A 69-year-old man presented with right hypochondriac pain accompanied by postprandial nausea and vomiting for 2 months. Additional symptoms included fever and fatigue for 4 days. There was associated history of weight loss of approximately 6 kg over the past few months. Vital signs were normal, and he was febrile (38.3°C). His skin and sclerae were mildly icteric. He had no signs of liver failure. His abdomen was soft, with tenderness noted in the right hypochondriac region (Murphy sign positive); no tenderness was noted elsewhere, and there was no evidence of ascites. The tip of the gallbladder was palpable in the right 9th costal margin. Laboratory evaluation revealed mild conjugated hyperbilirubinemia (total bilirubin level, 2.1 mg/dL; direct bilirubin level, 1.1 mg/dL), with normal levels of transaminases and alkaline phosphatase. Mild hypoalbuminemia was present. Other investigations were unremarkable. On the basis of the clinical and laboratory findings, the patient was evaluated for obstructive jaundice, and ultrasonography (US) was performed.

**IMAGING FINDINGS**

US revealed an abnormally thick gallbladder wall measuring 3 cm in thickness. The wall thickening gave the appearance of an endophytic mass causing near-total obliteration of the lumen. Multiple intraluminal and intramural calculi were seen (Fig 1A). Few echogenic intramural foci were also seen. No color uptake was noted on power Doppler evaluation (Fig 1B). Sonographic Murphy sign was absent, and there was no pericholecystic fluid collection. Interval cholecystectomy was performed 4 weeks after initial presentation. At laparotomy, diffusely enlarged gallbladder was seen, which was firm and showed multiple adhesions. A gross cholecystectomy specimen showed diffusely enlarged gallbladder weighing 63 g and measuring 7.5 × 5.5 × 2.5 cm. On cut sections, the gallbladder was firm, with grayish thickened wall measuring up to 2.5 cm and velvety granular mucosa containing numerous multifaced intraluminal calculi. The gallbladder wall showed areas of hemorrhages and contained multiple pockets, many of which also contained calculi. Microsections showed ulcerations and edematous gallbladder mucosa and myoepithelial hyperplasia with abundant granulation tissue composed of myofibroblasts. Inflammatory cells, such as neutrophils, plasma cells, and macrophages, were also present, with congested vessels (Fig 2). The final diagnosis of adenomyomatosis of the gallbladder was confirmed by the characteristic histopathologic appearance of muscular and epithelial hyperplasia contributing to mural thickening, with epithelial invaginations forming the pathognomonic intramural diverticula known as Rokitansky-Aschoff sinuses (Fig 2). No evidence of malignancy was found.

**PATHOLOGIC EVALUATION**

Adenomyomatosis is not an uncommon mimic of the gallbladder carcinoma, identified in 1% to 8.5% of cholecystectomy specimens. A Table 1 summarizes the clinicoradiopathological features of gallbladder adenomyomatosis. It is most often an incidental finding, has no intrinsic malignant potential, and usually requires no specific treatment. Varied names have been applied to this lesion in the literature, including adenomyomatosis, adenomyoma, diverticular disease, intramural diverticulosis, cholecystitis cystica, and cholecystitis glandularis proliferans. It is more commonly seen in women than in men, the majority
presenting with complaints of chronic right upper quadrant pain. Frequent coexistence with cholelithiasis is seen; however, no causative relationship has been proved. Adenomyomatosis occasionally produces abdominal pain, and in some cases, cholecystectomy may be indicated for relief of symptoms.

Dysplasia, carcinoma in situ, and invasive carcinomas may arise from the epithelium of adenomyomatous hyperplasia. However, most authors believe that the cause for development of carcinoma in adenomyomatous hyperplasia is the presence of stones, chronic inflammation, and metaplastic changes rather than adenomyomatous hyperplasia itself. Thus, adenomyomatous hyperplasia is not considered a premalignant lesion.

US is considered as the baseline imaging modality to investigate the hepatobiliary system, and adenomyomatosis of the gallbladder is a not-infrequent pathology, seen in approximately 2% of patients. Evaluation of gallbladder wall thickness plays an important role in the sonographic study of the biliary system. The gallbladder wall is no more than 2 mm thick in 97% of healthy subjects, if the short axis of the gallbladder is at least 2 cm in diameter. Diffuse gallbladder wall thickening has a differential diagnosis that includes the more common inflammatory and noninflammatory causes of wall thickening. The various causes include hepatitis, artifacts induced by the presence of pericholecystic fluid, hypoalbuminemia, portal hypertension, right-sided heart failure, incomplete gallbladder distention, cirrhosis, hepatitis, and cholecystitis. In addition, focal thickening occurs in gallbladder carcinoma and adenomyomatosis. However, gallbladder malignancy should be suspected when there are features of a focal mass with locoregional lymphadenopathy, metastases, and features of biliary obstruction at the level of the porta hepatis.

The pathognomonic pathologic features of the adenomyomatosis are thickened gallbladder wall and intramural diverticula containing bile, with cholesterol crystals, sludge, or calculi that show a distinct correlation with the modality imaging findings. Longstanding Rokitansky-Aschoff sinuses of adenomyomatous hyperplasia result in calcification of the intramural sludge, cholesterol, or stones. Rarely, abdominal radiograph may show them as nondependent calcific opacities in the right upper quadrant.

On ultrasonography, gallbladder involvement by adenomyomatous hyperplasia is variable in location and extent, which varies from focal to diffuse gallbladder wall thickening. Luminal narrowing...
may be seen in the diffuse and segmental variants that may produce a characteristic hourglass configuration.

The diagnostic sonographic hallmark on ultrasonography is the presence of the anechoic or echoenic intramural diverticula. Anechoic diverticula contain bile, whereas those that contain sludge, cholesterol, or intramural calculi are seen as echoenic foci.4,7 Comet-tail/V-shaped reverberation artifact is due to echogenic sound reverberation emanating from the small echogenic foci in the gallbladder wall into the central anechoic lumen. Similar appearance may be caused by intraluminal or intramural air, as seen in emphysematous cholecystitis; however, the mobile nature of the air with dirty echogenic shadowing on ultrasonography helps in differentiating them. In equivocal cases, computed tomography (CT) plays an important role. CT findings of adenomyomatous hyperplasia usually correlate to the sonographic findings. All three pathologic forms (localized, segmental, and diffuse) are apparent on CT scans. Intramural cystic spaces and calculi demonstration on CT scan is not possible, but they are easily picked up sonographically because of reverberation artifact. This makes ultrasonography a primary diagnostic imaging modality for the diagnosis of adenomyomatous hyperplasia. The Rokitansky-Aschoff sinuses that are large enough may be seen on CT scan, giving a characteristic appearance, the rosary sign, which is due to the enhancing epithelium within intramural diverticula surrounded by the relatively unenhanced hypertrophied gallbladder muscularis.9 Magnetic resonance imaging (MRI) plays an important role in distinguishing adenomyomatous hyperplasia from malignant lesions; hyperintense intraluminal cavities visualized on T2-weighted MRI are suggestive of Rokitansky-Aschoff sinuses and have been reported to be useful.10 When arranged in a curvilinear pattern, they give an appearance of pearl necklace sign.11 The intramural calculi are seen as signal void because of the mineral content. The pearl necklace sign is specific for adenomyomatosis of the gallbladder and is not seen in gallbladder carcinoma.11 Differentiation of echogenic intramural foci from abnormal enhancement requires a multiphasic MRI protocol with intravenous contrast material. Diffusion weighted imaging has been found useful in differentiating gallbladder adenomyomatosis from gallbladder carcinoma and significantly improves the diagnostic accuracy.11a

In our case, US revealed an abnormally thick gallbladder wall measuring 3 cm in thickness.

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Table 1 – Summary Table for Clinicoradiopathological Features of Gallbladder Adenomyomatosis

| Etiopathogenesis | Adenomyomatosis is a rare disease of the gallbladder characterized by epithelial proliferation and formation of mucosal pouches through the thickened muscular layer of the gallbladder wall—the so-called Rokitansky-Aschoff sinus. Despite the name, this condition does not involve any adenomatous changes in the gallbladder epithelium and is not a premalignant condition.
| Incidence | 1%-8.5% |
| Sex ratio | Male:female = 1:3 |
| Age predilection | Predominantly fifth decade |
| Risk factor | None known; mostly an incidental finding. |
| Clinical presentation | The clinical picture can vary from asymptomatic (60%) to symptomatic patients. These symptoms can be dyspepsia, pain in the right hypochondrium, fever of unknown origin, acute or chronic cholecystitis. |
| Treatment | The treatment of choice for these tumors is surgical resection, both in symptomatic and asymptomatic cases, accompanied or not by cholecystitis, because of the uncertain evolution of this disease and the difficulty of differential diagnosis with carcinoma. Cholecystectomy is suitable when the process is located in the gallbladder. When the tree biliary is affected, surgical resection with free margins and enterobiliary derivation is indicated. |
| Prognosis | Favorable |
| Ultrasound | Mural thickening: can be diffuse, focal or annular
Comet-tail artifact: echogenic intramural foci from which emanate V-shaped comet-tail reverberation artifacts. |
| CT | CT rosary sign as a result of enhancing epithelium within intramural diverticula surrounded by the relatively unenhanced hypertrophied gallbladder muscularis |
| MRI | Hyperintense on T2-weighted images and hypointense on T1-weighted images; pearl necklace sign as a result of the characteristically curvilinear arrangement of multiple rounded hyperintense intraluminal cavities visualized at T2-weighted MRI and magnetic resonance cholangiopancreatography of adenomyomatosis. On diffusion weighted imaging, the cystic areas of the adenomyomatosis show high signal intensity. |

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.
The wall thickening gave an appearance of endo-
phytic mass causing near-total luminal oblitera-
tion. Multiple intramural and intraluminal calculi
were seen with few echogenic intramural foci,
which did not show the classic comet-tail rever-
beration artifacts. The cause for the diagnostic
dilemma was the absence of the comet-tail/V-
shaped reverberation artifact, which is the diag-
nostic sonographic hallmark of adenomyomato-
sis. Its absence can be explained on the basis of
the absence of central anechoic gallbladder lu-
men because of gross dense fibrous wall thicken-
ing causing near-total luminal obliteration.12

Although the imaging features of adenomyomatosis
can be distinctive enough to allow confident diag-
nosis, findings such as gallbladder wall thickening
and enhancement are somewhat nonspecific. The
differential diagnosis includes adenomatous, hyper-
plastic, and cholesterol polyposis, papillomatosis,
adenoma, portal hypertension, total parenteral nu-
trition, hypoalbuminemia, congestive heart failure,
and cystadenoma, as well as malignancies such as
gallbladder adenocarcinoma, carcinoid tumor, and
metastatic melanoma of the gallbladder (Table 2).

Metabolic characterization with [18F]fluorodeoxy-
glucose (FDG) positron emission tomography
may be a useful adjunct in problematic cases.13
Adenomyomatosis does not show any FDG uptake
on positron emission tomography study, which
makes it a problem-solving tool in differentiating
it from malignant gallbladder wall thickening,
which shows focal or diffuse FDG uptake.13 Though
the FDG uptake within these lesions represents the
metabolic activity of the underlying pathological
tissue (cancerous cells), false positive results
may also be seen in cases with associated active
inflammatory process such as cholecystitis.14

In conclusion, great difficulty arises in differenti-
ating the diffuse variant of adenomyomatous hy-
erplasia that simulates a gallbladder malignancy,
especially in the absence of the diagnostic hallmark
comet-tail/V-shaped reverberation artifact, which
may be absent in cases of total luminal obliteration by
the pathology. Surgical resection may be indicated in
symptomatic cases and when nonspecific find-
ings present a diagnostic dilemma.

DOI: 10.1200/JGO.2016.005249
Published online on jgo.ascopubs.org on June 15, 2016.

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### Table 2 – Differential Diagnosis for Adenomyomatosis of the Gallbladder and Their Imaging Characteristics

| Diagnosis                     | Ultrasound                                                                 | CT                                                                               | MRI                                                                 |
|-------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------|
| Gallbladder adenomyomatosis   | Echogenic intramural foci from which emanate V-shaped comet-tail reverberation artifacts | CT rosary sign as a result of enhancing epithelium within intramural diverticula surrounded by the relatively unenhanced hypertrophied gallbladder muscularis | Rokitansky-Aschoff sinuses as intramural lesions that are hyperintense on T2-weighted images, hypointense on T1-weighted images, and nonenhancing. On diffusion weighted imaging, the cystic areas of the adenomyomatosis show high signal intensity, which represents the Rokitansky-Aschoff sinuses. |
| Gallbladder carcinoma         | May completely fill the gallbladder lumen                                 | Hypoattenuating or isoattenuating mass in the gallbladder fossa                  | The tumor is usually bright on T2-weighted images and is poorly margined. On T1-weighted images, relative to the liver, the gallbladder carcinoma ranges from isointense to hypointense. Ill-defined early enhancement is a typical appearance of these tumors at dynamic gadolinium-enhanced MRI. On diffusion weighted imaging, the tumor shows lower signal intensity on the ADC maps. |
| Cholelithiasis                | The characteristic findings of gallstones are a highly reflective echo from the anterior surface of the gallstone, mobility of the gallstone on repositioning the patient (typically in a decubitus position), and marked posterior acoustic shadowing. | Gallstones appear as single or multiple filling defects within the gallbladder and are densely calcified, rim calcified, or laminated or have a central nidus of calcification. | Most gallstones have no signal on MRI and present as signal-void filling defects within the gallbladder. These are most apparent on T2-weighted sequences where signal-void stones are contrasted against high-signal bile. |

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.
AUTHOR CONTRIBUTIONS
Manuscript writing: All authors
Final approval of manuscript: All authors

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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No relationship to disclose
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No relationship to disclose

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