



## Review Article

# Algorithmic approaches to the diagnosis of gallbladder intraluminal lesions on ultrasonography

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## Abstract

Ultrasound is a frequently used diagnostic tool for gallbladder diseases. Polypoid lesions are commonly depicted at routine abdominal ultrasonography (US). The characteristics of these lesions vary. Since most early malignant tumors in the gallbladder are asymptomatic, differentiation between malignancy and benignity is crucial. Knowledge of gallbladder polypoid lesions is important so that they can be appropriately included in the differential diagnosis in patients presenting with intra-gallbladder nodules on US. This article summarizes the algorithmic approach to the diagnosis of these lesions and our recent experience with contrast-enhanced US. The clinical and imaging features of gallbladder polypoid lesions are reviewed. Copyright © 2018, the Chinese Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Adenocarcinoma; Gallbladder; Polypoid lesions; Pseudotumors; Ultrasound

## 1. Introduction

Polypoid lesions of the gallbladder are common findings at abdominal ultrasonography (US). The term “polypoid” is defined as a focal elevation or a protrusion into the gallbladder lumen from the wall.<sup>1,2</sup> However, not all polypoid lesions are malignant. In fact, most incidentally found polypoid lesions in the gallbladder are benign.<sup>3</sup> Since most malignant tumors in the gallbladder are asymptomatic and usually diagnosed when advanced, differentiation between malignancy and benignity is crucial.<sup>4,5</sup> Mellnick and colleagues classified different types of

gallbladder lesions into pseudotumors, benign tumors and malignant tumors.<sup>1</sup> To evaluate a gallbladder polypoid lesion on US, we suggest confirming a “true” polypoid lesion first. After a “true” polypoid lesion is established, the next step is to distinguish pseudotumors from true tumor lesions. Finally, the differential diagnoses should be grouped into benign and malignant tumors separately. Several clinical factors have also been described to aid the differential diagnosis, including age, comorbidities and presence of clinical symptoms.

The study was performed following the ethical principles. Approval was waived for our study because the results for publication only involved unidentified imaging.

## 2. Intraluminal polypoid mimickers

The first step of evaluation of a gallbladder polypoid structure is to rule out the pseudo-mucosal lesions. A

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gallbladder polypoid lesion is defined as a mucosal lesion elevating or protruding into the gallbladder lumen.<sup>1,2</sup> Since a polypoid structure is derived from the gallbladder mucosa, it should be connected to the gallbladder wall. However, some intraluminal lesions contacting the mucosa can mimic the mucosal connection, and may thus be misdiagnosed.

Gallbladder sludge is a mixture of precipitates of cholesterol crystals, calcium bilirubinate pigments and other calcium salts.<sup>6</sup> It is mostly seen in fasting patients, especially those who are on parenteral nutrition. Typically, it is a mobile intraluminal lesion and without connection to the gallbladder wall. However, some sludges may not show significant mobility due their relatively sticky or stiffened nature.

Among these pseudo-mucosal lesions, gallbladder sludge is the most common, especially tumefactive sludge (Fig. 1). Gallbladder sludge, including tumefactive sludge, presents no real blood flow signal on color Doppler US. Only occasionally pseudoflows or twinkle artifacts are present because of the engulfed larger crystals or small stones (Fig. 2).<sup>7,8</sup> Posterior acoustic shadowing may be observed due to occasional contents of calcium or engulfment of a gallstone. It may be difficult to differentiate a gallbladder sludge from a true polypoid lesion when atypical, and follow-up study is needed in case of malignancy.

The formation of a tumefactive sludge is a process of coacervation and thixotropy. According to Ando and associates, tumefactive sludge is a precipitate of inspissated bile, multiple calculi, pigmented granules, cholesterol crystals, hemobilia and, possible, purulent bile or pus.<sup>9</sup> These particles tend to separate in the bile due to coacervation and precipitate to the dependent portion of the gallbladder due to thixotropy. Because of the relatively weak forces between particles and unstable folding, tumefactive masses may turn into numerous small particles when external strong tapping force is applied. The tapping maneuver may aid in the differential diagnosis when changes of the position have failed to demonstrate the mobile nature of the tumefactive masses.



Fig. 1. **Tumefactive sludge.** A tumefactive sludge (arrow) presents with polypoid appearance.

Gallstones may mimic polypoid lesions on US. Posterior acoustic shadowing is often present and may be obscured by the superimposed bowel gas or prominent fatty tissue. Although gallstones are often noted in patients with acute or chronic cholecystitis, the presence of gallstones does not rule out the possibility of malignancy.<sup>10</sup>

### 3. Polypoid lesions

After a “true” polypoid lesion is established, the next step is the differentiation of pseudotumors and true tumor lesions. Although there is an existence of mucosal connection to the polypoid lesion, it may not be clearly depicted on US, especially when they are small in size. Polypoid lesions can be observed as sessile, with stalk, or infiltrative (Fig. 3). Most lesions with stalk are relatively benign as compared with sessile lesions.<sup>2</sup> Infiltrative lesions are mostly malignant.

### 4. Pseudotumors

Some of the polypoid lesions of the gallbladder are non-tumorous lesions. These pseudotumors comprise mostly cholesterol polyps, adenomyomatosis and inflammatory polyps.

Cholesterol polyps are derived from engulfment of triglyceride by phagocytes. Typical cholesterol polyps accumulate on the gallbladder wall, presenting a “balls on the wall sign” (Fig. 4). Less commonly, cholesterol polyp may present as a solitary polypoid lesion with subtle vascularity (Fig. 5). Heterogeneous enhancement of the lesion is also noted on contrast-enhanced US (CEUS) (Fig. 6). To further differentiate these atypical cholesterol polyps from other polypoid malignancies, endoscopic ultrasonography (EUS) is recommended.<sup>11</sup> On EUS, cholesterol polyp tends to have a thin visible stalk and display homogeneous echogenicity, while gallbladder adenocarcinoma presents with a thick stalk and heterogeneous echogenicity.<sup>12</sup> Other imaging characteristics, including incomplete gallbladder wall and invasion of the adjacent liver parenchyma, often indicate malignant nature. It is also generally believed cholesterol polyps have barely any risk of malignant changes.<sup>13–15</sup>

Adenomyomatosis are bile acid crystal precipitates in the intramural diverticula (also known as Rokitansky-Aschoff sinuses) of the gallbladder. Multiple interfaces are formed due to crystals, and therefore produce the typical comet-tail artifacts (Fig. 7).<sup>16,17</sup> On color Doppler US, the crystals in the intramural diverticula may present with twinkle artifacts (Fig. 8).<sup>18</sup> Adenomyomatosis often coincides with thickening of the gallbladder wall.<sup>19</sup>

Different morphological changes may present with three types of adenomyomatosis, namely diffuse, segmental and focal types.<sup>20</sup> Ootani and colleagues proposed that segmental adenomyomatosis had strong relation with gallbladder cancer after reviewing over 3000 gallbladder specimens (Fig. 9).<sup>21</sup>

The formation of inflammatory polyps is due to chronic cholesterol precipitates and chronic inflammation, which stimulate the mucosal wall and further form granulation and fibrosis. Inflammatory polyps may proceed to mucosal dysplasia.

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