Opinion

Redefining acute acalculous cholecystitis: insights into its systemic inflammatory implications

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Richard C Semelka MD,[1] Miguel Ramalho MD[2]
[1]Richard Semelka Consulting, PLLC, USA
[2]Department of Radiology, Hospital da Luz, Portugal

Correspondence: Richard Semelka MD, Richard Semelka Consulting, PLLC, 3901 Jones Ferry Road, Chapel Hill, NC 27516, USA, Email richardsemelk@gmail.com

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The eyes don't see what the mind does not look for (modified quote originally attributed to DH Lawrence)

Opinion

Acute acalculous cholecystitis, biliary dyskinesia, and ampullary dysfunction are part of a family of gallbladder and biliary tree conditions in which no calculi are present, but the system is either inflamed or dysfunctional.[1,2] Traditionally, delayed passage of radiotracer in the biliary tree with hold-ups in nuclear medicine studies has been the imaging modality relied on to make the diagnosis.[1-3] Acute acalculous cholecystitis has been treated with cholecystectomy because of prolonged and sustained RUQ pain despite the absence of cholelithiasis. Patient symptom relief has been marginal, with at best 40% experiencing symptom relief following cholecystectomy.[4,5] More recently, authors have proposed that acute acalculous cholecystitis may be a systemic disease, explaining why cholecystectomy does not relieve symptoms in most sufferers.[6,7]

Over the last three years, we have observed a consistent finding in individuals who did not have gallstone disease, with clinical pictures of: "evaluate for RUQ pain," "evaluate for bile duct dyskinesia," or similar. The finding was that these subjects all had circumferential inflammatory changes of the proximal duodenum, alone or in combination with extension to and asymmetric involvement of the gallbladder (greater inflammation adjacent to the duodenum). This was especially noticeable when these organs abutted one another (Figure 1). In patients with suspected biliary or ampullary dysfunction, whether or not the gallbladder was present or surgically absent, circumferential duodenal inflammation was evident abutting the CBD or surrounding the ampulla and tracking up the distal CBD.[8] Regional inflammation in acute cholecystitis is relatively common.[9-15] Prior reporting has suggested that in a non-negligible number of cases, regional inflammation may be a triggering factor for acute cholecystitis.[11]

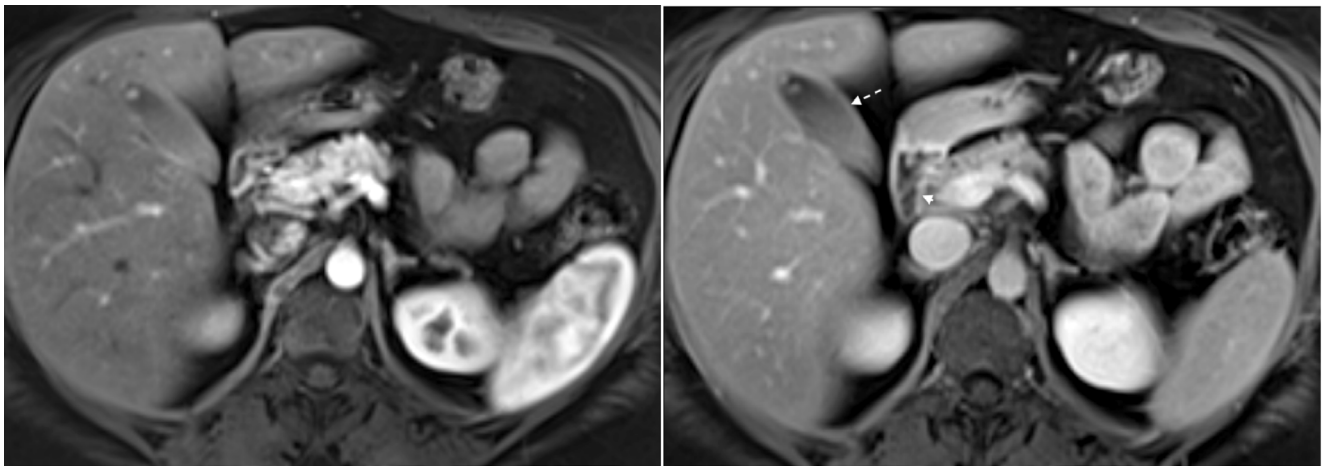

Figure 1 Chronic acalculous cholecystitis with simultaneous upper GI inflammation. Axial T1-weighted images acquired in the arterial phase (a) and the interstitial phase (5-minute delay) (b). Progressive increased mural enhancement of the duodenum is observed in the interstitial phase (short arrow, b). Moderately increased enhancement of the gallbladder is shown as enhancement of the gallbladder wall that shows progressively increased intensity from arterial phase to interstitial phase enhanced images (dashed arrow, b). Incidental gallbladder polyp was observed.

One author (RCS) who interpreted more than 1000 cases of individuals with hepatosteatosis over two years from 2021- 2023[8] observed in all subjects who had suspected gallbladder or biliary disease, with no biliary stone disease identified, which numbered in excess of 100, that all of them showed prominent duodenal inflammation. Interestingly, despite being published extensively on abdominal MRI, including in a definitive textbook,[16] why were these observations not made previously? The explanations probably reflect: 1) up to the present time, the primary indications for abdominal MRI studies have been investigating malignancy, 2) the increasing

incidence of obesity in the population, 3) this finding of inflammation is best shown on images acquired 5 minutes post GBCA contrast injection, and traditionally we have acquired the final postcontrast images at 2 minutes. Our current experience has informed us that 5 minutes postcontrast is the optimal time to observe inflammation, especially mild inflammation, which may not be apparent at 2 minutes postcontrast. Our theory for the heightened appearance of inflammation at 5 minutes is that it takes time for the combination of leakiness of capillaries and prolonged retention of contrast in the extracellular matrix to be consistently evident. In traditional imaging practice, various abdominal pain settings not related to cancer are imaged by ultrasound or CT. In all patients in our recent experience, ultrasound studies, which were commonly performed in this group, were interpreted as negative, which reflected that ultrasound is poor at visualizing the bowel, especially in overweight adults. Similarly, CT, if obtained, did not appreciate the inflammation of the proximal duodenum, which is accounted for by the poorer definition of increased enhancement due to inflammation than observed on MRI, which has been known for at least 32 years. This was the case also when looking retrospectively at the current collection of cases: the bowel findings were not evident on CT.

The findings of this duodenal inflammation are best shown as moderately intense enhancement on 5-minute post-GBCA MR images. Most cases showed mildly increased enhancement on late arterial phase images obtained 30 seconds after injection. We have termed this progressively intense enhancement from late arterial to late venous phase images.

It is also essential to recognize that MRI with GBCA should be used prudently, as some individuals may develop a toxicity termed Gadolinium Deposition Disease.[17] If GBCA is not used in the MR study, on a non-contrast MRI study, low B value Diffusion Weighted Imaging (DWI) can appreciate high signal in the wall of the second portion of the duodenum, suggestive of inflammation, but it is considerably less sensitive than 5-minute post-GBCA imaging. Noncontrast MRI may suffice for some individuals, especially if it is a follow-up study. Our focus now is not to generate more abdominal MRI studies with GBCA but rather to ensure the patient receives the maximum amount of information available on the MR study when it is performed. This means looking for progressively intense enhancement of the gallbladder and the biliary tree on 5-minute post-GBCA images is imperative. Our current theory then for the majority of these conditions: acute acalculous cholecystitis, biliary dyskinesia, and ampullary dysfunction is that they represent primary duodenal inflammation, and secondarily gallbladder-biliary system inflammation. These structures experience sympathetic inflammatory changes secondary to the principal inflammation, which is of the duodenum.

Based on this theory, the primary treatment for these gallbladder and biliary conditions is not surgery, specifically not cholecystectomy or drugs directed at the biliary function, but rather focused attention on mitigating/ resolving the cause of duodenal inflammation. This may simply represent a rigorous change in diet.

Acknowledgments

None.

Conflicts of interest

None.

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