Malignant neoplasms of gallbladder and biliary tract: not an uncommon diagnosis in emergencies. Differential diagnosis, complications and diagnostic imaging.

Poster No.: C-2210
Congress: ECR 2013
Type: Educational Exhibit
Authors: A. Marin Canete, I. Santos Gomez, M. Simonet, A. M. Sanchez Laforga, N. Rojo Sanchis, B. Y. Barragan Requena, M. R. Cambra Marti; Sant Boi de Llobregat/ES
Keywords: Obstruction / Occlusion, Neoplasia, Cancer, Contrast agent-intravenous, Cholangiography, Ultrasound, MR, CT, Pancreas, Emergency, Biliary Tract / Gallbladder
DOI: 10.1594/ecr2013/C-2210

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

To recognize biliary tract and gallbladder pathology in the emergency patient, including common and uncommon signs of malignant disease, as well as the potential complications that can be associated.
Background

The most prevalent gallbladder and biliary tract disorders seen in the emergency setting are infectious and obstructive pathologies. However, a considerable number of patients may present with neoformative disease, which may mimic the imaging and clinical signs of the inflammatory, infectious and obstructive diseases, and even, may associate them.

The role of the radiologist shall be essential to determine the origin of the patients disorders, as well as to exclude common complications in order to ease the initial clinical decisions.

One the one hand, there is a high prevalence of gallstones in the occidental population (12%), and approximately the 1-2% every year develop acute disease; on the other hand, neoplastic disease involving gallbladder and biliary tract may affect up to 5 to 10 patients per 100,000 inhabitants.
We illustrate the different signs of gallbladder and bile duct neoplasms, in early and advanced stages, through radiological images acquired in our hospital.

Concomitant thoracic and abdominal additional complications during the clinical process of the disease (either infectious, obstructive or neoplastic) are also exhibited.

1.- INTRODUCTION:

In the emergency department of almost every hospital, diagnosis, management and treatment of acute biliary pathology forms part of the daily routine.

The high prevalence of cholelithiasis in the European population, ranging between 10% and 12%, classically derives in two clinical scenarios:

1. Each year, approximately 1-4% of patients with vesicular lithiasis present hepatic colic episodes, and of these, 20% will definitely suffer superinfection that can culminate in acute cholecystitis.
2. Moreover, throughout their lives, the 6-9% of patients with cholelithiasis will suffer migration of the stones to the bile ducts, causing partial or complete obstruction with consequent infection in the end, engaging in a pattern of acute cholangitis.

Less frequently, we may find the clinical scenarios described but with a different etiology from the vesicular lithiasis. We specially refer to gallbladder carcinoma and cholangiocarcinoma in their varied patterns of presentation. Although they represent a low percentage of final diagnosis, given the high prevalence of acute biliary pathology, these "exceptions" are relatively common in the emergency box.

Not all gallbladder and biliary cancers present emergently in the box setting, but those who do, as a result of the invasion and obstruction of the gallbladder and the biliary trees, mimic clinical and radiological signs of acute or chronic cholecystitis, acute colangitis and choledocolithiasis. An accurate diagnosis on time permits an optimum management and treatment of the clinical process.

2.- CHOLECYSTITIS & CHOLANGITIS: COMMON ACUTE BILIARY DISEASE:
2.1.- ACUTE CHOLECYSTITIS:

The main symptom of cholelithiasis is hepatic colic, which occurs when a stone obstructs the cystic acutely, leading to a sudden expansion of the gallbladder that results in pain. This is the most frequent cause of right upper quadrant abdominal pain. Its persistence in time, usually more than 6 hours, should make us think of acute cholecystitis. As time goes by, there is a progressive ductal ectasia, more chemical irritation of the mucosa and finally wall ischemia, considering the infection as a secondary phenomenon.

However, not all patients present all symptoms from their entrance in the emergency room, and, just a little more than one-third of patients suspected of having acute cholecystitis after initial clinical evaluation are ultimately proved to have a different diagnosis.

Ultrasound (US) is the primary imaging modality used to evaluate acute right upper quadrant pain, as it is an accurate, non-radiating, safe, inexpensive and accessible imaging modality. Computed Tomography (CT) is the second choice and an excellent complement for US, specially in complex cases and when visibility with US is limited. When it is needed to discard acute biliary ductal disease, mostly when suspicion of choledocholithiasis, magnetic ressonance (MR) imaging is the most accurate diagnostic imaging method.

US: (Fig. 1 on page 22)

Most sensitive findings (both combined have a positive predictive value of 92%):

- **Cholelithiasis.**
- Maximal tenderness over the sonographically localized gallbladder **(sonographic Murphy sign)**.

Secondary findings, neither specific nor sensitive, may help:

- Gallbladder wall thickening >3 mm, sometimes with edema.
- Pericholecystic fluid.
- Wall hyperemia a Doppler US.
- Tumefactive sludge: as it may present a pseudomass appearance, it is imperative to distinguish it from polypoid gallbladder cancer, by changing the position of study of the patient (sludge moves and reubicates while a polypoid mass remains identical) and employing Doppler US (a polypoid mass shows internal flow, sludge shows no flow signal). It is prior to establish that difference, specially when there is the diagnosis of acute cholecystitis, because the surgical therapeutical approach is different if
gallbladder carcinoma cannot be discarded (laparoscopic cholecystectomy vs open cholecystectomy with resection of segments V and IVB of the liver). Contrast-enhanced CT can therefore be helpful.

**CT:** (Fig. 2 on page 22)

Imaging signs found with contrast-enhanced CT are more locally limited than the US (no evaluation of the Murphy sign, no movement of the patient, sludge often not seen), but also give us a more extended point of view, mainly in the extent of the pericholecystitic liquid and inflammatory affection.

The differential diagnosis for acute cholecystitis is extensive and includes choledocholithiasis, acute pancreatitis, peptic ulcer disease, acute hepatitis, liver abscess, liver or gallbladder neoplasm with complication, pneumonia and heart disease. There should also be included entities conditioning sympathetic thickening of the gallbladder wall, as perforated duodenal ulcer, right-sided diverticulitis, and even acute right-sided pyelonephritis.

**Complicated acute cholecystitis** in many occasions shall require both US and CT study:

1. **Gangrenous cholecystitis** (2-38%)(Fig. 3 on page 23): continuously increased intraluminal pressure may produce gallbladder wall ischemia, which can turn into necrosis, developing a gangrenous process. Up to 50% of patients show diffuse, peritonitic pain; though, *sonographic Murphy sign may be negative* in up to 66% of them, due to denervation of the wall. Perforation is more common. At CT, common findings are gas in the wall or lumen, intraluminal membranes, irregular or absent wall, and abscess.

2. **Emphysematous cholecystitis** (Fig. 4 on page 24): produced by a gas-forming bacteria, is more common in diabetic men, and frequently associates gangrene and perforation. Wether *intraluminal and intramural gas* findings are the more specific signs.

3. **Gallbladder perforation** (10%)(Fig. 5 on page 25): serious complication detectable either with CT or US, with a 19-24% rate of mortality, which can be acute (10%, generalized peritonitis, worst prognosis), subacute (60%, generally contained, pericholecystic abscess) or chronic (30%, duodenal or common bile duct fistula).

4. **Cholecystoenteric fistula** (Fig. 6 on page 26)(Fig. 7 on page 27): consequence of a chronic perforation, usually presents communication with duodenum; we may see air pass from the bowel to the gallbladder and stones from the gallbladder into the bowel, sometimes causing mechanical obstruction in the ileum (*gallstone ileus*) or less frequently at other segments of the gastrointestinal tract (Bouveret syndrome when at the duodenum).
5. **Gallbladder torsion**: distended, tender gallbladder with an abnormal orientation remote from the gallbladder fossa. CT and MR imaging may show tapering and twisting of the cystic duct.

### 2.2.- CHRONIC CHOLECYSTITIS:

Although called chronic, it is the most common form of clinically symptomatic gallbladder disease and is almost invariably associated with gallstones. Signs and symptoms are vague and include abdominal distention, epigastric discomfort, and nausea.

In many patients with gallstones, the persistence of hepatic colics or subtle episodes of acute cholecystitis, can turn the gallbladder into small and contracted, with irregular and thickened walls, being considered characteristics of chronic cholecystitis (sclero-atrophic gallbladder when is small, contracted and probably full of lithiasis), which are evaluable either with US, CT or MR (Fig. 8 on page 28).

In addition to the signs described, contrast-enhanced CT and MR shows that the gallbladder wall enhances less intensely than in acute cholecystitis. The enhancement is usually smooth, slow, and prolonged, unlike in gallbladder carcinoma, in which it is usually irregular, early, and prolonged, and which is the main differential diagnosis.

Prolongued persistence of irritating intraluminal factors may lead to lineal calcification of the gallbladder walls; then it is referred as a "**gallbladder in porcelain**" (Fig. 9 on page 29). 20-25% of these patients will develop a gallbladder cancer during their life.

### 2.3.- XANTHOGRANULOMATOUS CHOLECYSTITIS:  (Fig. 10 on page 30)

Uncommon destructive inflammatory disease, probably induced by intramural extravasation of bile from the Rokitansky-Aschoff sinuses or from superficial mucosal ulcerations, leading to an inflammatory response in which histiocytes predominate as they ingest the chemically irritating cholesterol crystals. So, macroscopically the gallbladder shows a thickened, nodular and poorly-defined walls.

It is common to find invasion of the surrounding fat and nearby organs, like the colon and duodenum, many times complicated by fistulous or abscess formation.

Lymphadenopathy and biliary obstruction may be associated findings, and even gallbladder cancer may coexist.
The disease usually manifests as an acute episode of cholecystitis in women 60-70 years of age and tends to persist even for years.

At CT, xantogranulomatous cholecystitis closely resembles gallbladder carcinoma, with diffuse or focal gallbladder wall thickening, heterogeneous wall enhancement with **continuous linear enhancement** of the mucosa (distinctive from gallbladder carcinoma), and **hypoattenuating intramural nodules** occupying more than 60% of the thickened wall area (xanthogranulomas). Sonographic signs are also similar.

**2.4.- ADENOMYOMATOSIS:**

Adenomyomatosis, or diverticular disease of the gallbladder, is a non-inflammatory benign condition that consists in an excessive proliferation of surface epithelium with deep and branching invaginations into the thickened tunica muscularis of beyond.

It can either be a diffuse entity, that manifests with diffuse mural thickening and luminal narrowing, or segmental, when seen as a focal circumferential thickening in the midportion of the gallbladder, ("hourglass" appearance) or as a semilunar, crescentic solid mass.

Dysplastic changes and even carcinoma may arise from adenomyomatous epithelium, especially in segmental type disorders.

Depending on the imaging technique, we find these typical findings:

**US:** wall thickening with echogenic intramural foci which condition V-shaped "**comet tail**" reverberation artifacts.

**CT:** abnormal wall thickening with enhancement after administration of endovenous contrast material, with the "**rosary sign**" (enhancing epithelium within intramural diverticula surrounded by the relatively unenhanced hypertrofied gallbladder muscularis.

**MR:** gallbladder wall thickening with Rokitansky-Aschoff sinuses as intramural lesions that are hyperintense on T2-weighted images, hypointense on T1-weighted images, and nonenhancing, showing the "**pearls necklace sign**" or "**string of beads sign**", that is highly specific (92%) in diagnosing gallbladder adenomyomatosis versus gallbladder cancer.
In approximately 70% of patients, the contrast enhancement pattern of adenomyomatosis is indistinguishable from that of gallbladder cancer.

Moreover, it is common to find gallstones and sludge in the lumen of the pathologic gallbladder.

2.5.- ACUTE CHOLANGITIS: (Fig. 12 on page 32)(Fig. 13 on page 33)

Ascending cholangitis is the consequence of an infection of the obstructed biliary tree, mainly by common bile duct lithiasis. Clinically, it is diagnosed on the basis of classical Charcot's triad of fever, jaundice and right upper quadrant abdominal pain (only exhibited in 50-70% of patients). In severe disorders, patients may develop shock and an altered mental status known as Reynolds' pentad.

In the urgent US we may see thickening of the walls of the bile ducts, which can be accompanied of dilatation of the biliary ducts, with choledocolithiasis, pus and/or debris in the lumen.

3.- NEOPLASMS MIMICKING ACUTE BILIARY DISEASE:

Most gallbladder carcinoma and cholangiocarcinoma diagnoses are made through rapid diagnostic units, usually from an outside hospital setting, after an insidious and long evolution disease. Still, it is noteworthy that a small percentage of patients, not inconsiderable, are diagnosed of gallbladder carcinoma or cholangiocarcinoma in a clinical process in the emergency department, most of them after an episode of acute biliary disease or some other acute complications.

We also include imaging of the pathologically confirmed diagnostics arising from our emergency department within the last two years, which are: adenocarcinoma (4), cholangiocarcinoma (3), hepatocholangiocarcinoma (1) and biliary duct papillary adenocarcinoma (1). There are 3 more patients without citologic confirmation due to their advanced stage.

On the following lines, we develop the details about gallbladder carcinoma and, posteriorly, cholangiocarcinoma.
3.1.- GALLBLADDER CARCINOMA:

3.1.1.- EPIDEMIOLOGY:

Primary gallbladder carcinoma is an uncommon, aggressive malignancy that affects women more frequently than men. Its diagnosis increases with the age of the patient, with a peak of presentation in the 7th and the 8th decades of life. The highest incidence rates are found in Chile, north-east Europe, Israel, North Japan and countries with Native Americans and Hispanic Americans. In Europe, in number of patients in the 7th decade and on, it is classified as the 4th gastrointestinal cancer in women and the 6th in men.

3.1.2.- RISK FACTORS:

There are several demonstrated risk factors which have to be considered in the clinical routine: beyond the female sex and the age, the postmenopausal status, cigarette smoking, chronic infection of *Salmonella typhii* and exposure to chemicals used in rubber, automobile, wood finishing, and metal fabricating industries.

Moreover, cholelithiasis, and subsequent chronic cholecystopathy and/or porcelain gallbladder, as well as patients with primary sclerosing cholangitis or those with congenital developmental anomalies, that facilitate the chronic stasis of biliary secretions and the reflux of pancreatic secretions, have an increased risk.

The given conditions ease a gallbladder and ductal mucosal metaplasia which can subsequently turn into carcinoma.

3.1.3.- CLINICAL DIAGNOSIS:

There is not a typical clinical presentation established for the gallbladder cancer.

Most of the patients develop progressively indolent symptoms as chronic abdominal pain, anorexia or weight loss, and show clinical signs as a palpable mass in the right upper quadrant or hepatomegaly. Jaundice is more often an indirect sign of advanced disease, as the result of malignant obstruction of the biliary ducts. Given these features, due to the nonspecificity of the symptoms and their usually painless progression, the vast majority of these patients will show advanced disease at diagnosis.
A few patients will present infectious or inflammatory signs in relationship with a gallbladder cancer, due to biliary drainage problems, which can be associated either with early and advanced stages. Those who arrive at the emergency setting with a clinical presumptive diagnosis of cholecystitis, cholangitis or choledocolitiasis, or even probable biliary colics, may have an incidental diagnosis of early-staged gallbladder carcinoma.

It is reported an incidental diagnosis of gallbladder cancer in the 1% of patients affected of gallstones undergoing cholecystectomy, and turns into de 2.5-3% in cholecystectomized patients in case of acute cholecystitis. This percentage rises up to the 8-10% in patients with scleroatrophic gallbladder, and almost to the 25% in those showing porcelain gallbladder.

3.1.4.- PATHOLOGIC FEATURES:

Microscopically, the normal gallbladder wall is composed of four layers: mucosa (with a single layer columnar epithelium), lamina propria, an irregular muscle layer, and connective tissue. The 98% of all gallbladder malignancies have an epithelial origin, being the 90% of them adenocarcinomas. There are several histologic variants of adenocarcinoma recognized: papillary, intestinal, mucinous, signet-ring cell, and clear cell.

Macroscopically, gallbladder carcinomas are tumors with origin in the fundus (60%), less commonly in the body (30%) or the neck (10%). We have to distinguish between three different patterns of presentation: the big majority of gallbladder adenocarcinomas are diffuse, infiltrating masses with origin in the fundus that replace the gallbladder with direct invasion of neighboring organs (specially the liver), although sometimes they may present as wall thickening or nodularity and occasionally as intraluminal polypoid growth.

3.1.5.- RADIOLOGIC FEATURES:

An abdominal radiography shall be the first radiological examination, either in a patient with fever and right upper quadrant pain in the emergency room, and also in the one with months-long abdominal discomfort and subtle jaundice. We can find calcified gallstones or a porcelain gallbladder, as well as gas collections in a fistulized gallbladder or in the biliary tree. Though not showing us the whole pathology, important indirect signs may be seen.
Next imaging steps include US or CT (MR), an election to be made based on the clinical context and machine availability. Different signs will be found depending on the pattern of growth:

3.1.5.1.- Mass replacing the gallbladder (40-65%): (Fig. 14 on page 34)(Fig. 15 on page 35)

US:

- mass with irregular margins replacing totally or partially the gallbladder, sometimes invading the liver and the biliary tree (without solution of continuity),
- heterogeneus echotexture (reflecting the degree of necrosis)
- with echogenic areas with acoustic shadowing (coexisting gallstones, calcified walls or tumoral calcifications).
- and hypoechoic foci of trapped bile.

CT /MR:

- hypodense/intense or isodense/intense mass in the gallbladder fossa (low attenuation related to necrosis),
- with soft-tissue invasion of the liver,
- up to 40% show enhancement areas (viable tumor), peripheral in arterial phase and central in portal and delayed phases (retained in stromal fibrous components).
- calcifications (porcelain walls or calcified gallstones),
- usually with secondary biliary dilatation and obstruction (38%).

DIFFERENTIAL DIAGNOSIS:

When finding this presentation of gallbladder carcinoma, specially in urgent cases seen in the emergency department that associate acute inflammatory or infectious clinical signs and analytic figures, the most common diagnosis we should care about is the acute cholecystitis complicated with a liver abscess, mostly infiltrating the IVB and V segments.

Moreover, there are other neoplastic ethiologies to have in mind:

- Hepatocellular carcinoma.
- Cholangiocarcinoma.
- Metastatic disease.
3.1.5.2- **Focal or diffuse wall thickening (20-30%)**: (Fig. 16 on page 36)(Fig. 17 on page 37)

- Mimics the appearance of the common acute and chronic inflammatory pathologies of the gallbladder, but wall thickening tends to be thicker than 1 cm with associated irregularity or conditioning asymmetry.
- Contrast-enhanced CT or MR: marked arterial enhancement that becomes isodense or isointense to the liver in portal venous phase, heightens suspicion of gallbladder carcinoma.
- When associated lymphadenopathy, soft-tissue extension or hematogenous metastases, carcinoma is the most probable diagnosis.
- Contrast-enhanced CT is extremely useful to distinguish cancer from complicated cholecystitis.
- MR useful to distinguish adenomyomatosis and chronic cholecystitis from gallbladder carcinoma.

**DIFFERENTIAL DIAGNOSIS:**

- Chronic cholecystitis.
- Xantogranulomatous cholecystitis.
- Adenomyomatosis.
- Diffuse hepatic or systemic diseases: acute hepatitis, portal hypertension, congestive heart failure.

3.1.5.3- **Intraluminal polypoid mass (15-25%)**: (Fig. 18 on page 38)

**US:**

Well-defined, round or oval shape mass, in relation with gallbladder wall, with a thickened implantation base. Modification with the position changes of the patient helps to diagnose a pseudotumor of tumefactive sludge or a clot.

**CT / MR:**

hypodense/intense or isodense/intense polyp, with ill-defined early enhancement after intravenous contrast administration. Ct or MR imaging is more subtle than US to determine extension beyond the wall.

**DIFFERENTIAL DIAGNOSIS:**

- Tumefactive sludge.
• Adenomatous polyps.
• Hyperplastic cholesterol polyps.
• Carcinoid.
• Melanoma metastases.

3.1.6.- TUMORAL EXTENSION:

Nodal involvement may be seen in the hilar region, progressing through the hepatoduodenal ligament and the head of the pancreas to the superior mesentery, celiac and para-aortic lymph nodes.

Gallbladder carcinoma commonly spreads to neighboring organs by direct invasion, rather than following the lymphatic and vascular paths, which is facilitated by the thin gallbladder wall. Intraductal, intraperitoneal and neural spread are anecdotal.

When direct extension is seen, the liver is the most frequently involved (65%), followed by the colon (15%), duodenum (15%) and pancreas (6%). Affectation of the omentum and the vascular structures of the mesentery may also be seen in punctual cases (Fig. 19 on page 39).

3.1.7.- COMPLICATIONS:

There are several kinds of complications to take in consideration.

With the local progression, independently of the pattern of presentation of the gallbladder cancer, it is possible to find direct invasive extension to the neighboring organs, recently explained a few lines above. Logically, those who behave as a mass replacing the gallbladder show earlier infiltrative signs than the other tumoral patterns.

When involving the liver, the tumoral growth shall condition obstruction with retrograde dilatation of the biliary trees, tumoral thrombosis or infiltration of the portal vein and hepatic artery branches (Fig. 20 on page 40). The chronic biliary obstruction eases the addition of inflammatory changes and secondary infections. Furthermore, the growth of the tumoral mass may lead to a bigger necrotic central content; added to the obstructive conditions, infections may become even more usual.

When the gallbladder tumor invades the gastrointestinal tract, either the duodenum or the hepatic angle of the colon, several grades of obstructive pathology may be found. In
advanced stages of invasion, endoluminal duodenal (and sometimes colonic) prosthesis may be essential to maintain the gastrointestinal transit (Fig. 21 on page 41). In other occasions, as occurs in chronic cholecystitis, transient fistulas with duodenum and colon may appear, with migration of gallstones into the gastrointestinal lumen. When migrating to the colon, lithiasis can be clinically silent, but in the occasions they migrate to the duodenal lumen, depending on their size, subocclusive or occlusive symptoms can be associated (gallstone ileus), requiring surgical removal in many episodes (Fig. 22 on page 42).

In cases of pancreatic involvement, obstruction of the duct of Wirsung can develop acute panchreatitis, which may turn into chronic. Not only the tumor but the adenopathic masses may produce panchreatic involvement, though it is easier that only by compression phenomenons. With chronicity, pancreatic atrophy may be a consequence (Fig. 23 on page 43).

3.2.- CHOLANGIOCARCINOMA:

3.2.1.- EPIDEMIOLOGY:

Cholangiocarcinoma is the second most common primary malignancy of the liver, showing its highest prevalence in Southeast Asia.

3.2.2. RISK FACTORS:

Known risk factors listed share in common the feature of chronic biliary inflammation.

- Liver flukes (Opistorchis viverini, Clonorchis sinensis).
- Hepatolithiasis (recurrent pyogenic cholangitis): 10% develop cholangiocarcinoma.
- Primary sclerosing cholangitis (regardless of activity).
- Viral infection (HIV, HBV, HCV, EBV).
- Anomaly and malformation (anomalous pancreaticobiliary junction and choledocal cyst, fibrocystic liver diseases).
- Enviromental or occupational toxin (thorotrast, dioxin, polyvinyl chloride).
- Biliary tract-enteric drainage procedures.
- Heavy alcohol consumption.

3.2.3.- PATHOLOGIC FEATURES:
Cholangiocarcinomas are malignant tumors that arise from the epitelial cells of the bile ducts, being more than 90% of them adenocarcinomas. Mass-forming cholangiocarcinomas usually are poorly differentiated, whereas periductal-infiltrating cases tend to be well-differentiated and the intraductal-growing tumors are considered papillary adenocarcinomas.

3.2.4.- DIAGNOSTIC IMAGING:

Cholangiocarcinomas are catalogued according to the morphologic classification proposed by the Liver Cancer Study Group of Japan. It permits the establishment of a differential diagnosis, a prognosis and also a prediction of the probable tumor dissemination. Three groups are distinguished:

3.2.4.1- Mass-forming cholangiocarcinoma:

Well-circumscribed fibrous stromatous tumors, usually large when located intrahepatically and small when extrahepatically, as they can grow considerably without causing significant symptoms of disease.

**US:**

Homogeneus intrahepatic mass with an irregular but well-defined margin, hiperecoic when larger than 3 cm and hypo / isoecoic when less than 3 cm, that shows a peripheral hypoechoic rim (35%).

**CT:** (Fig. 24 on page 44)

Homogeneus attenuation, irregular peripheral enhancement, **gradual centripetal enhancement (specially in delayed phases)**, with capsular retraction, satellite nodules, vascular encasement without gross tumor thrombus formation, hepatolithiasis.

**MR:** (Fig. 25 on page 45)

Hyperintense at T2 WI, hypointense at T1 WI, peripheral and centripetal enhancement at dynamic contrast-enhanced imaging (active cells in the periphery of the tumor, central fibrosis and necrosis).
Regardless of the imaging technique employed, it is frequent to find dilatation of the biliary trees in the tumor periphery, when referring to intrahepatic tumors. When extrahepatic tumors do not usually achieve a significant growth at the diagnosis, as they cause clinical symptoms in the patient, and do not present all the typical imaging findings (Fig. 26 on page 46)(Fig. 27 on page 47).

In the **differential diagnosis** for the intrahepatic mass-forming cholangiocarcinoma we have to consider mature abscesses and hepatic tuberculosis, as they present as hepatic masses with infectious clinical and analitical parameters.

We also have to consider the hepatocellular carcinoma (HCC) with cirrhotic stroma, the sclerosing HCC and combined HCC-cholangiocarcinoma / hepatocholangiocarcinoma (Fig. 28 on page 48) (especially in patients with chronic liver disease), as well as metastasis.

### 3.2.4.2- Periductal infiltrating cholangiocarcinoma:

**Intrahepatic** type is a tumoral entity characterized by a growth along a dilated or narrowed bile duct formation without mass formation, seen as an elongated, spiculated or branch-like abnormality.

**US:**

Small, masslike lesion or diffuse bile duct thickening with or without obliteration of the bile duct lumen.

**CT & MR:**

Diffuse periductal thickening with increased enhancement, abnormally dilated or irregular narrowed duct.

The **differential diagnosis** shall include periportal lymphangitic metastasis from an extrahepatic tumor.
**Extrahepatic** type is shown as a diffuse, annular thickening of the extrahepatic bile ducts with severe luminal stenosis, in occasions presenting extension through de intrahepatic ducts.

**US:** focal or diffuse thickening of the bile duct, of difficult evaluation.

**CT & MR:** focal or diffuse thickening of the bile duct, ring-like enhancing in contrasted studies. MR-cholangiography is an important tool to help in the diagnosis.

Both intrahepatic and extrahepatic periductal-infiltrating cholangiocarcinomas, have to be taken in consideration in patients with urgent clinical processes similar to acute cholangitis or that have story of choledocolithiasis.

### 3.2.4.3.- Intraductal-growing cholangiocarcinoma:

Small, sesile or polypoid papillary adenocarcinomas, which tend to spread superficially along the mucosal surface. The progressive growth of the intraluminal masses cause obstruction and retrograde dilatation of the biliary tree. In very advanced stages, only in extrahepatic intraductal cholangiocarcinomas, it is possible to identify invasion of the wall and the surrounding tissue.

There are five patterns of presentation:

- Diffuse and marked ductectasia with a visible papillary mass.
- Diffuse and marked ductectasia without a visible mass.
- Intraductal polypoid mass within localized ductal dilatation.
- Intraductal cast-like lesions within a mildly dilated duct.
- Focal stricture-like lesion with mild proximal ductal dilatation.

**US:**

Localized or diffuse ductectasia with or without an echogenic intraductal polypoid lesion.

**CT & MR:** *(Fig. 29 on page 49)(Fig. 30 on page 50)*

Show us the tumors following the patterns of presentation described above, emphasizing that when the intraductal mass is discovered, it is hypo- or isoattenuating relatively to the surrounding liver at precontrast CT and enhances at contrast-enhanced CT (or as an intraductal mass which enhances at MR).
The **differential diagnosis** shall be made with benign tumors of biliary ducts (adenoma and papilloma), specially in early stages.

### 3.2.5.- Tumoral extension:

**Mass-forming** cholangiocarcinomas, specially when intrahepatic, tend to grow in the three axis, with propensity to invade small portal venous branches, showing peripheral, marginal little tumors. Extrahepatic tumors easily cause obstruction at an early stage, and are usually small at the time of the diagnosis, so do not tend to spread.

Intrahepatic **periductal-infiltrating** cholangiocarcinomas spread along the bile duct wall via the nerve and perineural tissue, following the axis of the bile duct like a branch of a tree.

When extrahepatic, there is no sizable mass associated, only the thickening of the bile duct wall is seen.

**Intraductal-growing** cholangiocarcinomas spread superficially along the mucosal layer. When they grow to a certain size, may slough spontaneously from the wall of the bile ducts, floating inside them, and growing considerably by imbibing nutrients from the bile juice.

### 3.2.6.- Complications:

Arising from cholangiocarcinomas, in relationship with the local progression, the growth on intrahepatic tumors shall condition obstruction with retrograde dilatation of the biliary trees, tumoral thrombosis or infiltration of the portal vein and hepatic artery branches. The chronic biliary obstruction eases the addition of inflammatory changes and secondary infections, specially repetitive cholangitis.

### 4.- POST-CHIRURGICAL MIMICKERS:

### 4.1.- SURGICAL THERAPEUTICAL PROCEDURES:

After an episode of acute cholecystitis, and on punctual occasions secondarily to other urgent biliary disease, it is necessary to practice a therapeutical cholecystectomy, usually by laparoscopical approach.
When there is suspicion of gallbladder cancer or it cannot be discarded, open cholecystectomy with resection of the hepatic segments IVB and V, and sometimes the left hepatic lobe, will be the treatment in election.

Intrahepatic cholangiocarcinomas have to be treated with hepatic tumoral resection, with a free-of-tumor peripheral margin of 1 cm, with segmentectomy / lobectomy when needed. Hilar cholangiocarcinomas surgical therapy consists in affected bile ducts resection, with lymphadenectomy and biliodigestive anastomosis.

Resectable distal bile duct cholangiocarcinomas are treated by cephalic duodenopancreatectomy.

Choledocolithiasis are sometimes confirmed and therapeutically removed with endoscopic retrograde cholangiopancreatography (ERCP), with associated sphincterotomy or papillotomy sometimes needed to extract the gallstones.

4.2.- SURGICAL COMPLICATIONS MIMICKERS OF ACUTE BILIARY DISEASE:

Postoperative complications may be seen in up to 0-16% in laparoscopic cholecystectomy, whereas in open surgery it may present in up to 9-26% of the patients.

It is common to find early post-surgery findings in the vesicular fossa, consisting in a trabeculation of the fatty tissue and sometimes small seromas, liquid density, intensity or echogenicity in US, CT or MR studies, that is gradually reabsorbed in a few days (Fig. 31 on page 51).

Occasionally, persistent bile leakage of the cystic duct remnant can lead to an infection of the surgical bed in the gallbladder fossa (infected biloma), which may appear as an abscess in imaging technics.

There are other complications associated with the cystic duct remnant, like stricture, fistula formation, retained stones in the cystic duct remnant, "amputation neuromas" and suture granulomas of the cystic duct remnant. The most common problem associated with the cystic duct remnant is retained calculi, which occurs in up to 5% of patients undergoing cholecystectomy. These pathologies mean about 10% of repeat surgeries performed after cholecystectomy, usually in relationship with reappearance of right upper quadrant abdominal pain. When they cause obstructive disease, infection can be associated and an abscess may develop in the surgical bed.
Anecdotally, during difficult cholecystectomy procedures, gallstone dislodgement from the cystic duct remnant may be complicated with migration of the gallstones into the peritoneal cavity, that shall condition severe peripheral inflammatory changes, with abscess in some occasions or generating fistulous tracts with neighboring organs in the abdomen, or even in the chest (Fig. 32 on page 52).

Cholecystectomies accompanied of partial liver resections can show more frequently abscess spread from the vesicular fossa into the liver (Fig. 33 on page 53)(Fig. 34 on page 54).

Patients with a partial liver or bile ducts resection, mostly when associated with biliodigestive anastomosis, apart from intrahepatic abscess they may be more susceptible to the formation of bilomas, which can also suffer superinfection and spread into the peritoneal cavity.

Pneumobilia is a common sequela of procedures such as endoscopic sphincterotomy and ductoenteric anastomosis and often manifests as air in the bile ducts.

An extraordinary mention requires the possibility of local recurrence in patients with bile duct cancer, either suffering gallbladder carcinoma and cholangiocarcinoma, most of times in the surgical bed, sometimes in the the input paths of the laraparoscopic trocars (Fig. 35 on page 55).
Images for this section:

**Fig. 1**: US Signs in Acute Cholecystitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 2:** CT signs in Acute Cholecystitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 3: US & CT signs in Gangrenous Cholecystitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 4: CT signs in Emphysematous Cholecystitis.

Emphysematous Cholecystitis: hydropic gallbladder with intraluminal and intramural gas, with diffuse wall thickening and edema, pericholecystic fluid and inflammatory changes.
Fig. 5: Gallbladder perforation.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 6: CT signs of cholecystoenteric fistula with gallstone ileus.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 7: Cholecystoenteric fistula with gallstone ileus (Bouveret Syndrome)

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 8:** US & CT findings in chronic cholecystitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 9:** Porcelain gallbladder & US added choecystitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 10: Xanthogranulomatous cholecystitis.

**Fig. 11:** Adenomyomatosis signs.

© RadioGraphics 2006; 26:941–946
Fig. 12: Acute intrahepatic focal cholangitis secondary to liver abscess.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 13:** Acute extrahepatic cholangitis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 14:** Gallbladder cancer. Mass replacing the gallbladder.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 15: Gallbladder carcinoma. Mass replacing the gallbladder.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 16:** Gallbladder cancer. Wall thickening with liver mass.

Gallbladder (GB) wall thickening predominantly in fundus, with mass extension into the liver. Dilatation of intrahepatic biliar ducts is associated, and also prominent metastatic lymphadenopathic masses are present in the gastrohepatic ligament, mesentery root, hepatic hilum and peripancreatic levels.
Fig. 17: Porcelain gallbladder cancer showing wall thickening with liver masses.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 18:** Gallbladder cancer. Polypoid intraluminal mass with liver extension.

Tumoral papillary polypoid lesion in the body of the gallbladder, with mass extension into the liver. Dilatation of intrahepatic biliary ducts is associated, and also prominent metastatic lymphadenopathic masses are present in the mesentery root, hepatic hilum and peripancreatic levels.
Fig. 19: Temporal evolution of a gallbladder cancer as a mass replacing the gallbladder.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 20: Portal tumoral partial thrombosis in patient with gallbladder carcinoma with liver extension.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 21**: Local recurrence and progression in cholecystectomized patient with gallbladder carcinoma.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 22: Gallstone ileus secondary to bilioduodenal fistula in patient with gallbladder carcinoma progression.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 23:** Pancreatic chronic atrophy secondary to extension of a metastatic lymphadenopatic mas.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 24: Mass forming intrahepatic cholangiocarcinoma (CT).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Mass-forming intrahepatic cholangiocarcinoma (MR & CT): Irregular mass*, hypointense in T1 WI, hyperintense in T2 WI, DWI* (MR), hypodense (CT), with progressive enhancement after contrast administration; in this patient, no significant enhancement was described in MR, while in CT it was very subtile (Hypodense in arterial & portal phases, isodense in delayed phase).

Fig. 25: Mass-forming intrahepatic cholangiocarcinoma (MR & CT).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 26: Mass-forming extrahepatic cholangiocarcinoma.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Mass-forming extrahepatic cholangiocarcinoma: Intraductal soft-tissue mass, periductal-like wall thickening, but without periductal extension (so, not a periductal-infiltrating type, though similar) with retrograde biliar dilatation. In MR, discretely hypointense in T1 and slightly hyperintense in T2.

**Fig. 27:** Mass-forming extrahepatic cholangiocarcinoma.
**Fig. 28:** HCC-cholangiocarcinoma.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 29:** Intraductal-growing cholangiocarcinoma (CT).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
**Fig. 30:** Intraductal-growing cholangiocarcinoma (MR).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 31: Temporal difference between normal and pathologic post-cholecystectomy fluid collections in the surgical bed.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 32: Gallstone migration into the peritoneal cavity after difficult dislodgement of the lithiasis.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 33: Liver abscesses (US & CT):

Hypoechoic (US) or hypodense (CT) lesions, with ill defined margins, usually multiple, with peripheral enhancement and central necrotic tissue identified as hypoechoic (US) or hypodense and non-enhancing (CT).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Liver abscesses (MR):
Hypointense lesions in T1 WI, heterogeneally hyperintense in T2 WI, with ill defined margins, with peripheral enhancement and central necrotic tissue identified as hypointense, non-enhancing and markedly hyperintense in T2 WI.

Fig. 34: Liver abscesses (MR).

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Fig. 35: Local recurrence around the metallic clip post-cholecystectomy.

© Diagnostic Imaging, Parc Sanitari Sant Joan de Déu, Parc Sanitari Sant Joan de Déu - Sant Boi de Llobregat/ES
Conclusion

Neoformative ethiology should be considered in the differential diagnosis in the emergency gallbladder and biliary disease, given its relatively high incidence, aside from inflammatory, infectious or obstructive pathology.

Awareness of these conditions by the radiologist is important to provide an accurate and prompt diagnosis, assess the extent of the disease and guide the initial clinical management of the patients.
References


