Gallbladder Masses: Multimodality Approach to Differential Diagnosis

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Introduction

Gallbladder masses are commonly encountered on diagnostic imaging examinations. Distinguishing between benign and malignant conditions is critical, in terms of clinical significance, management, and follow-up. It is important to be familiar with the differential diagnoses of gallbladder masses, recognize imaging features that are diagnostic for each condition, and understand the utility and limitations of each of the cross-sectional imaging modalities currently available.

Gallbladder pathology is a frequent source of patient complaint, to include acute or chronic right upper quadrant pain, jaundice, or dyspepsia. As such, the gallbladder is a routinely imaged structure either directly to exclude or characterize gallbladder pathology or in general abdominal imaging for nonspecific complaints or imaging related to adjacent structures.

Gallbladder masses as part of the spectrum of gallbladder pathology are commonly encountered at imaging. It is important for the diagnostic imager to be familiar with the broad differential of gallbladder masses. While most gallbladder masses are benign and do not present a diagnostic dilemma, they may present with unusual or nonspecific imaging appearances, or on a modality that is not typically used to characterize gallbladder pathology.

The purpose of this article is to review the spectrum of gallbladder masses (Table 1) and mass-like lesions on US, CT, and MR, providing the reader with the ability to recognize benign disease, identify worrisome imaging features, and review the diagnostic information each cross-sectional modality may provide.

Benign Masses

Cholelithiasis.

Cholelithiasis, or gallstones, represents the most commonly encountered gallbladder mass. They affect

Table 1. Differential Diagnosis of Gallbladder Masses

Benign
  Common
    Cholelithiasis
    Tumefactive Sludge
    Polyps
      Cholesterol
      Adenomatous
  Uncommon
    Adenomyomatosis
    Hematoma
    Varices
  Rare
    Xanthogranulomatous Cholecystitis
    Choristoma/Heterotopia
    Granular Cell Tumor
    Neurofibroma

Malignant
  Primary Gallbladder Adenocarcinoma
 Metastasis
    Melanoma (Most Common)
    Hepatocellular Carcinoma
    Renal Cell

over 25 million individuals or about 10% of the U.S. adult population, affecting women more than men by a ratio of 2:1; the risk increases with age.[1] Consequently, they typically are not a diagnostic challenge but remain important to recognize on all modalities, so as not to be confused with more ominous lesions. Common associations include diabetes, oral contraceptives, estrogen replacement, obesity, ileal disease, total parenteral nutrition, cirrhosis, and certain medications.[2] Gallstones are present in up to 95% of cases of acute cholecystitis, 65% of adenomas, 95% of porcelain gallbladders, and 90% of gallbladder adenocarcinomas. [3, 4, 5] Eighty percent of stones are cholesterol stones (contain greater than 50% cholesterol; 10% being pure cholesterol), and the remaining 15-20% are pigmented
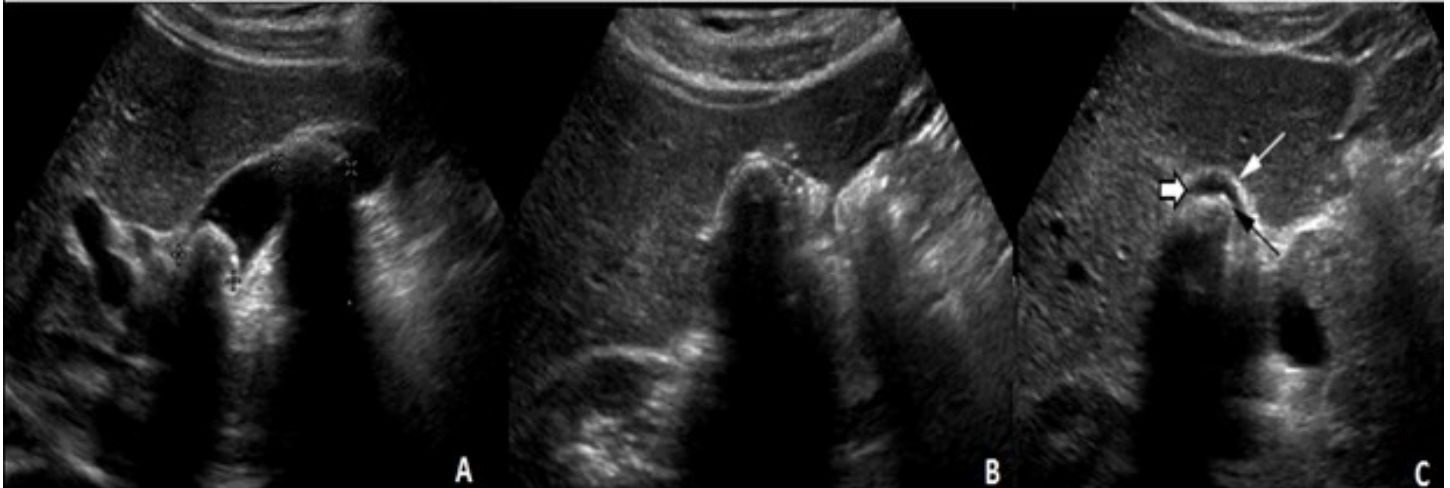
Figure 1. WES sign –Cholelithiasis. Sagittal **(A)** and transverse **(B and C)** ultrasound images of the gallbladder demonstrate the wall-echo-shadow complex **(C)** comprised of an outer echogenic line representing the gallbladder wall (thin white arrow), an outer hypoechoic line representing the gallbladder lumen (thick open arrow), an inner echogenic line (thin black arrow) representing the margin of the gallstone, and then hypoechoic posterior acoustic shadowing.

stones (contain <25% cholesterol), which are primarily composed of calcium bilirubinate and glycoproteins.

Ultrasound is the most common modality employed for initial evaluation of the gallbladder. Sonography is highly sensitive and specific for cholelithiasis, detecting >95% for stones over 2mm. Gallstones are classically mobile and strongly echogenic with marked posterior acoustic shadowing.[6] Demonstrating the posterior acoustic shadowing is variable and dependent upon technique when imaging the patient. Occasionally numerous or very large stones can fill the gallbladder, resulting in a wall-echo-shadow complex (WES). The anterior wall of the gallbladder is echogenic, followed by a thin hypoechoic line of intraluminal bile, then an echogenic line representing the superficial margin of the stone. Posterior shadowing obscures the deeper stones (Fig. 1).[4,7] The WES complex is specific to gallstones and is important in diagnosing benign stone disease versus a soft tissue mass filling the gallbladder lumen.

CT sensitivity for detection of gallstones is much less than sonography, typically about 75%-80% for stones ≥5mm (Fig. 2).[8] Calcium containing stones are well seen, even as small as 2mm; however, pure cholesterol stones may be iso- or even hypoattenuating to bile, decreasing detection rates. Considering this finding, attempts have been made to characterize stones based on density. Overall, pigmented stones tended to have higher Hounsfield units (HU) than cholesterol stones. However, the accuracy of CT characterization is significantly diminished due to attenuation overlap between the two types of stones, which is attributed to varying calcium content. Another consideration is that decreased tube voltage also decreases CT detection of choleliths, regardless of stone size. Optimal voltage for detecting stones has been reported at 140kVp with sensitivities of 73-86%; the sensitivity declines to 40-68% at 80kVp.[9] This is important to remember when employing low-dose CT protocols. Some calcified stones may contain a triradiate or triangular area of
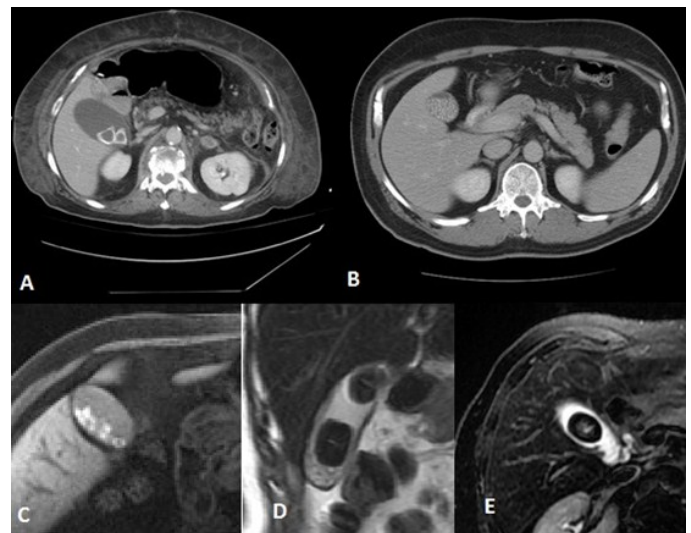
Figure 2. Cholelithiasis. Various CT and MR appearances of cholelithiasis **(A thru E)**. CT with IV contrast – A and B; Axial LAVA T1 GRE with fat suppression **(C)**; Coronal T2 SSFSE **(D)**; Axial T2 FRFSE-XL with fat suppression **(E)**.

central low or even air density representing contained nitrogen gas. This has been described as the "Mercedes-Benz" sign and was originally described as a radiographic finding.[10] This may be the only visible feature to suggest the presence of isodense stones.[11]

MR detection of gallstones is best appreciated on T2 - weighted images, especially magnetic resonance cholangiopancreatography (MRCP) sequences. Overall MR sensitivity is approximately 90-95%. Gallstones are typically hypointense on T1 and T2 weighted images. Less common appearances include a T1 or T2 hyperintense central focus surrounding by low signal or a predominantly T1 hyperintense appearance. The imaging appearance has been attributed to the relative amount of protein or pigment; pure cholesterol stones are typically uniformly low in T2 and T1 signal, and highly pigmented stones are predominantly hyperintense in T1 signal.[5] This can be an important feature for deciding management of impacted stones, as the pigment stones are softer and may be easier to treat endoscopically; pure cholesterol stones are more solid, making endoscopic treatment more difficult.

Gallbladder Polyps.

Another commonly encountered mass is the gallbladder polyp. Incidence of gallbladder polypoid lesions has been reported in 3 - 5% of the adult population.[12] Gallbladder polyps represent a spectrum of processes presenting with similar morphology and appearance at imaging. Most of these are benign, including cholesterol polyps and benign adenomas which are discussed here; malignant lesions are discussed separately.

Cholesterol polyps comprise about 50% of gallbladder polyps, are typically less than 10mm in size, and are completely benign with no malignant potential. They represent lipid-laden macrophages covered by normal gallbladder epithelium and project into the lumen [3, 13].

Adenomatous polyps of the gallbladder represent true neoplasms and are rather uncommon, representing about 5% of polyps.[14] They have an increased incidence in polyposis syndromes, such as Peutz-Jeghers and familial adenomatous polyposis.[15, 16] Subtypes of adenomas include tubular, papillary, and tubulopapillary. Most lesions measure less than 20mm in size and 10% are multiple.[3] It has been theorized
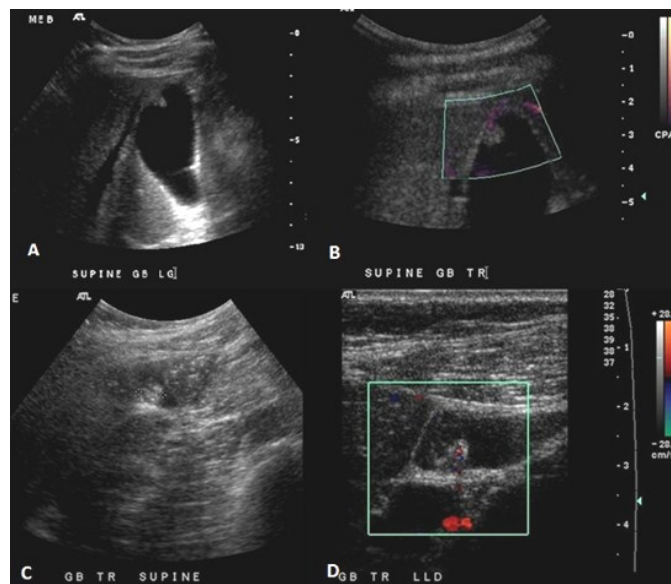
Figure 3. Gallbladder Polyps. Gray scale US images in two different patients (A and C) demonstrate focal echogenic, non-shadowing polyps projecting into the gallbladder lumen: one in the fundus (A) and one near the neck (C). Vascular flow is demonstrated within each polyp on Power (B) and color (D) Doppler, distinguishing these from avascular choleliths.

that adenocarcinomas may arise from benign adenomas in an adenoma-carcinoma sequence similar to that of colonic polyps.[12] This would suggest that accurately diagnosing small adenomas (<10mm) may help in identifying at risk individuals who require close follow up or early surgical intervention. This has been challenged, however, in several recent studies, which report that gallbladder cancers are genetically dissimilar from adenomas and lack residual adenomatous tissue at pathologic evaluation.[17,18]

Both cholesterol and adenomatous polyps appear sonographically as non-mobile, echogenic, non-shadowing masses. They may be sessile or pedunculated, have a stalk which may or may not be visible, and may show internal vascularity (Fig. 3). Adenomas and cholesterol polyps are usually smooth but may also be lobular or cauliflower-like. One important feature is that the gallbladder wall adjacent to a benign polyp should be normal; any irregularity or focal thickening >3mm should raise the suspicion for malignancy.

On unenhanced CT, adenomatous polyps are typically iso- or hypodense to liver parenchyma and are more easily seen than cholesterol polyps.[19] Cholesterol polyps are difficult to detect with

unenhanced CT, as their attenuation characteristics are similar to bile. Polyps enhance, making them more easily detectable on enhanced CT. However, the stalk may be undetectable, resulting in an appearance identical to a small stone or tumefactive sludge.[20]

The MR appearance of polyps is nonspecific with polyps having intermediate signal intensity on T1 and T2 weighted images. The appearance overlaps with gallbladder carcinoma. Irie et al. reported that malignant polypoid lesions more often have increased signal on diffusion images with lower ADC values than benign polyps at high b-values.[21] Also, it has been described on both MR and CT that while both benign and malignant polypoid lesions enhance in the arterial phase, benign lesions washout while malignant lesions tend to persistently enhance.[5,22]

Despite the available number of imaging modalities, there remains significant overlap between the appearance of benign polyps and malignant lesions. There has been considerable controversy over the years as to the proper follow-up and management of incidentally discovered polyps. Despite lack of consensus, the most consistently reported independent risk factor prompting intervention is size.[23] Many have advocated a strategy of cholecystectomy for polyps equal to or greater than 10mm and sonographic imaging follow-up for those less than 10mm. This results in many unnecessary follow ups and many unnecessary surgeries. However, Corwin et al. recently reported a series of 346 patients with gallbladder polyps followed for more than 5 years with no progression to carcinoma. The authors suggested that no additional follow up may be required for incidental polyps less than 6mm in size.[24] Another risk factor that should prompt earlier intervention is polyp morphology. Sessile polyps are significantly more likely to represent malignancy than pedunculated polyps and should prompt either cholecystectomy or close follow-up.[12,19]

Adenomyomatosis.

Adenomyomatosis, also known as adenomyomatous hyperplasia or diverticular disease of the gallbladder, represents one of two acquired benign hyperplastic cholecystoses. It is found in approximately 1-8% of cholecystectomy specimens.[25,26] The pathologic hallmark of adenomyomatosis is intraluminal
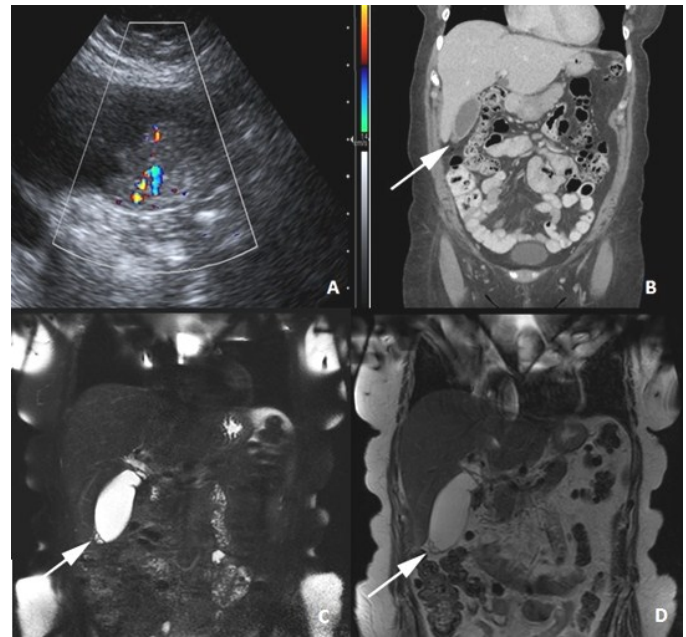
Figure 4. Focal Adenomyomatosis. Color Doppler US image **(A)** demonstrates focal gallbladder wall thickening with a polypoid appearance and vascular flow. Contrast-enhanced CT **(B)** and T2 weighted coronal MR sequences without and with fat saturation **(C and D)** demonstrate the focal gallbladder wall thickening with a characteristic cystic appearance (white arrows), favoring adenomyomatosis which was confirmed following cholecystectomy.

cholesterol deposition that becomes trapped within dilated Rokitansky-Aschoff sinuses, along with bile salts, sludge, and calculi. There is associated wall thickening from hyperplasia of both the mucosa and muscularis propria.[25] Cholecystosis is the second benign hyperplastic cholecystosis process, and represents cholesterol and triglyceride deposition in the lamina propria. This results in the classically described "strawberry gallbladder" appearance.

Adenomyomatosis is commonly encountered on ultrasound. The most common findings are nonspecific wall thickening (either focal fundal, segmental or diffuse), often associated with sludge, or calculi; focal fundal mass-like thickening is most common (Fig. 4).[3] Segmental adenomyomatosis may result in focal luminal narrowing of the gallbladder body. Echogenic intramural foci with associated V-shaped comet tail reverberation artifacts are characteristic and represent cholesterol crystals within Rokitansky-Aschoff sinuses. This is highly specific for adenomyomatosis and should not be confused with the "dirty shadowing" of intramural air seen in emphysematous cholecystitis, which is more irregular and linear in configuration.[3]

Contrast-enhanced MDCT is limited in the evaluation of adenomyomatosis. One retrospective review by Ching et al. of 36 cases of either adenomyomatosis or gallbladder carcinoma demonstrated a sensitivity of only 36% for the twenty-two pathologically proven cases of adenomyomatosis with a negative predictive value of only 44-48%.[26] However, if wall thickening (focal or diffuse) had a clearly cystic appearance (representing the Rokitansky-Aschoff sinuses), the specificity was 79-93%. It is important to note that there are case reports of adenomyomatosis coexisting with gallbladder carcinoma. If suspicious features, such as local organ invasion, adenopathy, or biliary obstruction are present, carcinoma should remain the primary diagnosis.[26] So while CT cannot be used to effectively exclude adenomyomatosis, if well-defined cystic gallbladder wall thickening is encountered in the absence of other suspicious findings, it is reasonable to conclude the diagnosis of adenomyomatosis.[26,27]

The most commonly described feature of adenomyomatosis on MR imaging is the "pearl necklace" sign, which results from the dilated Rokitansky-Aschoff sinuses.[25,28] A previous study evaluating 66 patients with gallbladder lesions demonstrated this finding best on T2 weighted images, ideally using single shot fast spin echo techniques or fast spin echo breath hold T2 techniques. The finding could also be seen T1 weighted dynamic contrast enhanced sequences but with significantly less sensitivity.[29] A later study compared 47 patients with either adenomyomatosis or primary gallbladder carcinoma using single shot fast spin echo T2-weighted magnetic resonance cholangiopancreatography sequences. It was demonstrated that the "pearl necklace" sign could be used to diagnose adenomyomatosis and exclude carcinoma with a mean sensitivity, specificity, and accuracy of 62 %, 92%, and 74%, respectively.[28]

The value of contrast-enhanced MR to discern between adenomyomatosis and carcinoma is highly questionable. Yoshimitsu et al. described that both adenomyomatosis and primary carcinoma enhance from the arterial phase through the delayed phase, but there were differences in their enhancement distribution.[29] Focal adenomyomatosis showed early, smooth, homogeneous mucosal enhancement that was continuous around the gallbladder epithelium;

this finding was rare in a few cases of carcinoma. Diffuse adenomyomatosis showed similarly early mucosal enhancement with delayed serosal enhancement, as well as a T2 hyperintense serosal layer. These individual findings were demonstrated in 38-50% of the primary carcinomas; however, these combined findings were seen in only 13% of carcinomas.[29] In a similar study, Haradome et al., reported that contrast enhanced MR demonstrated that enhancement patterns were indistinguishable between adenomyomatosis and carcinomas in 70% of their patients.[28]

Tumefactive Sludge.

Biliary sludge represents highly viscous bile with high bilirubin content. It is usually the result of biliary stasis from prolonged fasting or hyperalimentation. Tumefactive sludge is typically associated with cholelithiasis, and evolution of tumefactive sludge to calcium bilirubinate stones has been described.[30] Tumefactive sludge is most commonly encountered as an incidental finding on ultrasound evaluation for right upper quadrant pain.

While most biliary sludge presents as a layering slowly mobile dependent fluid-fluid level, tumefactive sludge presents as an intraluminal polypoid, echogenic, non-shadowing mass, which may mimic a tumor.[31] The key features separating the two are demonstration of tumefactive sludge as a mobile mass with no internal vascularity.[3,31] Unfortunately, this is not always possible, as sludge can be adherent to the wall or move very slowly; the lack of vascularity alone is not sufficient to effectively exclude tumor, especially with small masses. It has been suggested that in cases where tumefactive sludge is suspected on the initial exam but not conclusive, reimaging after a fatty meal and/or performing a short interval follow-up ultrasound in several weeks may show resolution or decreased size of the mass, which would exclude a neoplasm.[31,32]

Biliary sludge on CT can appear as layering increased density in the gallbladder or as a tumefactive soft tissue attenuation mass (>25HU). It should not enhance; however, vicarious excretion of iodinated contrast may confound evaluation for enhancement.[33] CT is limited as a primary evaluation tool for sludge with a sensitivity between 44-64%.[33] Tumefactive
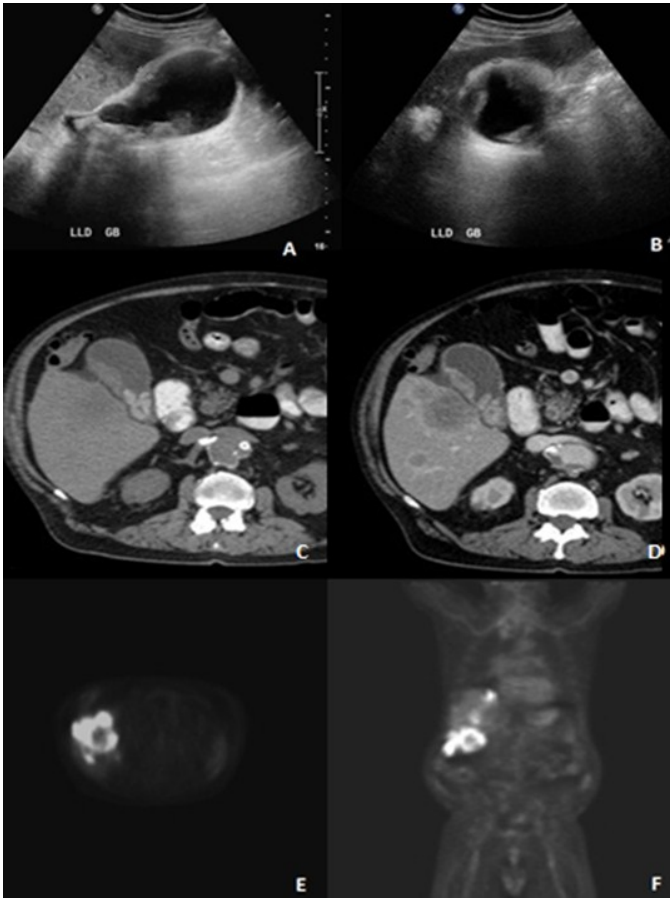
Figure 5. Primary Gallbladder Adenocarcinoma. Longitudinal **(A)** and transverse **(B)** gallbladder ultrasound images demonstrate irregular gallbladder wall thickening. Axial CT images without **(C)** and with **(D)** contrast reveal an enhancing eccentric gallbladder wall mass, as well as layering non-enhancing intraluminal sludge and stones. Multiple rim enhancing hepatic lesions are consistent with hepatic metastases **(D)**. F18 FDG-PET in axial **(E)** and coronal **(F)** planes show hypermetabolic activity associated with the primary gallbladder carcinoma and multiple hepatic metastases.

sludge on MR is not separately well described in the literature to our knowledge; however, biliary sludge in general has been described as iso- to mildly hyperintense on T2 weighted images and hyperintense on T1 weighted images. The T1 hyperintensity results from water resorption and concentration of cholesterol and bile salts during fasting.[5] Similar to CT, any enhancement demonstrated within the mass excludes sludge and is suspicious for neoplasm. The recent ability to perform subtraction images for post-contrast sequences greatly increases the ability to identify or exclude true enhancement and leads to a more confident diagnosis.[34]

Rare Benign Entities.

Additional rare entities that the radiologist should have a passing familiarity with are listed in (Table 1). A detailed discussion of most of these entities is beyond the scope of this article and is well described in a review by Levy et al.[3] Of these entities, xanthogranulomatous cholecystitis (XGC) may be the most important to know. This represents a histiocyte-predominant inflammatory process from bile extravasation into the gallbladder wall through ulcerated Rokitansky-Aschoff sinuses.[3,5] It most often presents with clinical symptoms identical to typical cholecystitis. Its imaging appearance mimics that of aggressive invasive carcinoma, as the infection may spread into local adjacent organs. It has also been described as an associated risk factor of primary gallbladder carcinoma[3] Wall thickening is the most common finding but is nonspecific. The typical sonographic appearance has been described as wall thickening with multiple hypoechoic bands or nodules. CT findings suggestive of XGC include a low attenuation nodule involving more than 60% of the thickened gallbladder wall area and a continuous line of mucosal enhancement.[3] These same findings are seen on T2 and post-contrast T1 MRI sequences. Intramural T2 hyperintense foci correspond to the low density nodules on CT and represent abscesses and foci of xanthogranulomatous inflammation.

Malignant Masses

Primary Gallbladder Carcinoma.

Primary gallbladder carcinoma is uncommon with approximately 7,000 cases reported annually.[35] Reported risk factors include female gender, advanced age, cigarette smoking, ethnicity (specifically Hispanic, Northern Japan, Native American, and Israeli), and occupational exposure to chemicals from rubber, automobile, wood finishing, and metal fabrication industries.[36,37] Mean age of presentation is 72 years. More than 90% are adenocarcinomas, and there are several histological subtypes, including papillary, clear cell, signet cell, and mucinous. Adenosquamous, squamous, small cell, and undifferentiated types are quite rare. Many gallbladder carcinomas contain a mixture of different subtypes.[36,38] The overall five-year survival rate of gallbladder carcinoma is dismal (less than 5%) with a median survival of 6 months. Papillary

carcinomas have a slightly better prognosis (median survival 20 months), as they tend to fill the gallbladder before becoming invasive.[36]

The cross-sectional appearance of gallbladder carcinoma for US, CT, and MR is that of a mass replacing the gallbladder (40-65%), focal or diffuse wall thickening (20-30%), or an intraluminal polypoid mass (15-25%) (Figures 5-7).[39] Most gallbladder carcinomas present at an advanced stage and are not diagnostically challenging. There is typically local invasion of liver or adjacent organs, which significantly limits therapeutic options. It is important to be aware of the utility of cross sectional imaging in staging and prognosis of gallbladder carcinoma.

Sonography is not useful in staging of gallbladder carcinoma; Bach et al. reported that only 37% of patients with advanced disease could be identified on US.[40] In another study, Tsuchiya described that 30% of early carcinomas may be missed by ultrasound.[41] Endoscopic ultrasound improves success in both characterizing local disease and identifying regional nodal spread versus conventional ultrasound.

CT and MR are more useful in staging, as they more accurately define local extent of disease, regional adenopathy, and distant metastases. CT sensitivity for hepatic invasion is 65% if <2cm and 100% if >2cm. Sensitivity for nodal spread has been reported as 36% for N1 and 47% for N2 disease; there is 99% specificity for nodes >10mm.[42] CT has a reported an overall T stage accuracy of 84% and an accuracy of 85% in determining resectability. MR has a variable reported sensitivity between 67-100% for hepatic invasion, although the depth of invasion is underestimated in approximately 10% of cases. MR sensitivity for lymphadenopathy has been reported between 56-92%.[5,39] MR and CT are also useful in detecting vascular invasion by tumor.

Diagnosis of early stage gallbladder carcinoma is a distinct challenge. The imaging features of early gallbladder carcinoma have significant overlap with those of benign gallbladder diseases previously described. There are several features, however, that may be useful in characterizing a mass as suspicious for malignancy. Malignant polypoid lesions are typically greater than 1cm. Also, any focal or diffuse wall thickening >1cm or asymmetric thickening are suggestive of carcinoma.[39]
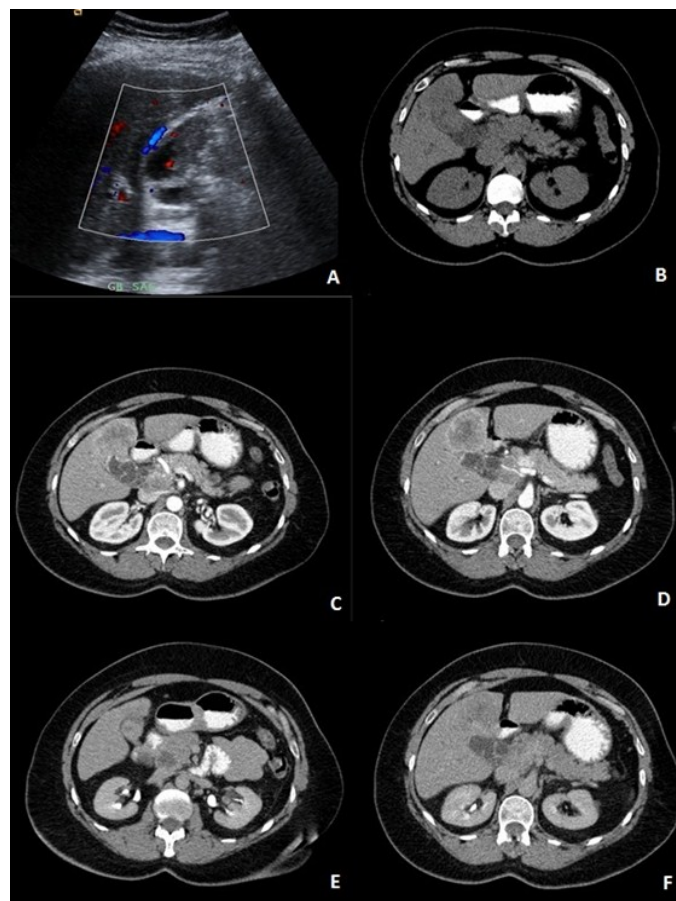

Figure 6. Primary Gallbladder Small Cell Carcinoma. RUQ transverse ultrasound image with color Doppler **(A)** demonstrates an intraluminal echogenic mass with increased color flow and irregular gallbladder wall thickening. Unenhanced **(B)**, arterial phase **(C and D)**, and 5 minute delayed **(E and F)** CT images through the gallbladder show the irregular gallbladder mass directly invading the liver parenchyma. Central low density of the mass on all phases likely represents necrosis. Primary small cell carcinoma was confirmed at biopsy. The prominent enhancement on arterial phase with progressive washout through the delayed phase is typical of neuroendocrine tumors.

Sonographic imaging of gallbladder carcinoma typically demonstrates heterogeneous echotexture within the mass, which reflects varying degrees of necrosis, or irregular wall thickening. Echogenic foci typically represent gallstones versus the much less common porcelain gallbladder (Fig. 8).[43] Both gallstones and porcelain gallbladder are well described risk factors, although the association between gallbladder carcinoma and porcelain gallbladder may not be as evident as previously thought. This risk/association is primarily based on reports from the early to mid-20th century, which found gallbladder carcinoma in 20% of cases of porcelain gallbladder. A

Figure 7. Primary Gallbladder Adenocarcinoma. Sagittal grayscale ultrasound image of the RUQ **(A)** demonstrates irregular polypoid gallbladder wall thickening. Axial **(B and C)** and coronal **(D)** contrast-enhanced CT images of the gallbladder show markedly irregular gallbladder wall thickening with heterogeneous enhancement and loss of distinction between the gallbladder wall and surrounding liver margin, consistent with direct invasion. Extensive metastatic adenopathy is present in the peripancreatic and periaortic regions **(B and C)**.
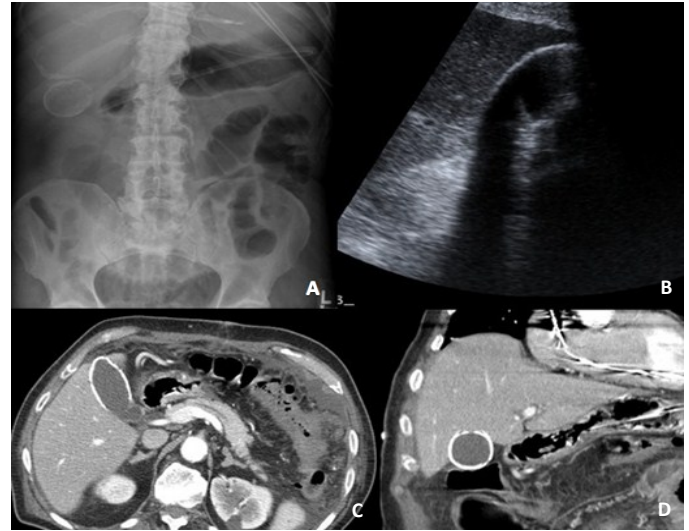
Figure 8. Porcelain Gallbladder. Abdominal AP radiograph **(A)**, transverse RUQ gray scale ultrasound **(B)**, and axial **(C)** and coronal **(D)** contrast-enhanced CT images of the upper abdomen each demonstrate thin intramural calcification of the gallbladder wall, diagnostic of porcelain gallbladder. Marked posterior acoustic shadowing is seen on US **(B)**.

recent retrospective review by Kahn et al. of seven published series encompassing over 60,000 cholecystectomies found gallbladder carcinoma in 15% of porcelain gallbladders; gallbladder carcinoma in itself had an overall incidence of 0.2%. They also retrospectively reviewed an additional 1,200 consecutive cholecystectomies with 1.1% having porcelain gallbladders, as well as an additional series of 35 gallbladder carcinomas; none of the patients in these two series had both gallbladder carcinoma and porcelain gallbladder. Their conclusion was that porcelain gallbladder and gallbladder carcinoma are only weakly associated.[44]

On unenhanced CT, gallbladder carcinoma is typically hypodense; 40% demonstrate hypervascular foci equal to or greater than liver parenchyma with IV contrast. On MR, gallbladder carcinoma has nonspecific intermediate T1 and moderately hyperintense T2 signal intensity. On both CT and MR, intense irregular enhancement may occur at the periphery of the lesion on arterial phase imaging with persistent portal venous and delayed enhancement from fibrous stromal elements. The persistent delayed enhancement is suggestive of malignancy, as opposed to early washout which is more characteristic of benign polyps.[5,22,39]

F18-FDG PET-CT is a relatively recent addition to the work-up of gallbladder malignancies. Several studies have reported a sensitivity of 75-80 % and specificity of 82-87% for gallbladder malignancy with a high negative predictive value of 90%.[45,46] Reported false positives include adenomyomatosis, xanthogranulomatous cholecystitis, and tuberculoid granulomatosis.[47] False negatives include mucinous carcinoma, which is a well described limitation of PET. Focal intense increased FDG activity is the most commonly described appearance for gallbladder malignancy, although rim-like intense activity (which is more typical of acute cholecystitis or chronic cholestasis) has also been described.[47]

Metastases and Other Rare Malignancies.

Approximately 98% of gallbladder malignancies represent primary carcinoma.[42] The next most common malignancy is metastases. Malignant melanoma is the most common primary tumor to metastasize to the gallbladder, representing just over

50% of reported cases.[48] The sonographic appearance of melanoma metastases is one or more hyperechoic mural masses >1cm in diameter. Unfortunately, a study of 464 patients with malignant melanoma by Holloway et al. demonstrated that while 15-20% of patients had gallbladder involvement at autopsy, only 4.1% had detectable disease on ultrasound.[49] The CT appearance is that of a polypoid enhancing mass or irregular wall thickening. Most of the lesions are serosal, but they may also be intraluminal. The typical MR appearance is that of a T1 and T2 hyperintense mass. The T1 hyperintensity has been attributed to both the melanin content, which can be variable, as well as hemorrhage or necrosis. Because of the pre-contrast T1 hyperintensity, post-contrast imaging may not be helpful. The enhancing gallbladder wall may become isointense with the lesions, decreasing detection.[50] Other reported metastases to the gallbladder include renal cell carcinoma and hepatocellular carcinoma.

Other rare malignancies reported to occur in the gallbladder include primary non-Hodgkin lymphoma (approximately 13-20 cases reported), which typically presents with a nonspecific appearance on US, CT, and MR that mimics gallbladder carcinoma; typical imaging findings include an intraluminal mass or a mass replacing the gallbladder, along with cholelithiasis, biliary sludge, porta hepatic adenopathy, liver invasion, or biliary obstruction. MR reveals a T1 hypointense and T2 hyperintense mass relative to liver parenchyma.[5,48] There are also case reports of primary gallbladder sarcomas, including Kaposi sarcoma, malignant fibrous histiocytoma, angiosarcoma, leiomyosarcoma, and rhabdomyosarcoma.[48]

Summary

There are numerous causes of gallbladder masses, benign much more common than malignant, which are frequently found on imaging. Familiarity with the diverse etiologies of these masses and their presentations on various cross-sectional imaging modalities is critical. This knowledge provides the radiologist with the ability to make earlier and more confident diagnoses and assist referring clinicians in facilitating appropriate management. At times, costly diagnostic workups and interventions may be avoided.

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