



# Differential Diagnosis of Benign and Malignant Lesions with Imaging

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## Introduction

With the exception of advanced gallbladder cancer, the differential diagnosis of gallbladder lesions is still considered challenging. However, differentiating benign polypoid lesions from neoplastic lesions is essential. Although the incidence of benign polypoid lesions is much higher than neoplastic lesions, especially for smaller lesions less than 1.0~1.5 in size, neoplastic lesions have to be identified because gallbladder cancer has poor prognosis. In addition, when gallbladder wall thickening is present, benign lesions such as adenomyomatosis or xanthogranulomatous cholecystitis and early-stage gallbladder cancer should also be differentiated. The gallbladder is a superficially located organ that is rarely in the abdomen. Hence, US plays an important role in differential diagnosis along with MR and CT. This chapter discusses the types of diseases that require differential diagnosis and characteristic imaging findings of each.

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## Differential Diagnosis of Polypoid Lesions in the Gallbladder

Gallbladder polypoid lesions can be defined as lesions that protrude into the gallbladder lumen [1]. Differential diagnoses of polypoid lesions include gallbladder stones, cholesterol polyps, adenomyomatosis, inflammatory polyps, adenomas, carcinomas in situ and other rare lesions such as leiomyomas, lipomas, neurofibromas, and carcinoids [2]. Definite mass-like lesions should be classified as gallbladder cancer rather than gallbladder polypoid lesions [1]. Cholesterol polyps, adenomyomatosis, and inflammatory polyps are also called pseudotumors or pseudopolyps [1, 2]. Cholesterol polyps account for two-thirds of the polypoid lesions in the gallbladder, while only about 4% of these lesions are adenomas (Table 1) [2].

## Imaging for the Differential Diagnosis of Gallbladder Polypoid Lesions

Gallbladder stones can easily be differentiated from polyps when acoustic shadowing is observed in the posterior aspect of the lesion (Fig. 1). However, acoustic shadowing might not be seen in obese patients or when stones are deeply set in the gallbladder neck. [3]. In

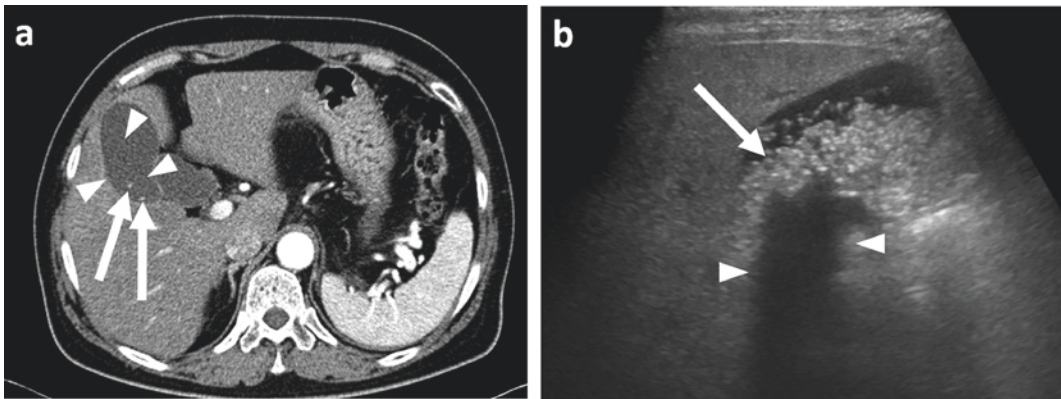
**Table 1** Incidence of polypoid lesions in the gallbladder [2]

Cholesterol polyps	60%
Adenomyomatosis	25%
Inflammatory polyps	10%
Adenomas	4%
Rare miscellaneous polyps	1%

this case, changing the patient's position from supine to the left or right decubitus is helpful because stones usually move to the dependent

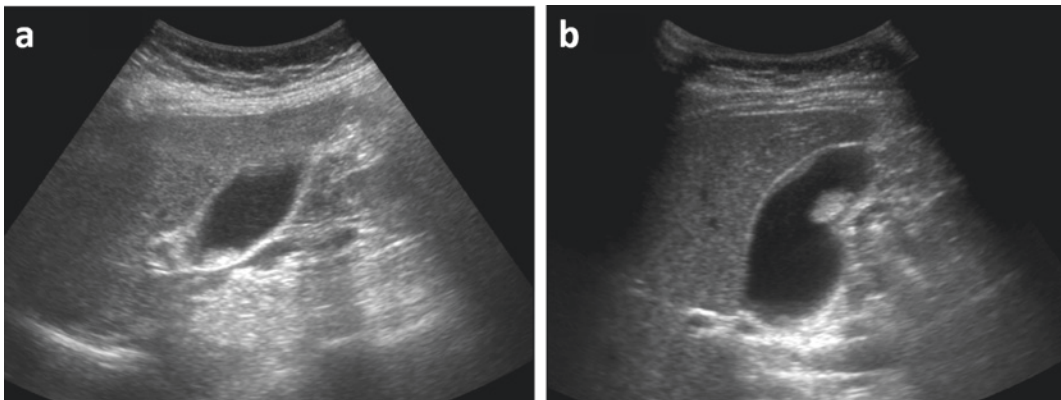
part, while true polypoid lesions do not (Fig. 2). Using the ultrasound probe to induce abdominal movement can also nudge sticky stones or sludge balls to move that did not with just position change. Neoplastic polyps with stalks can also appear to move after position changes, so the radiologist needs to confirm that they have moved completely from their original position (Fig. 3)

With the exception of gallbladder stones, it is important to differentiate benign polypoid lesions and neoplastic lesions. This is because the incidence of gallbladder polyps is relatively



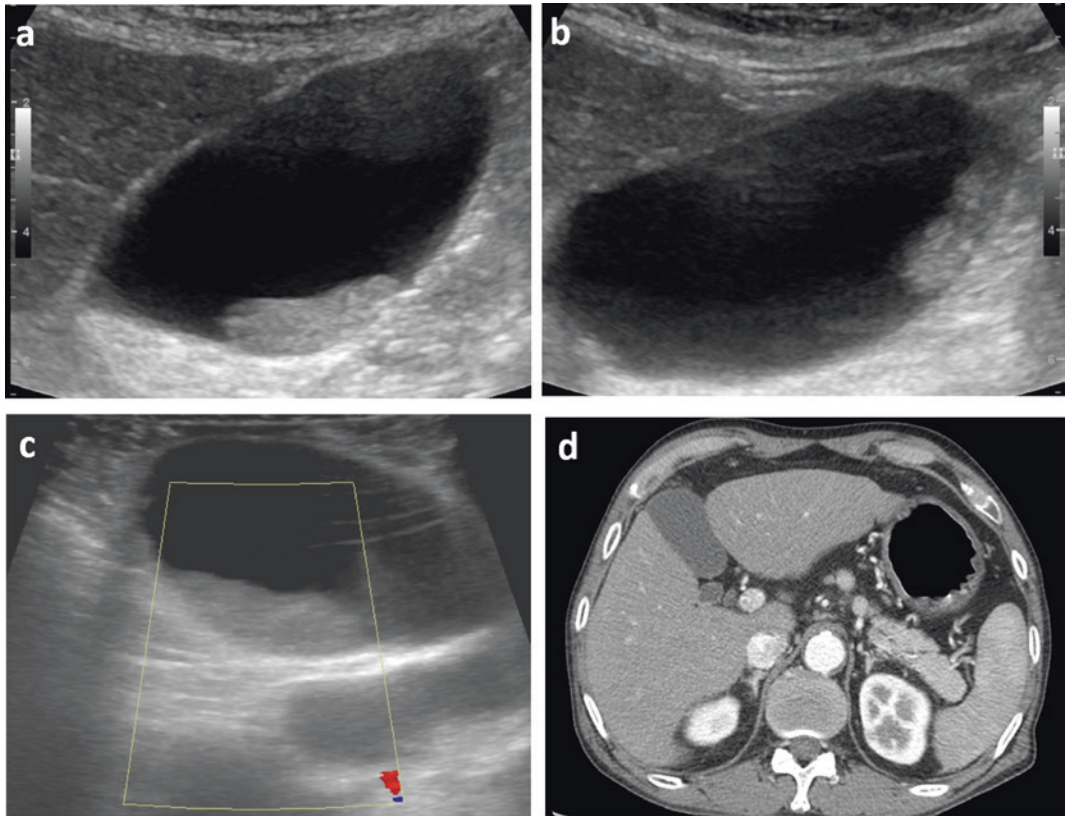
**Fig. 1** Gallbladder stone and sludge. **a** On CT, several small high attenuating lesions are seen in the gallbladder (arrowheads). Iso- to slightly high attenuating material surrounds (arrows).

the gallbladder stone (arrowheads). **b** On US, sludge is noted in the gallbladder (arrow). Acoustic shadowing is also seen (arrowheads), which suggests combined gallbladder stones



**Fig. 2** Gallbladder stone without acoustic shadowing. **a** Stone was initially located around the GB neck. **b** After

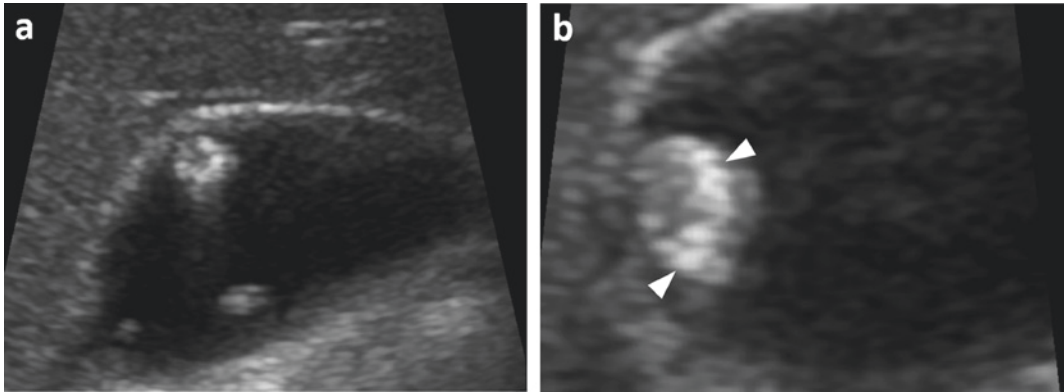
the patient changed from the supine position to the left decubitus, the stone moved to the fundus



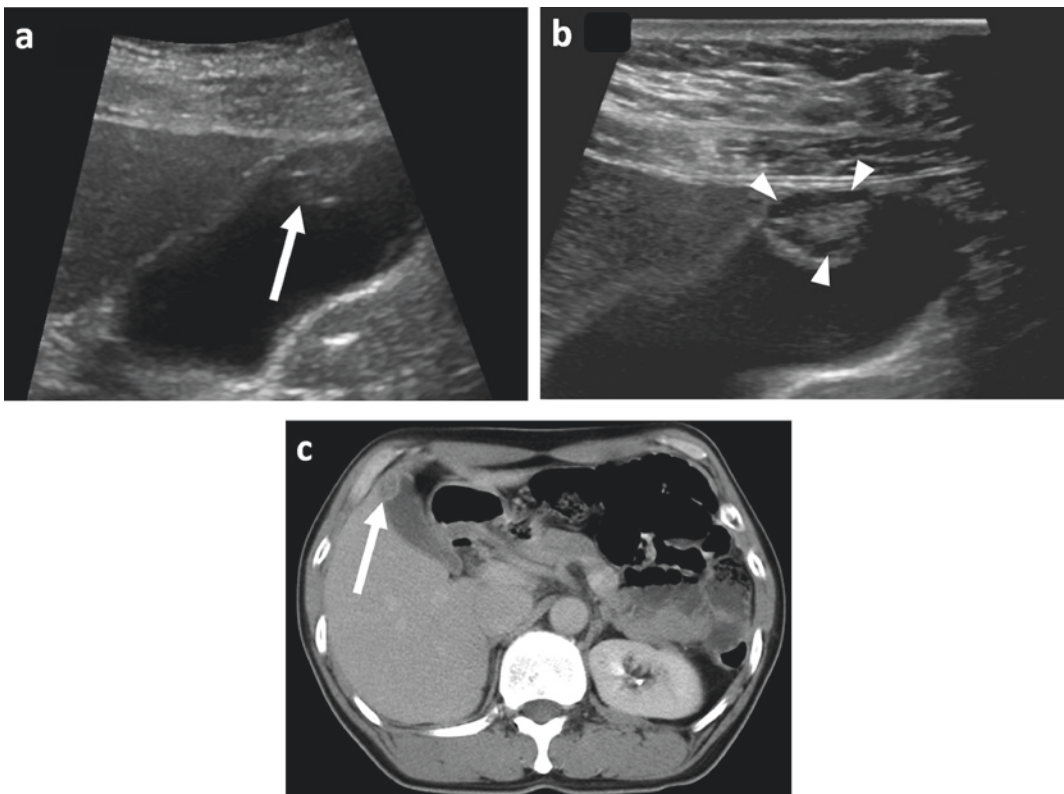
**Fig. 3** Gallbladder adenoma. **a, b** After position change, the polypoid lesion appeared to move on US. **b** On Doppler US, no blood flow signal is observed within the lesion. **d** On CT, the polypoid lesion is not detected within the gallbladder. The first impression of this lesion was sludge or stone, but it was confirmed as adenoma after cholecystectomy

high at approximately 4–7% in healthy subjects [4, 5], and the prognosis for gallbladder malignancy is devastating. According to previous studies, risk factors for neoplastic polyps are larger lesion size (>10–15 mm), accompanying stones, single lesion, older age (>50 years old), sessile shape, rapid growth, and presence of associated symptoms [4, 6–13]. Based on these clinical parameters, most guidelines recommend cholecystectomy for gallbladder polyps with associated symptoms and those larger than 1 cm or more in size [1, 2, 14]. However, these criteria might not be sufficient to indicate cholecystectomy because approximately 50–70% of gallbladder polypoid lesions larger than 1.5 cm have been confirmed as benign [4]. Furthermore, past studies have found the incidence of some

cancers including hepato-biliary, pancreatic, and colon cancer to increase after cholecystectomy [15–17], making the non-invasive diagnosis of gallbladder polyps increasingly more important as cholecystectomy might be avoided for benign polypoid lesions. US is usually used for the detection and differential diagnosis of gallbladder polypoid lesions. On US, cholesterol polyps may be high- to iso-echogenic compared to the most lateral layer of the gallbladder wall, and tiny hyperechogenic foci which represent cholesterol crystals (Fig. 4). Adenomyomatosis usually shows multiple microcysts which are Rokitansky–Aschoff sinuses in the thickened wall (Fig. 5). Comet tail artifacts on US or twinkling artifacts on Doppler US can accompany adenomyomatosis, whereas neoplastic



**Fig. 4** Cholesterol polyp. **a, b** The echogenicity of the polyp is similar to the most lateral layer of the gallbladder wall. There are also multiple high echogenic foci within the polyp (arrowheads)



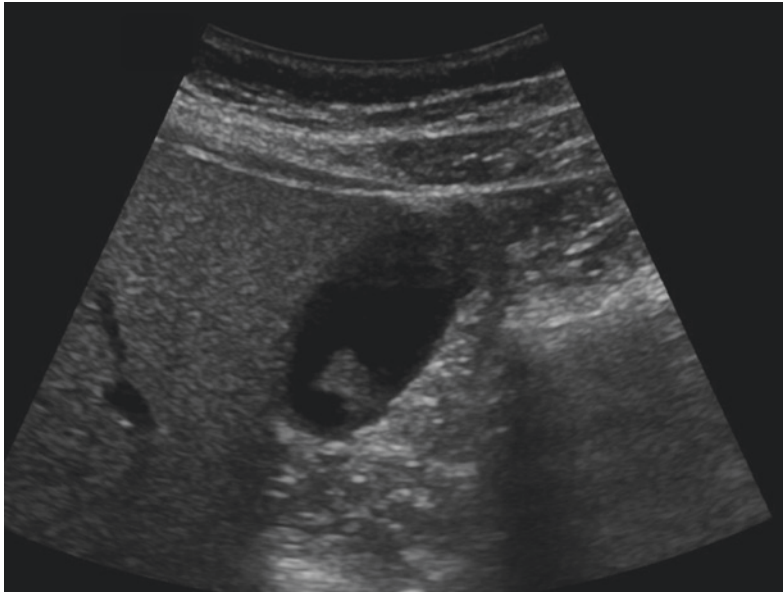
**Fig. 5** Adenomyomatosis. **a** A polypoid lesion is noted in the gallbladder fundus (arrow). **b** Multiple microcysts which suggest Rokitsky-Aschoff sinuses are seen

within the polypoid lesion. **c** On CT, an oval-shaped lesion is noted in the gallbladder fundus (arrow). This lesion was confirmed as adenomyomatosis

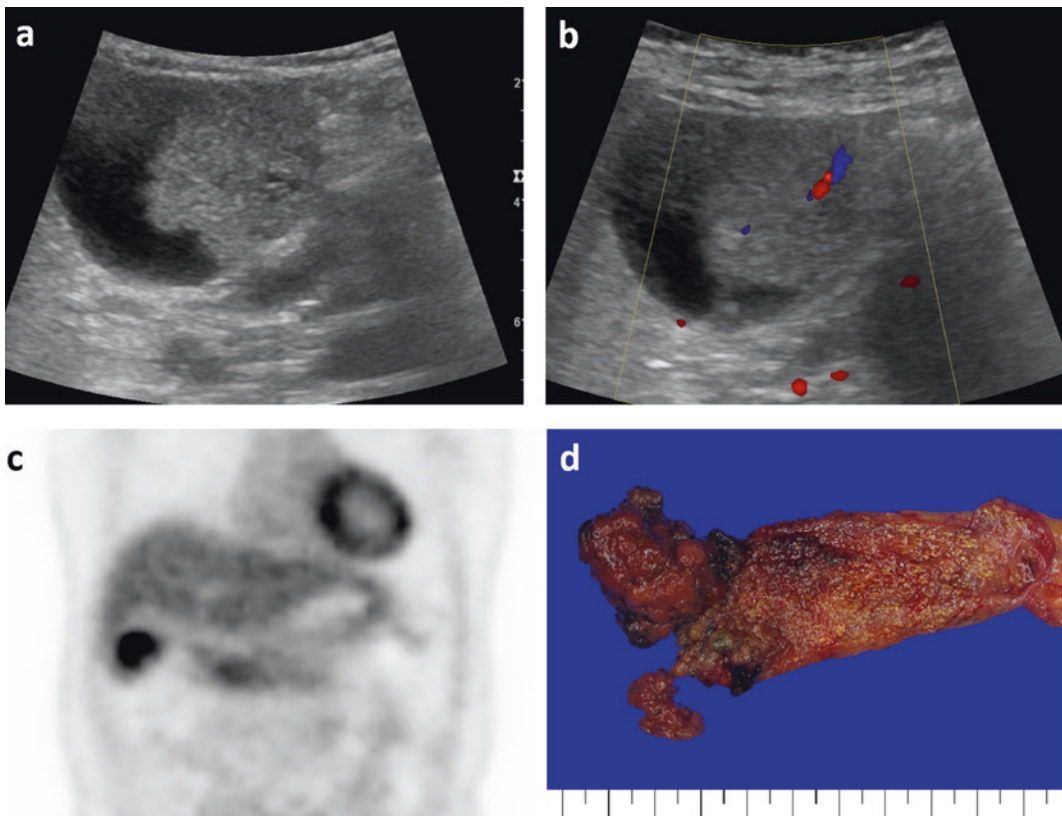
polyps show homogeneous hypo- to iso-echogenic internal echoes with nodular surfaces [18–20] (Figs. 6, 7 and 8). Traditionally, EUS

has shown better diagnostic performance for the differentiation of benign and neoplastic polypoid lesions (sensitivity and specificity: 78–92%



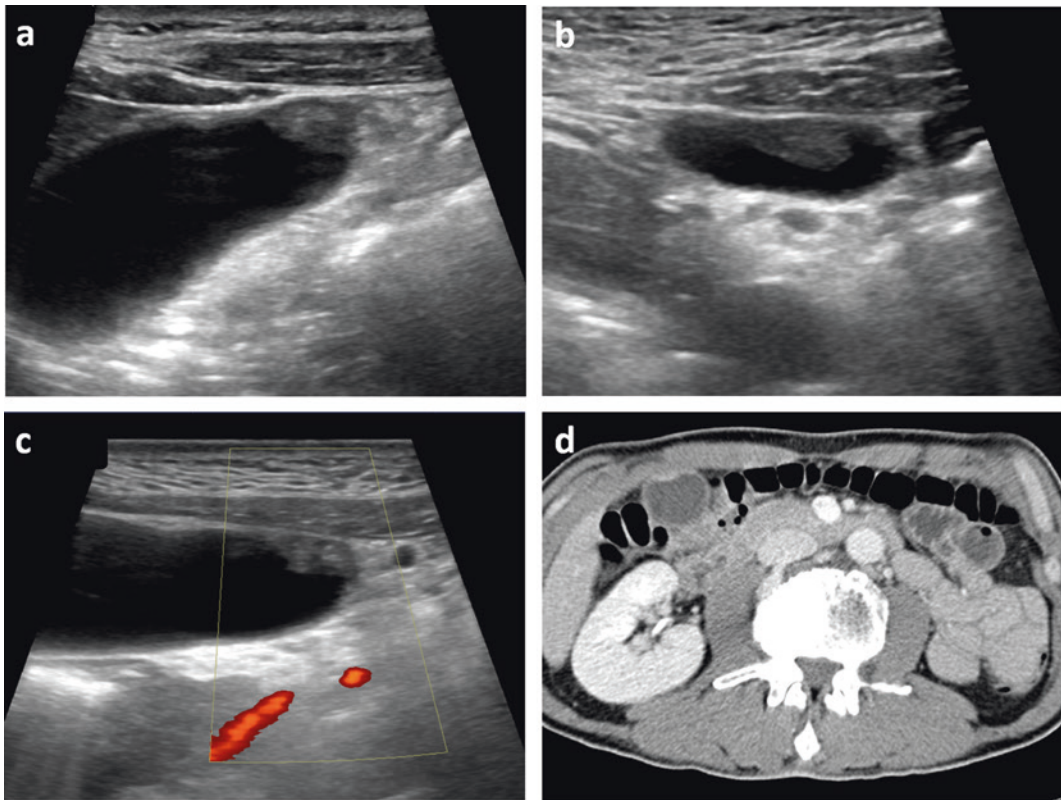


**Fig. 6** Gallbladder adenoma. A low echogenic polypoid lesion is noted near the gallbladder neck



**Fig. 7** Gallbladder cancer. **a** On US, a polypoid lesion is seen in the gallbladder. Gallbladder wall discontinuity is noted. **b** On Doppler US, a blood vessel is detected in the stalk. **c** On PET scan, increased 18F-FDG uptake can be

observed in the polypoid lesion. **d** This lesion was confirmed as adenocarcinoma with invasion of the perimuscular connective tissue (T2)

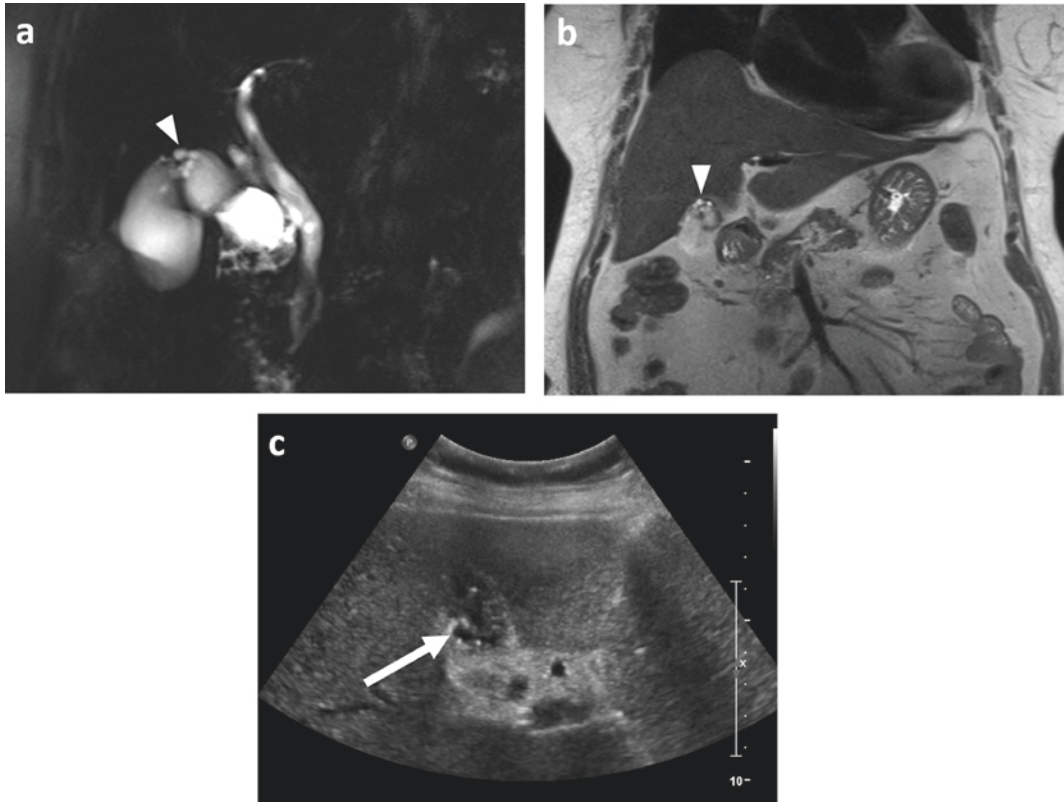


**Fig. 8** Pyloric gland adenoma. **a, b** On US, focal wall thickening or a polypoid lesion is noted in the gallbladder fundus. Microcysts are not seen within the lesion. **c** On Doppler US, there is no blood flow or twinkling

artifacts within the lesion. **d** On CT, focal wall thickening is noted in the gallbladder fundus. The initial impression was fundal adenomyomatosis, but the lesion was confirmed as pyloric gland adenoma

and 83–88%) than transabdominal US (54%, 54%) [19, 20]. However, a recent meta-analysis showed that transabdominal US can successfully detect gallbladder polyps with a pooled sensitivity of 84% and specificity of 96% along with sufficient diagnostic accuracy, but found it to be less accurate (sensitivity, specificity: 79%, 89%) compared with EUS (86%, 92%) for the differential diagnosis of benign and neoplastic polyps [21]. The recently introduced high-resolution gallbladder US is performed with a high-resolution linear probe rather than a low-frequency convex probe, showing the highest sensitivity (90%) for the diagnosis of neoplastic polyps, followed by EUS (86%) and CT (72%) [5].

Contrast-enhanced US (CEUS) has also been attempted for the differentiation of benign and neoplastic gallbladder polypoid lesions. Homogeneous enhancement and an intact GB wall might suggest a benign lesion, whereas heterogeneous enhancement, disruption of the gallbladder wall beneath the lesion, and wider stalk width are more common in neoplastic polypoid lesions [22–25]. According to previous studies, presence of vascularity or certain vessel types such as branched or linear intralesional vessels can suggest neoplastic polyps [3, 22], whereas another study stated that vascular types cannot be used as a differential point between benign and neoplastic polyps [25]. Although, there



**Fig. 9** Segmental adenomyomatosis. On MR cholangiography (a) and a coronal T2-weighted image (b), there are multiple microcysts arranged in a round shape

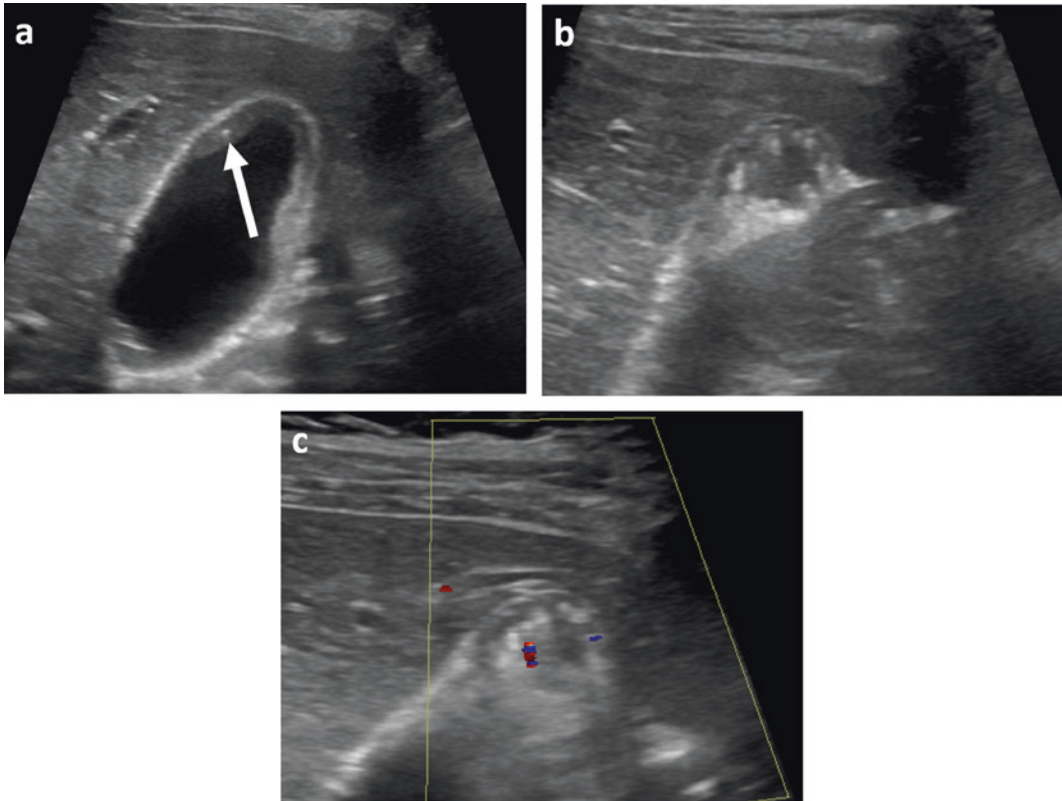
(arrowheads). (c) On US, microcysts are noted within the thickened gallbladder wall (arrow)

have been reports that enhancement pattern and washout time differ between benign and neoplastic polyps [25, 26], these are relative rather than absolute findings and care should be taken in their application. CEUS is reported to have a sensitivity of 75–100% and a specificity of 67–87% for differentiating benign and neoplastic lesions [23].

### Differential Diagnosis of Gallbladder Wall Thickening

For gallbladder wall thickening, a differential diagnosis is needed to distinguish early gallbladder cancer and diffuse or segmental type

adenomyomatosis and to distinguish between xanthogranulomatous cholecystitis and locally advanced gallbladder cancer. Early gallbladder cancer and segmental or diffuse adenomyomatosis can be present as uniform and mild gallbladder wall thickening. Adenomyomatosis can be diagnosed when small round foci with T2 high signal intensity are observed within the thickened gallbladder wall (i.e., pearl neckless sign) which are due to Rokitansky–Aschoff sinuses on MR cholangiography or T2-weighted images (Fig. 9) [27]. On US, symmetric wall thickening, intramural cysts, and intramural echogenic foci which are cholesterol crystals and twinkling artifacts may suggest



**Fig. 10** Adenomyomatosis. (a) On US, an intramural echogenic dot is seen within the thickened wall (arrow). Multiple comet tail artifacts on US (b) and

twinkling artifacts on Doppler US (c) are seen, suggesting adenomyomatosis

adenomyomatosis (Fig. 10), whereas gallbladder wall disruption or discontinuity and loss of multilayer pattern may suggest gallbladder cancer [28, 29].

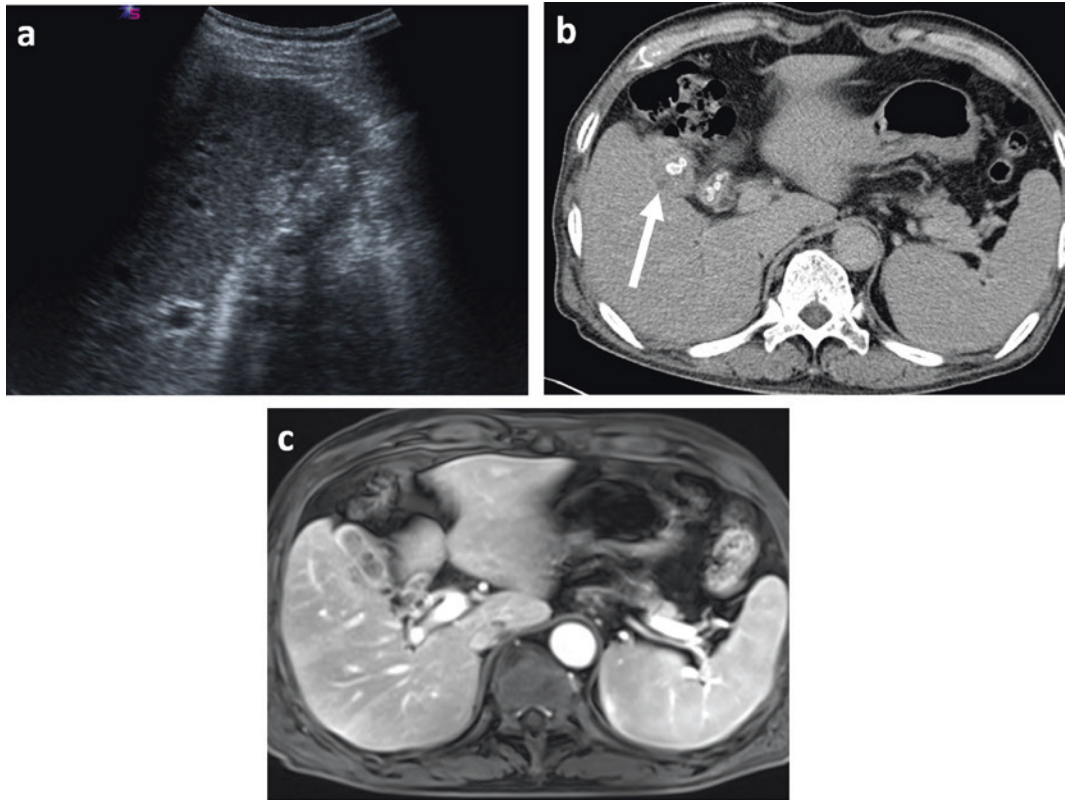
Irregular wall thickening with accompanying stones are frequently noted in xanthogranulomatous cholecystitis, which makes it difficult to reach a differential diagnosis from gallbladder cancer. If a hypoechogenic nodule sits in the thickened wall on US, an intramural low attenuating nodule with continuous linear mucosal enhancement on CT may suggest xanthogranulomatous cholecystitis (Fig. 11). On MR, a signal drop in the opposed phase compared to the in-phase can be seen in the thickened wall due to the fat content [30]. Xanthogranulomatous inflammation or

abscesses can be seen in high signal intensity foci on T2-weighted images [29, 30].

## Conclusion

It is important to make a differential diagnosis between benign and neoplastic gallbladder lesions because treatment plans and prognosis are quite different for the two lesions. Although there are still a lot of gray zones left to interpretation, several helpful findings have been suggested for accurate differential diagnosis. Gallbladder stones can be diagnosed with accompanying posterior acoustic shadowing or position change made by the patient. High- to iso-echogenic polypoid lesions with tiny hyperechogenic foci might suggest cholesterol





**Fig. 11** Xanthogranulomatous cholecystitis. **a** On US, irregular gallbladder wall thickening with multiple impacted stones is noted. **b** On non-contrast CT, a focal

low attenuating area is noted within the thickened wall (arrow). **c** On contrast-enhanced T1-weighted MR, gallbladder mucosa shows continuous linear enhancement

polyps and multiple microcysts in the thickened wall with comet tail artifacts or twinkling artifacts might suggest adenomyomatosis. On the other hand, hypo- to iso-echogenic polyps with nodular surfaces and larger than 1 cm in size might suggest neoplastic polyps. For gallbladder wall thickening, the pearl neckless sign on T2-weighted MR images is a specific finding for adenomyomatosis, whereas discontinuity or loss of gallbladder wall layers suggest gallbladder cancer. If there is a hypoechogenic nodule in the thickened wall on US or an intramural low attenuating nodule on CT, the findings would suggest xanthogranulomatous cholecystitis rather than gallbladder cancer. Careful imaging evaluation of the gallbladder enables accurate diagnosis of gallbladder lesions and can reduce unnecessary cholecystectomies.

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