Fig. 1. (A) CT at 6 weeks: large asymptomatic WON with left para-colic extension. (B) EUS at 6 weeks: Large WON. (C) CT at 11 weeks: WON has ruptured into descending colon with air in the cavity because of bowel communication.

patients, body of pancreas in 34 (79%) patients and tail of pancreas in 4 (10%) patients. Seven (16%) patients had WON extending to the paracolic gutter. None of the asymptomatic patients under went endoscopic or radiological or surgical drainage and were regularly followed up in outpatient clinic.

As these 43 patients were enrolled in the study at different time periods and therefore, had variable follow up period. The median follow up period was 7 months (range: 3 weeks–32 months). During follow up, 30 (70%) patients remained asymptomatic with WON resolving in 13 (43%) patients within 6.2 ± 3.4 months. In 11 (26%) patients, size of WON decreased from mean of 9.1 cm–4.8 cm whereas in 6 (13%) patients it increased from 9.3 to 12.6 cm but patients continued to be asymptomatic. No intervention was done in these asymptomatic patients despite increase in size of WON till the last follow up.

Thirteen (30%) patients became symptomatic or developed complications during mean follow up period of 3.2 ± 1.3 months. The complications or symptoms observed were: refractory abdominal pain (n = 7); infection (n = 4) and spontaneous rupture (n = 5; stomach in 3, duodenum in 1 and colon in 1). One patient had massive gastrointestinal bleeding from splenic artery pseudoaneurysm. Of seven patients with pain/infection, mean size of WON increased from 7.7 ± 1.7 cm to 10.8 ± 1.4 cm. Patients with abdominal pain and/or fever were successfully treated with EUS guided transmural drainage with fully covered self-expanding metallic stent or multiple plastic stents. The patients with spontaneous rupture into stomach or duodenum were successfully treated with endoscopic transmural drainage by enlarging the rupture site and placing multiple plastic stents with or without nasocystic drain (Figs. 1 and 2). The patient with spontaneous rupture into colon underwent successful surgical treatment. The patient with bleeding splenic artery pseudoaneurysm underwent successful angioembolisation followed by EUS guided transmural drainage.

All the complications developed within 6 months of an attack of ANP with median period of 10 weeks and none of the patients succumbed to the illness.There was no significant difference in the size of WON at presentation between patients who remained asymptomatic versus patients who developed symptoms/complications (8.0 cm vs 8.8 cm; p = .28). All 5 patients with WON located adjacent to head of pancreas developed symptoms or complications whereas all 4 patients with WON located adjacent to tail of pancreas had spontaneous resolution or remained asymptomatic.

4. Discussion

WON develops after an attack of ANP and evolves from an acute necrotic collection (ANC). The ANC gets encapsulated with an inflammatory wall within 4–6 weeks after an attack of AP leading on to formation of a heterogeneous collection comprising of mixture of solid and liquid necrotic content [1]. The WON may be symptomatic necessitating intervention or may remain asymptomatic. The asymptomatic WON is a therapeutic dilemma because of lack of availability of reliable information about natural history of ANC's and WON [9,10]. Based upon personal experience of experts and limited short term studies reporting instances of gradual resolution of asymptomatic PFC current guidelines recommend conservative non-interventional treatment of asymptomatic WON, regardless of size, duration and extent [3,4]. However, natural history of asymptomatic WON has not been systematically studied and actual frequency as well as factors responsible for spontaneous resolution is unknown. Also, consequences of expectant management are also not known.

In current study, we found that 70% of patients with asymptomatic WON remained asymptomatic during median follow up of 7 months with WON resolving or decreasing in size in 56% of patients. However, 30% patients developed symptoms or complications requiring intervention. Wroński et al. studied 16 patients with asymptomatic WON and found that 44% of patients remained asymptomatic during a median follow up of 17 months (range 7–53.5 months) [8]. In a short term follow up study of 6 months using EUS, we had previously reported that 23% of patients with WON needed intervention on follow up [7]. Also, WON resolved in 11% patients and completely liquefied in 40% patients at 6 months [7]. Patra et al. studied 39 patients with WON for 6 months and reported that WON either resolved or remained asymptomatic in 77% patients whereas intervention was needed in 23% patients [5]. However, another short term study of 3 months of 76 patients of WON, reported higher intervention rates of 70%) [6]. The authors hypothesized that higher intervention rates could be because of inclusion of more patients with organ failure and extensive pancreatic necrosis suggesting more severe disease. Majority of above mentioned studies suggest that more than 50% of patients with asymptomatic WON have spontaneous resolution or decrease in size of WON on follow up, thereby supporting current practice of careful surveillance and non-interventional expectant management.

In our study, 23% patients with WON developed complications with rupture into adjacent gastrointestinal tract and infection being the most common. Similar observations of infection and rupture being common complications of expectant management of WON have been reported by previous studies [5,8]. We also found that none of these complications occurred after 6 months of follow up and similar observation was also recorded by Wroński et al. where no complications occurred after 7 months [8]. These observations stress need for closed and rigorous surveillance for first few months after development of asymptomatic WON. In accordance with previously published studies, we also found that majority of complications could be successfully treated endoscopically and there was no mortality.

Erosion into the adjacent blood vessel leading on to massive life threatening haemorrhage is the most dreaded complication of expectant management of PFC's. Fortunately, only one patient (2%) developed arterial pseudoaneurysm leading on to gastrointestinal bleeding and could be successfully management using angioembolisation followed by endoscopic drainage. Similar observations of rarity of vascular complications following expectant management of asymptomatic WON have been reported by previous studies [5–8]. Also, these vascular complications associated with WON can be successfully managed using a combination of angioembolisation and endoscopic drainage [11].

As discussed above, 30–40% patients with asymptomatic WON develop symptoms and complications and it is important to identify this subset of patients who would need a close follow up. One of the obvious factors that could predict complications could be size of WON. But we found that there was no significant difference in thesize of WON at presentation between patients who remained asymptomatic versus patients who developed symptoms/complications. Wronski et al also found that there was no significant difference between either the size of WON or its extension into para-renal space between patients who remained asymptomatic versus patients who developed symptoms/complications [8]. These observations are in contrast to results obtained in patients with pseudocysts where size is an important factor predicting spontaneous resolution [12–15]. These studies have reported that pseudocysts less than 4 cm usually resolve spontaneously whereas pseudocysts larger than 6 cm in diameter are less likely to resolve spontaneously [12–15]. This difference in importance of size in predicting outcome in WON and pseudocysts could be because of different pathogenesis. Pseudocysts are usually formed due to pancreatic duct disruption and larger pseudocysts usually have major duct disruption that is less

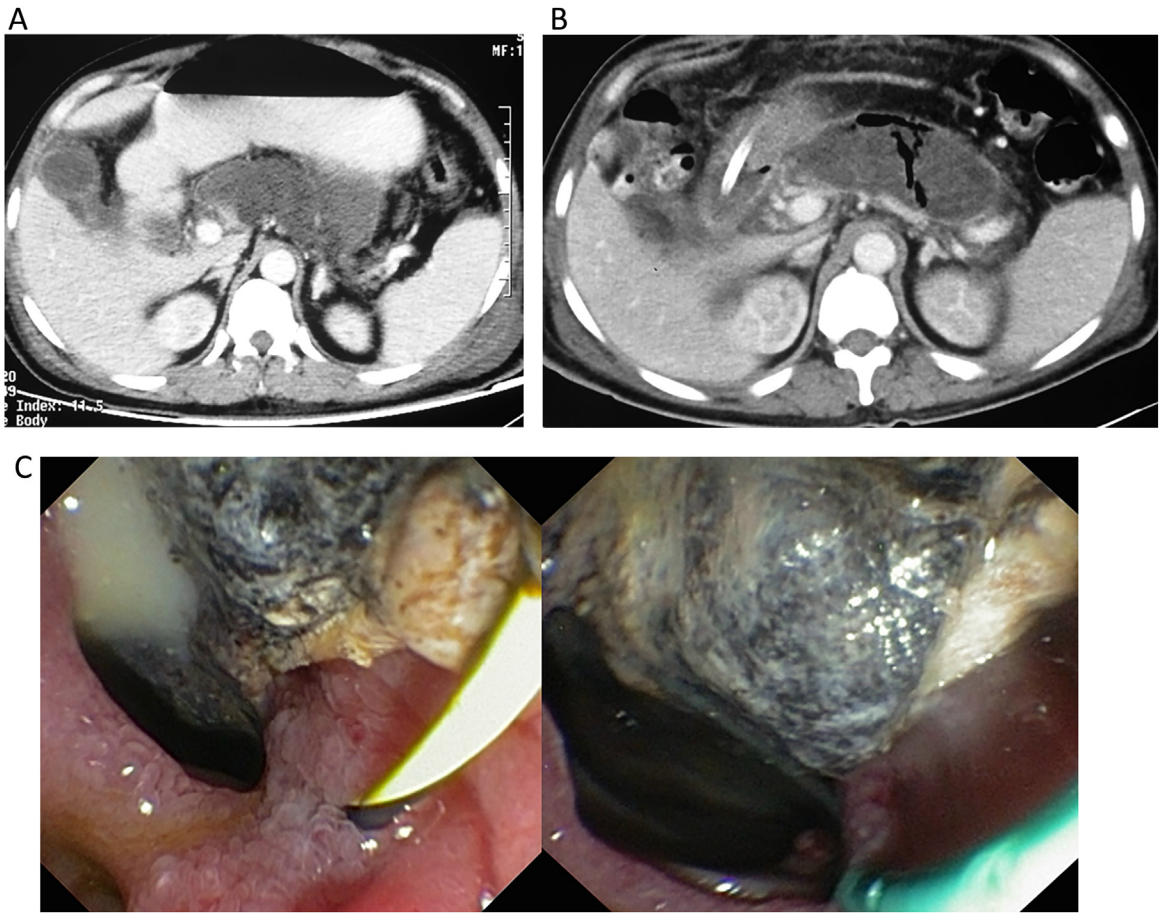

Fig. 2. (A) CT at 5 weeks: WON adjacent to body of pancreas. (B) CT at 14 weeks: air seen in WON cavity because of rupture into duodenum. (C) Endoscopy showing opening in the duodenum. Endoscopic drainage of necrotic material being done.

likely to heal spontaneously. WON is formed due to combination of pancreatic/extra-pancreatic necrosis and duct disruption. Many patients with large WON may not have duct disruption or develop pancreatic parenchymal atrophy because of extensive parenchymal necrosis, thereby, preventing further increase in size of WON by continued leakage of pancreatic juice. a None of the studies have looked at impact of pancreatic duct disruption on the outcome of asymptomatic WON and this area warrants further investigation. We also found that WON located in head were more likely to develop symptoms and complications and this could be because of limited space available for expansion.

Previous studies have also reported that patients with WON who developed complications or symptoms had higher admission packed cell volume and required more fluids in first 72 h, higher BISAP score, higher frequency of organ failure, and more pancreatic parenchymal necrosis at time of admission with ANP [5,6]. for further management of WON and therefore, we did not have baseline data of organ failure, fluids administered and indices of severity in many patients.

Although ours is the first study that has evaluated natural history of asymptomatic WON with a longer follow up of up to 3 years in some patients, it has few limitations also. Firstly, this is a retrospective study from a single centre but the data base was maintained prospectively with rigorous follow up and minimal drop outs. Also, as many of patients were referred from other centres, the baseline data of ANP and its management was not available. Moreover, follow-up is variable ranging from 3 to 32 months and short follow up in few of the enrolled patients is a major limitation of this study.

In conclusion, majority of patients with asymptomatic WON have an uneventful clinical course with WON spontaneously resolving in one third patients within 6 months. However, one third of patients will develop symptoms or complications that require interventional treatment. Further studies with large sample size are needed to study factors that can predict complications in patients with asymptomatic WON.

Conflict of interest

None declared.

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