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CYSTIC LIVER LESIONS: A COMPREHENSIVE REVIEW

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INTRODUCTION

The main hepatic cystic lesions are: simple cyst, hydatid cyst, alveolar echinococcosis, cystadenoma, cystadenocarcinoma and polycystic liver disease.

Cystic liver disease encompasses a heterogeneous group of fluid-containing lesions within the liver parenchyma. Liver cysts (HCs) are incidentalomas, most often discovered randomly on imaging tests. Detection of CHs is increasing due to the increased availability and use of abdominal imaging modalities such as ultrasound (USG), Computed Tomography (CT) and MRI Magnetic Resonance Imaging. Early detection presents two challenges: distinguishing a benign lesion from a malignant one, and choosing an imaging modality that is diagnostically accurate, cost-effective, non-invasive, and safe.[1]

CHs can be subdivided into simple and complex cysts based on lesion characteristics. The main means of differentiation is the propaedeutics by image. This type of examination made it possible to avoid invasive tests, such as biopsy or resection, in some cases.[1]

In this comprehensive review we aim to describe the different types of cystic liver lesions and how various imaging modalities are used to assess and diagnose them. We will also discuss treatment strategies.[1]

DEFINITION AND CLASSIFICATION

SIMPLE LIVER CYSTS

These are thin-walled, smooth-walled lesions lined by cubic epithelium, which secrete bile-like fluid. When associated with renal cysts and a positive family history, they can be classified as Polycystic Liver Disease.[1]

COMPLEX LIVER CYSTS

They are defined by the presence of complex features within a lesion, including septations, wall thickening or nodularity, fluid containing debris, radiographic enhancement, hemorrhagic or protein content. diverse etiologies. Hydatid or echinococcal cysts are lesions caused by infection by the parasite: *Echinococcus granulosus.* Hepatic cystadenoma are rare cystic tumors that form within the liver, currently being called non-invasive mucinous cystic neoplasm. Hepatic cystadenocarcinoma are rare malignant cystic tumors, currently called mucinous cystic neoplasm with invasive carcinoma.[4]

EPIDEMIOLOGY

The prevalence of CHs in the United States is 15-18%.[2]

Simple cysts are the most common, found in 2.5-18% of the population. These are congenital and more common in women aged 40 to 70 years, while acquired cysts, including hydatid cysts, for example, occur more in men aged 30 to 70 years.[1]

Mortality is generally low, however, the mortality rate varies with the etiology of the cyst and increases when complications occur.[1]

Cystoadenoma is rare, being more common in women between 40 and 50 years. Cystoadenocarcinoma affects more elderly people over 60 years of age.[4]

RISK FACTOR

The risk is inherent to the acquired disease. Therefore, the risk factor for hydatid cyst is living in rural areas or regions with an epidemic of echinococcosis.[9]

Cystoadenoma can progress to cystadenocarcinoma.[4]

For the other cysts, no associated risk factors were found.

PATHOPHYSIOLOGY

Most of these cysts are congenital and form from bile ducts that do not connect to the biliary system. Biliary hamartomas are derived from embryonic bile ducts.[4] A proposed alternative mechanism is a defect in the bile cilia, leading to hyperproliferation of cholangiocytes and generation of cysts.[6]

There is a rare disease that presents with multiple simple cysts, but of biliary origin. Caroli's disease is autosomal recessive and is characterized by cavernous ectasia of the bile ducts.[5] Simple hepatic cysts range in size from less than 1 to 30 cm in diameter and may contain up to 2 septa, unlike complex cysts, which are typically multiseptate.[1]

Hydatid or echinococcal cysts occur due to infection with Echinococcus granulosus, a parasite ingested through contaminated food. After ingestion, the eggs hatch in the small intestine. The parasite then enters the bloodstream, where it can migrate to its target organs - the lungs and liver. Cysts first appear in the liver 3 to 4 weeks after infection.[9]

GENETICS

Liver liver disease is the one with the most genetic influence. It includes a heterogeneous group of diseases characterized by multiple liver cysts. Isolated cysts are caused by mutations in protein kinase C substrate 80K-H (PRKCSH), SEC63 and LDL receptor-related protein 5 (LRP5), while mutations in polycystic kidney disease 1, 2 and hepatic and renal polycystic liver disease cause renal cysts often accompanied by liver cysts. Glycosidase II alpha subunit (GANAB) has been reported to cause both phenotypes. These mutations, along with newly identified ones in SEC61B and Alpha-1,3-Glucosyltransferase (ALG8), can be found in about 50% of patients with isolated polycystic liver disease. Second-hit somatic mutations are hypothesized to be the driving force leading to cystogenesis. Subsequently, the loss of heterozygosity in cystic tissue exacerbates disease progression. All genetic mutations lead to reduced levels of functional polycystin-1. This ciliary protein is therefore considered the central factor in the development and severity of liver cysts.[7, 8]

CLINICAL CONDITION

Most CHs are asymptomatic and as they increase in size, they can become symptomatic due to compression (15-16% of cases).[3] Symptoms are nonspecific and may include abdominal pain, early satiety, nausea or vomiting.[2] Patients may have a palpable mass or hepatomegaly on physical examination, depending on the size of the cyst.

Hydatid cysts are symptomatic and include abdominal pain, fever, chest pain, and dyspnea.[9]

DIAGNOSIS

SIMPLE CYST

Clinical Symptoms

Totally asymptomatic, it is an incidental imaging finding.[11]

Laboratory exams

In simple cysts, laboratory tests are usually normal or with a slight increase in gammaglutamyltransferase (GGT).[9] Some studies have shown that the levels of Carcinoembryonic Antigen (CEA) and Carcinogenic Antigen 19-9 (CA 19-9) both in the cyst fluid and in the serum dosage are elevated.[10]

Imaging exams

The characteristics described by the USG are: anechoic content and no septations, thin and well-defined borders. It is an oval and well-defined image in the midst of the liver parenchyma.[11] CT shows a hypodense and well-defined image and MRI shows, in the T2 sequence, an image with hypersignal and

non-contrast uptake. In T1 it is a hypointense image.[1, 12] Although CT and MRI have higher sensitivity and specificity than US - which is about 90% - this test is low cost, available, effective and non-invasive. Therefore, the most used.[13]

HYDATID CYST

Clinical Symptoms

The diagnosis follows the criteria: epidemiology of the endemic region, clinical symptoms of abdominal pain, fever, chest pain and dyspnea.[14]

Laboratory exams

Immunodiagnostic tests. Anti-Echinococcus granulosus antibodies have a sensitivity of 93.5% and specificity of 89,7%.[16]

Imaging exams

USG shows an oval lesion with anechoic content and debris.[14] CT can be used for surgical planning and MRI has not proven to be cost-effective.[15]

There is a specific type of presentation of this disease that is Alveolar Echinococcosis. This presents typical USG aspects. About 70% of cases include irregular shape and border, hyperechoic outer ring and hypoechoic center, multivesicular appearance, and posterior shadowing due to calcified areas.[18] Unlike what occurs in the hydatid cyst, in alveolar echinococcosis, MRI is superior to CT in detecting the margins of the lesion.[11] The similarity between the two presentations of E. granulosus infection are high diagnostic sensitivity (90%-100%) and specificity (95%-100%) achieved with serodiagnostic tests. [16]

CYSTOADENOMA AND CYSTOADENOCARCINOMA

Clinical Symptoms

Usually asymptomatic.[19]

Laboratory exams

Liver function tests do not change. In up to 23% of cases there is an elevation of GGT and Alkaline Phosphatase (FA).[19] Serum levels of CEA in 14% and of CA 19-9 in 36%.[20] Therefore, laboratory tests are not useful to differentiate cystadenoma and cystadenocarcinoma from other cystic lesions of the liver.

Imaging exams

USG demonstrates a lesion with a round or oval shape, irregular border, hypoechoic echo pattern with hyperechoic septations or solid structures that are papillary projections, wall enhancement and posterior acoustic shadowing due to calcified areas. This makes the technique useful for differentiating these lesions from simple cysts. [21] The characteristics of CT and MRI are similar. So, in most cases the differentiation between cystadenoma and cystadenocarcinoma is not possible in the same way as for hydatid cyst because both can have intracystic hemorrhage, calcifications and septations. [22]

POLYCYSTIC LIVER DISEASE

Clinical Symptoms

Usually asymptomatic, but complaints may arise from mechanical compression. Hemorrhagic and infectious complications are rare and occur in the presence of large cysts, which leads to symptoms of acute abdomen.[2]

Laboratory tests

There is an increase in canalicular enzymes (FA and GGT). An increase in aspartate aminotransferase (AST) may be found. When there is renal involvement, creatinine may be increased, but in isolated liver disease, renal function is normal.[23]

Imaging exams

USG, CT or MRI may be used. The first

has the advantage of being non-invasive and inexpensive. It is necessary to respect some criteria to suggest the diagnosis, such as: more than 4 cysts and a positive family history. Renal involvement is seen in the same way.[23]

TREATMENT

SIMPLE CYST

Treatment is conservative, observing the lesions through imaging methods. If symptoms are present, aspiration with sclerotherapy or surgical roofing - laparoscopic or open - may be proposed, which are similar or even more effective in reducing symptoms, but have a significantly higher morbidity and mortality rate. [24]

HYDATID CYST

Treatment includes open or laparoscopic surgery; aspiration, injection and re-aspiration by puncture and chemotherapy. [25]

In the case of Alveolar Echinococcosis, the proposed treatment includes hepatectomy and chemotherapy.[25]

CYSTOADENOMA AND CYSTOADENOCARCINOMA

The primary treatment of cystadenoma and cystadenocarcinoma is liver resection.[21]

POLYCYSTIC LIVER DISEASE

Treatment is proposed for symptomatic disease. Aspiration and sclerotherapy, as well as surgical unroofing (open or laparoscopic) are indicated for large cysts that are confined to a limited part of the liver. In more extensive disease, hepatectomy and even liver transplantation may be indicated.[26]

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