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REVIEW

Gallbladder tumor and pseudotumor: Diagnosis and management



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Summary The most common gallbladder disease, by far, is cholecystolithiasis. Nevertheless, the discovery of abnormal thickening of the gallbladder wall or a tumorous lesion (with or without gallstones), is a frequent problem. The physician who confronts this finding must be aware of the various lesions to be considered in the differential diagnosis, whether neoplastic or pseudotumoral, epithelial or not, benign or malignant. Because of the particularly grim prognosis of gallbladder cancer, especially when discovered at a late stage, it is especially important to focus on the potential for malignant degeneration of any gallbladder lesion. Imaging plays an important role in distinguishing these lesions; ultrasound remains the key diagnostic tool for gallbladder disease, but other modalities including CT and MRI may help to characterize these lesions. The resulting treatment strategies vary widely depending on the risk of malignancy. A wide and extensive resection is recommended for malignant lesions; prophylactic cholecystectomy is recommended for lesions at risk for malignant degeneration while observation is indicated for purely benign lesions.

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Introduction

Gallbladder tumors are rare compared to gallstone disease which forms the bulk of gallbladder pathology. However, its prevalence varies from 3% to 7% in the general population [1], which makes it not infrequent in day-to-day surgical practice. On ultrasound exam, the presence of a tumorous lesion of the gallbladder, whether associated with gallstones or not, must be systematically sought. The main challenge of management of malignant or pre-malignant gallbladder tumors lies in early diagnosis; the diagnosis of gallbladder cancer is all too often delayed and the lesion is commonly at an incurable stage [1,2].

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Gallbladder adenocarcinoma, the most feared, has a mean 5-year survival rate of 5%, all stages combined [3], and the prognosis depends mainly on tumor stage at the time of diagnosis. Clinical context is essential to the diagnostic process but in most cases, an isolated gallbladder lesion needs to be accurately characterized by modern imaging methods. Abdominal ultrasound remains the first-line examination for patients with symptoms of biliary disease, but CT and MRI have become essential to characterize any abnormal appearance of the gallbladder parenchyma. Other tests (Contrast-enhanced ultrasound [CEUS], Endoscopic ultrasound, endoscopic ultrasound [EUS], and Positron emission tomography [PET]) are currently being evaluated [4,5]. These modern imaging techniques are needed to help distinguish between benign lesions, those at risk of malignant degeneration, and malignant lesions, in order to select the most appropriate surgical management. The objective of this systematic review is to define the various neoplastic and pseudo-tumorous pathologies of the gallbladder, based on data from the literature and on our own experience, and thereafter to establish a diagnostic strategy using available imaging modalities, and finally to define an appropriate therapeutic strategy.

Different gallbladder pathologies

Gallbladder lesions occur commonly; their prevalence on ultrasonography varies from 2% to 12% in the general population in different series [1,6]. Table 1 summarizes the various benign and malignant pathologies that can be seen. But signs of malignancy in lesions at risk for malignant degeneration must be sought in order to select an appropriate management strategy, particularly since the patient's prognosis depends on diagnosis at an early stage.

Benign lesions

Most gallbladder lesions are benign. In the study of Yang et al. [7] study, more than two-thirds of the 182 patients who underwent cholecystectomy performed were found to have benign lesions.

These included both polypoid lesions and also atypical thickening of the gallbladder wall (inflammation or infection), which can be diagnostically misleading because they mimic cancerous lesions.

Polypoid lesions

Cholesterosis and cholesterol polyps

Cholesterol polyps represent the majority of benign lesions, with a prevalence ranging from 60–90% in different studies [1,7]. These polyps arise from the accumulation of triglycerides and cholesterol esters within macrophages in the gallbladder wall, without any cellular proliferation. Polyps are small (usually 1–2 mm, always less than 10 mm) and multiple [7]. In gross appearance, they are yellow, relatively friable, carpeting the mucosal surface of the gallbladder lumen; they are often attached to the mucosa by a pedicle. Cholesterosis involves the gallbladder diffusely and has a mean prevalence of 10% in autopsy series [8]. This lesion is clinically asymptomatic as a rule but may occasionally manifest itself as biliary pain or even by distal migration provoking cholecystitis. Ultrasound imaging allows diagnosis based on findings of a hyper-echoic intraluminal polyp without posterior shadowing that remains in a fixed mural

location with change in position; it is typically round or slightly lobulated (Fig. 1). Other imaging techniques are not particularly useful [4]. The diagnosis of cholesterol polyp requires no further surveillance or treatment as long as no biliary symptoms are present. In case of doubt, repeat ultrasound imaging at six-month interval is indicated.

Inflammatory or fibrous polyps

These represent 10% of gallbladder polyps and result from secondary sequelae of fibrosis and chronic inflammation. They are small in size and ultrasound imaging is diagnostic of simple benign poly; the diagnosis of these non-cholesterol polyps is based on histologic exam [8,9].

Heterotopic polyps

These consist of ectopic tissue such as liver, gastric, pancreatic, adrenal or thyroid tissue lining the bile duct [9]. Only ectopic gastric or pancreatic tissue causes symptoms. A literature review found fifty cases of ectopic gastric and thirty cases of ectopic pancreatic tissue [10]. No risk factors for malignant degeneration could be identified. Non-surgical observation can be proposed but the unusual lesion is usually diagnosed by postoperative histological analysis.

Mesenchymal lesions

Rare benign tumors such as leiomyomas, lipomas and fibroids may develop from smooth muscle cells [11]. Macroscopically, these are solid, nodular and well-circumscribed lesions. Again, there is no specific indication for excision, but diagnostic uncertainty can lead to surgery.

Gallbladder wall thickening

Gallbladder inflammation or cholecystitis usually results in a diffuse thickening of the wall. Its presentation can be acute or chronic, of more or less serious gravity, and the diagnosis is suggested by non-specific thickening of the gallbladder wall.

Acute cholecystitis

Acute cholecystitis results from obstruction of the cystic duct or gallbladder by impaction of a gallstone in 95% of cases, with inflammation of the gallbladder wall, often associated with bacterial infection. Acute acalculous cholecystitis occurs in only 5% of cases, typically occurring in ICU patients or multiple trauma, where gallbladder inflammation is due to hemorrhagic or ischemic events or biliary stasis (parenteral nutrition) [12]. The diagnostic and therapeutic criteria of calculous cholecystitis are well described and codified with a set of recommendations (Tokyo Guidelines) published in 2007 and recently updated [13,14]. The diagnosis is suggested by the association of clinical signs (RUQ abdominal pain, guarding, mass, Murphy's sign) and laboratory findings of inflammation (leukocytosis, elevated CRP). The diagnosis is confirmed by ultrasound imaging showing gallstones, wall thickening ≥ 4 mm, peri-cholecystic fluid, and the elicitation of a positive Murphy sign on ultrasound examination. Management and the interval before surgical intervention depend on the severity of cholecystitis, but the curative treatment remains cholecystectomy [14]. Management of certain forms of acute cholecystitis should be individualized because of their severity and specific aspects of imaging:

- gangrenous cholecystitis is accompanied by ischemia and hemorrhagic necrosis of the gallbladder wall. CT scan shows an irregular wall, with thinning in places (necrosis), sometimes with air present within the wall or lumen of the gallbladder, a marked edema, and/or a peri-cholecystic

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