

## Intramural Hypoattenuated Nodules in Thickened Wall of the Gallbladder: CT Features According to Their Primary Causes<sup>1</sup>

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According to published reports, a common feature of xanthogranulomatous cholecystitis is the presence of intramural hypoattenuated nodules in thickened gallbladder wall. These nodules can, however, also be seen in pathological conditions such as acute cholecystitis, hyperplastic cholecystoses (cholesterolosis and adenomyomatosis), gallbladder cancer, and other inflammatory diseases such as tuberculosis. Retrospective review of the abdominal CT findings in 622 patients who for various reasons underwent cholecystectomy during a one-year period showed that intramural nodules were present in 60. In this pictorial essay we illustrate the imaging features of the many different pathological conditions which give rise to intramural hypoattenuated nodules in thickened wall of the gallbladder, correlating these features with the histopathological findings.

**Index words :** Gallbladder, CT  
Gallbladder, wall thickening

Intramural hypoattenuated nodules, which are occasionally found in thickened wall of the gallbladder, are caused by benign and malignant conditions such as hyperplastic cholecystosis, acute or chronic cholecystitis, xanthogranulomatous cholecystitis and gallbladder carcinoma. Although the presence of these nodules on radiological images sometimes provides a clue to diagnosis, it is not always easy - and sometimes impossible - to distinguish between the primary diseases which cause them. For correct diagnosis, an understanding of the pathologic basis of the nodules, as well as careful evaluation of a patient's clinical history or data, is important. Despite the difficulty involved, firm diagnosis on the ba-

sis of imaging studies obviates the need for wide surgical resection and sets the stage for prompt surgical intervention in patients in whom gallbladder disease involves the presence of intramural nodules.

The purpose of this essay is to describe the various pathological conditions in which CT scanning reveals the presence of hypoattenuated intramural nodules in thickened gallbladder wall, and to understand their histopathologic basis.

### Adenomyomatosis

Adenomyomatosis of the gallbladder, a common disease with an incidence of 2.8 - 5%, is characterized by the presence of Rokitsansky-Aschoff sinuses in its thickened wall (1). It presents as focal (fundal or segmental) or diffuse-type gallbladder wall thickening, occasionally simulating gallbladder carcinoma on imaging studies (1-3). Pathologically, adenomyomatosis shows epithelial proliferation and hypertrophy of the muscularis of the gallbladder, with outpouching of the mucosa into or

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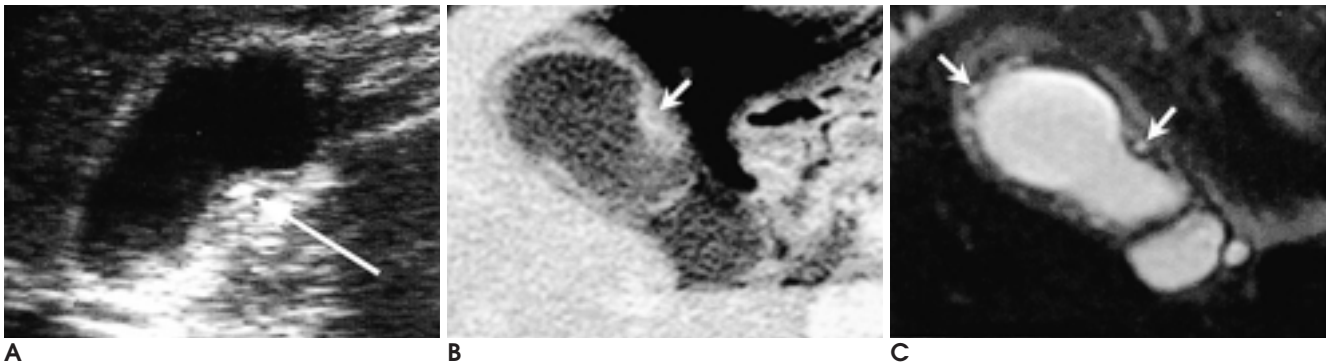
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through the thickened muscle layer, resulting in the formation of Rokitansky-Aschoff sinuses. To establish diagnosis, the detection of these is therefore necessary (1, 2, 4). Oral cholecystography easily demonstrates the presence of intramural diverticula filled with contrast medium (2), while ultrasound examination reveals diffuse or segmental thickening of the gallbladder wall, indicating adenomyomatosis of the gallbladder; intramural diverticula are anechoic, with or without echogenic foci and reverberation artifacts (2, 4). CT is useful for demonstrating focal or diffuse mural thickening as well as for detecting Rokitansky-Aschoff sinuses containing fluid or calculi (Fig. 1) (5), but with this modality, differentiation between a tumor and thickening due to adenomyomatosis is very difficult. In a study which analyzed MR imag-

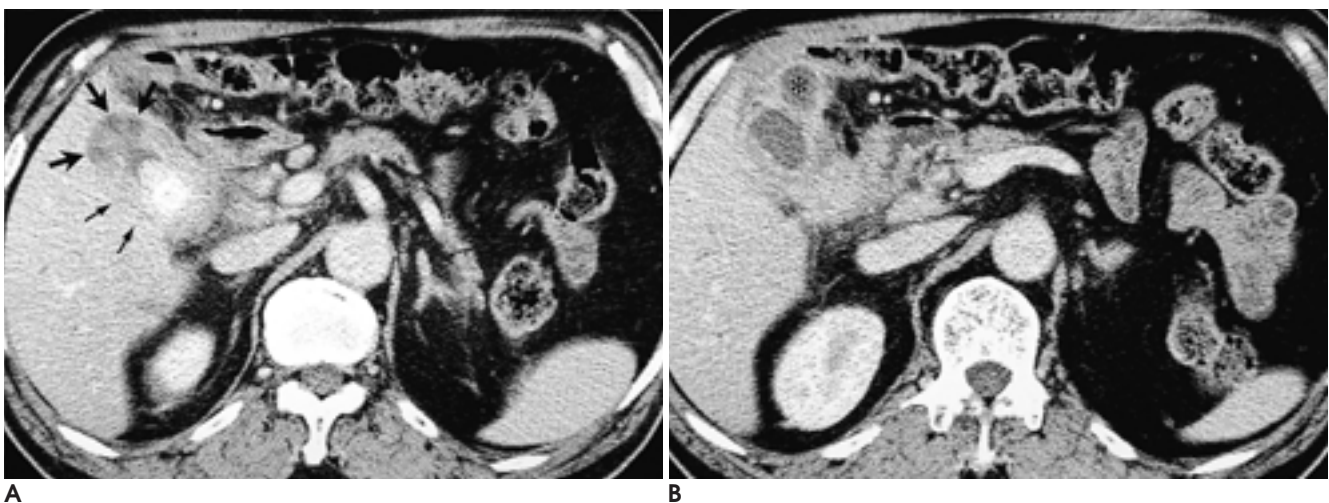
ing findings, T2-weighted images clearly showed multiple intramural Rokitansky-Aschoff sinuses as linearly arranged, discrete, hyperintense intramural cystic structures (5).

### Acute Cholecystitis

Acute cholecystitis usually occurs in patients with chronic biliary symptoms, the complete scenario for this condition comprising impaction in the cystic duct, local inflammation, worsening cystic duct obstruction, gallbladder distention, generalized wall edema, secondary ischemia, and transmural necrosis (6). CT findings of acute cholecystitis include gallstone, gallbladder wall thickening, indistinctness of the gallbladder - liver inter-



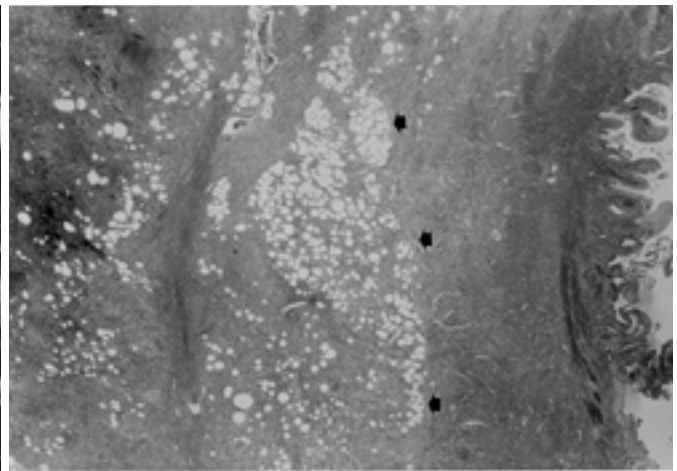
**Fig. 1.** 47-year-old man with adenomyomatosis of gallbladder.  
**A.** Abdominal ultrasonography shows asymmetrical wall thickening of the gallbladder without visible stone (arrow).  
**B.** Contrast-enhanced CT scan shows diffuse thickening of the gallbladder wall with focal intraluminal protrusion (arrow).  
**C.** Axial single-shot fast spin echo T2 weighted MR image also shows mild and diffuse mural thickening of the gallbladder. There are multiple intramural hyperintense foci (arrows) in the thickened wall as well as the focal protruding protion noted on the CT scan.



**Fig. 2.** 68-year-old man with acute cholecystitis.  
**A.** Contrast-enhanced CT scan shows diffuse gallbladder wall thickening (small arrows) with multiple hypoattenuated nodules (arrows) in the fundus of the gallbladder. Note large stone impacted in the narrowed lumen of the gallbladder.  
**B.** Contrast-enhanced CT scan below the level of (A) shows pericholecystic abscess (asterisk) adjacent to the fundic portion of the gallbladder.



**A**  
**Fig. 3.** 71-year-old woman with acute cholecystitis.

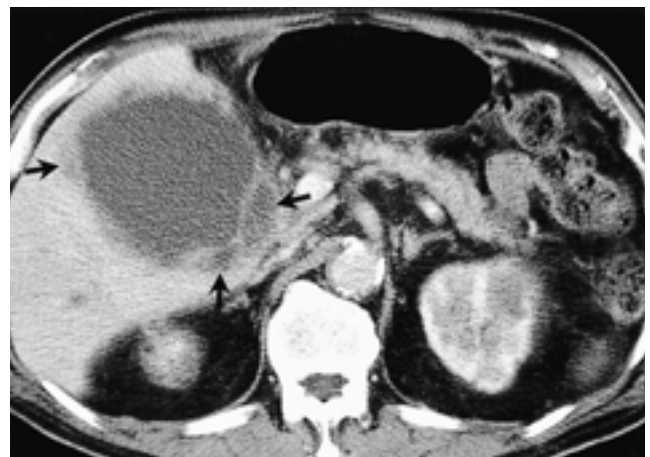


**B**  
**Fig. 3.** Photomicrograph of resected gallbladder specimen shows subserosal abscess (arrows) with thickened wall (H&E stain,  $\times 1$ ).

face, gallbladder distention, pericholecystic stranding, subserosal edema, pericholecystic fluid, high-attenuation bile, and the presence of luminal or mural gas (Fig. 2). The presence of intramural abscess may cause intramural hypoattenuated nodules (Fig. 3) (7, 8). Due to the onset of acute clinical symptoms and signs, correct diagnosis is not difficult.

### Hemorrhagic and Gangrenous Cholecystitis

Hemorrhagic or gangrenous cholecystitis can complicate acute cholecystitis (6). The pathologic designation of these entities relies upon the identification of inflammation, mucosal and intramural hemorrhage, and/or gangrene (9). Compared with gangrenous cholecystitis, the hemorrhagic variety is thought to represent an earlier and less severe complication of acute cholecystitis, though the two types often coexist pathologically (9). In gangrenous cholecystitis, inflammation is extensive and leads to ischemic infarction of the gallbladder wall, and the gallbladder may contain clotted blood mixed with bile and stones. Microscopically, the mucosa is eroded, and the wall may be extremely attenuated due to infarction and infiltration by neutrophils (Fig. 4). Hemorrhagic cholecystitis has a high mortality rate and is most commonly associated with cholelithiasis (9). Its clinical presentation and that of acute cholecystitis may be indistinguishable (9). In both hemorrhagic and gangrenous cholecystitis the sonographic findings are similar and include focal wall thickening, intraluminal membranes, and non-shadowing, and non-mobile intraluminal

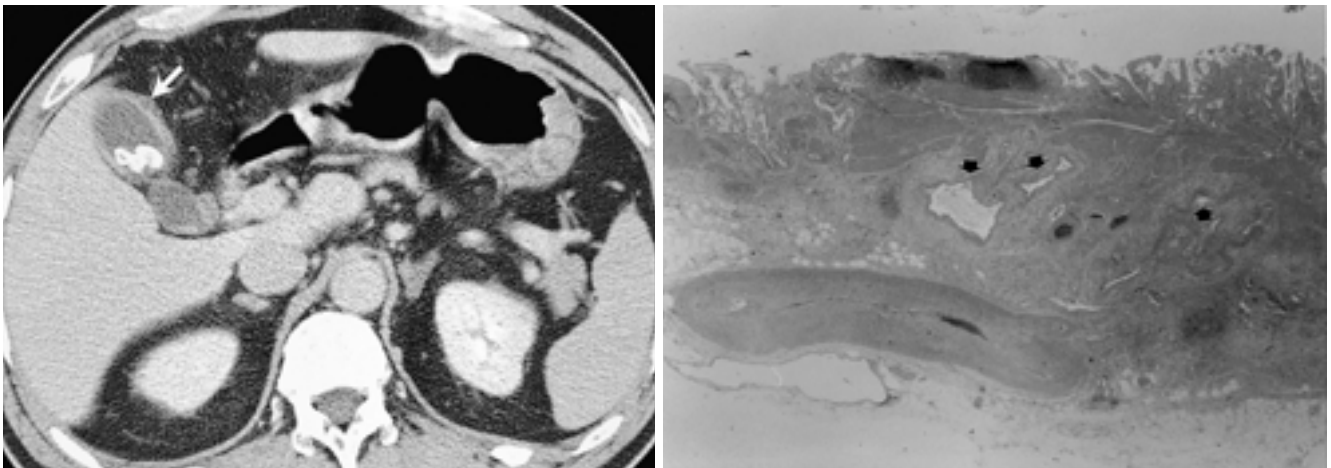


**Fig. 4.** 67-year-old man with gangrenous cholecystitis. Contrast-enhanced CT scan shows multiple variable-sized hypoattenuated intramural nodules (arrows) in the thickened wall of the distended gallbladder, with intramural abscess and mild pericholecystic fat infiltration. Mucosal line of the gallbladder is indistinct and the liver-gallbladder interface is obliterated. Note mild intrahepatic bile duct dilatation.

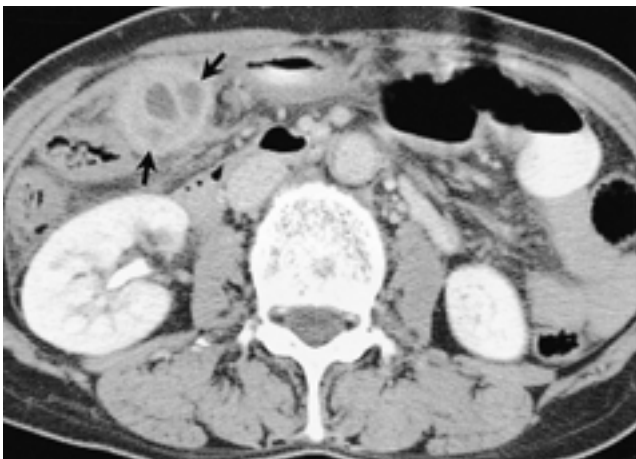
echogenic material (9, 10). CT, especially if unenhanced, helps to detect intramural hemorrhage.

### Chronic Cholecystitis

The morphologic changes occurring in nonspecific chronic cholecystitis are extremely variable. The gallbladder may be contracted, of normal size, or enlarged, with a wall thickness which varies but is rarely more than three times normal. Stones are present in almost all cases (Fig. 5), and dilatation of the Rokitsansky-Aschoff



**A** **Fig. 5.** 58-year-old man with chronic cholecystitis.  
**A.** Contrast-enhanced CT scan shows a small hypoattenuated intramural nodule (arrow) in the thickened gallbladder wall. Note multiple gallstones.  
**B.** Photomicrograph of the resected specimen shows dilated Rokitansky-Aschoff sinuses (arrows) in the thickened gallbladder wall (H & E stain,  $\times 1$ ).



**Fig. 6.** 58-year-old woman with chronic cholecystitis. CT scan shows multiple intramural hypoattenuated nodules (arrows) in the thickened gallbladder wall. On histopathological examination, there was chronic inflammation with dilated Rokitansky-Aschoff sinuses and edematous changes in the thickened gallbladder wall.

sinuses and hyperplastic cholecystosis are occasionally demonstrated (Fig. 6) (10).

### Xanthogranulomatous Cholecystitis

Xanthogranulomatous cholecystitis is an unusual focal or diffuse destructive inflammatory disease of the gallbladder that may occasionally mimic a malignant neoplasm (8). Its characteristic gross findings include irregular wall thickening with poorly demarcated, soft to firm, yellow or grayish-yellow variable-sized nodules; ulcera-



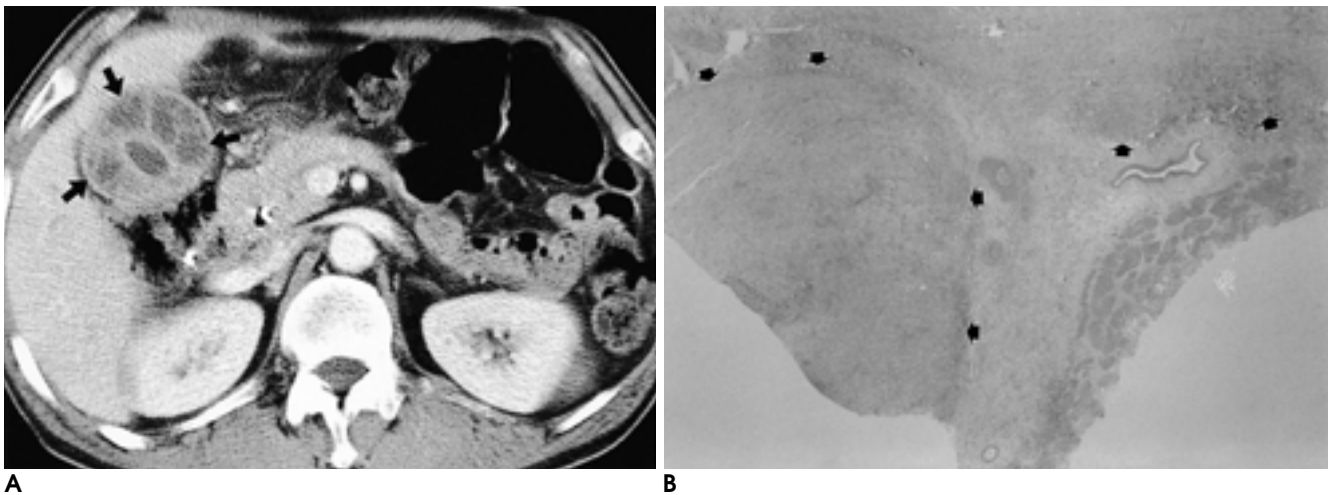
**Fig. 7.** 42-year-old man with xanthogranulomatous cholecystitis. Contrast-enhanced CT scan shows marked thickening of gallbladder wall with several hypoattenuated intramural nodules (arrows). In the narrowed lumen of the gallbladder, single gallstone is noted. Also note mild intra- and extrahepatic bile duct dilatation due to distal common bile duct stone (not shown). These intramural nodules were confirmed as xanthogranuloma on pathologic examination.

tion of the mucosa; and cholelithiasis (8). Although the pathogenesis of this lesion is not fully understood, it is generally agreed that rupture and intramural extravasation of inspissated bile and mucin from the occlusion of Rokitansky-Aschoff sinuses are the main causes of a xanthogranulomatous reaction in the gallbladder wall (11). Another possible primary cause of xanthogranulomatous cholecystitis is chronic infection and calculi as-

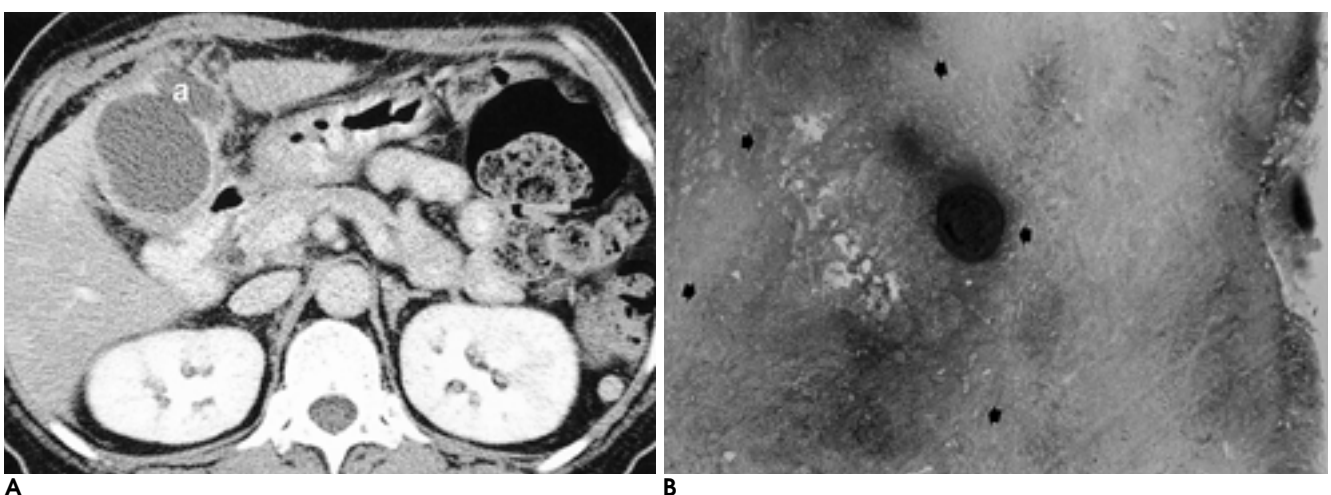


sociated with bile stasis; recurrent inflammation and calculi provoke degeneration and necrosis of the gallbladder wall with subsequent intramural abscess formation (Fig. 7) (11). Regardless of the primary cause, the intramural abscesses are replaced by xanthogranuloma with foamy histiocytic foreign-body giant cells (Fig. 8) (8, 11). Interestingly, in a series which attempted to differentiate between xanthogranulomatous cholecystitis and thickened wall-type gallbladder carcinoma (11), the CT features changed in appearance according to the age

of the lesion. When newer lesions were compared with older ones, areas of necrosis within a xanthogranuloma were much greater in the former. If intramural hypoattenuated nodules are not seen on CT, differentiation of xanthogranulomatous cholecystitis from gallbladder carcinoma or other forms of cholecystitis may be difficult or impossible (11). A recent study (8) showed that in xanthogranulomatous cholecystitis, hypoattenuated nodules do not always indicate xanthogranuloma and some may be due to an intramural abscess. If this is the



**Fig. 8.** 55-year-old man with xanthogranulomatous cholecystitis.  
**A.** Contrast-enhanced CT scan shows marked thickening of the gallbladder with multiple variable sized hypoattenuated intramural nodules (arrows). The mucosal lining is well preserved.  
**B.** Photomicrograph of the resected surgical specimen of the gallbladder shows segmental thickening of the gallbladder musosa. Note xanthogranuloma (arrows) in the thickened gallbladder wall (H&E stain,  $\times 1$ ).



**Fig. 9.** 58-year-old woman with adenocarcinoma of gallbladder.  
**A.** Contrast-enhanced CT scan shows uneven thickening of the gallbladder wall with a large intramural hypoattenuated nodule due to the presence of intramural abscess (a), as well as of focal discontinuity of the mucosal line. Note minimal pericholecystic fat infiltration.  
**B.** Photomicrograph of the resected specimen shows segmental thickening of the gallbladder wall consisting of fibroblast proliferation, inflammatory infiltration, and hemorrhage (arrows) (H & E stain,  $\times 1$ ).

case, the onset of symptoms is shorter (25 days) than in cases caused by xanthogranulomatous cholecystitis (70 days). Since this and gallbladder cancer can coexist (8, 12), early diagnosis is important. As the duration of symptoms of xanthogranulomatous cholecystitis increases, hypoattenuated intramural nodules become fewer, and the amount of fibrosis in the gallbladder wall grows, mimicking thickened wall-type gallbladder cancer.

### Tuberculosis of the Gallbladder

Tuberculosis of the gallbladder is extremely rare and very difficult to diagnose, and is most common in women over the age of thirty (13). Normal gallbladder is highly resistant to tuberculosis, but in patients with gallstones or cystic duct obstruction, secondary tuberculous infection can occur (13, 14). According to the route involved, infection may be classified as canalicular or hematogenous/lymphatic, depending on whether or not the gallbladder mucosa is involved histologically (13, 14). Histological lesions take the form of localized ulceration and there may also be typical tuberculous nodules of varying sizes and numbers in the thickened wall.

### Gallbladder Carcinoma

Because patients are often asymptomatic or present with signs or symptoms of chronic cholecystitis and/or cholelithiasis, early-stage carcinoma of the gallbladder is very difficult to detect. Gallstones are seen in 73 - 98% of such patients with calcification of the gallbladder wall in up to 25% of cases (15). Gallbladder carcinomas show three major patterns of histologic and radiographic presentation: 1) focal or diffuse thickening of the gallbladder wall; 2) a polypoid mass projecting into the lumen; and 3) most commonly, a mass replacing the gallbladder and often invading the adjacent liver (6).

Although rare, gallbladder cancer - especially where the tumor wall is thickened - may involve the presence of fluid within the mass, in which case hypoattenuated nodules appear on CT images. Fluid accumulation is usually caused by tumor necrosis, by a small collection of residual bile, or by an intramural abscess (Fig. 9) (16). In addition, multiple, dilated cancerous glands are reported to develop in these tumors (12), and are another cause of the hypoattenuated nodules revealed by on CT.

### Conclusion

Intramural hypoattenuated nodules in the thickened gallbladder wall develop under various pathologic conditions. Histopathologically, they indicate the presence of intramural abscesses, necrosis, hemorrhage, Rokitansky-Aschoff sinuses filled with inspissated bile or pus, xanthogranuloma, tuberculous granuloma or fluid collection in the necrotic area. Despite the nonspecificity of this finding, the detection of intramural hypoattenuated nodules by imaging studies may aid in the differential diagnosis of various gallbladder diseases.

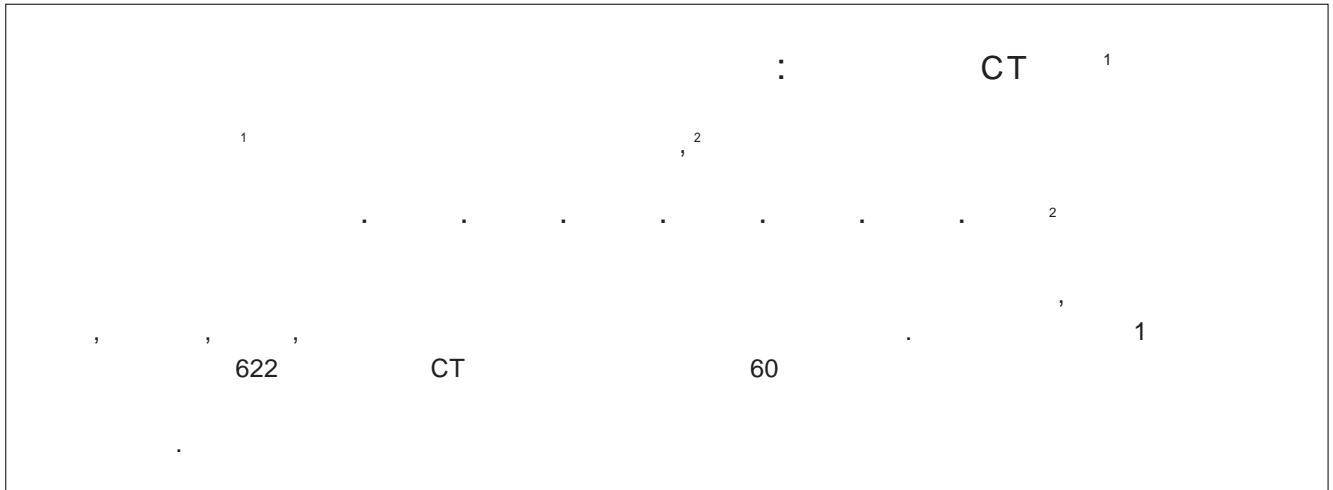
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