

# Diffuse Adenomyomatosis Of The Gallbladder: An Infrequent Disease Wth Difficult Preoperative Diagnosis

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## Abstract

Adenomyomatosis is a rare disease of the gallbladder characterized by epithelial proliferation and formation of mucosal pouches through the thickened muscular layer of the gallbladder wall: the so-called Rokitansky-Aschoff sinus. Most of the patients remain asymptomatic. Hence, adenomyomatosis is usually an incidental finding on ultrasonography performed for other reasons. We present a patient treated during the last year, a 35-year-old woman. She had dull pain in the right subcostal region, approximately 6 months before the diagnosis was established. Diagnosis of acute cholecystitis was made preoperatively on ultrasonography. Laparoscopic cholecystectomy was carried out. Diagnosis of diffuse adenomyomatosis was confirmed after histopathological study. Clinical findings, diagnosis and treatment are discussed.

## INTRODUCTION

Gallbladder adenomyomatosis (GBA) is an infrequent disease of unknown origin and of slow growth. It may be located in any place of the gallbladder, but fundamentally in the bottom. Occasionally, it can be located in the biliar conduits. Diagnosis is usually difficult because generally it is asymptomatic and not suspected. Patients developing symptoms present a clinical picture similar to that of the cholelithiasis. Abdominal ultrasonography and computed tomography (CT) are the most useful tests to guide the diagnosis; however, it is the histopathological study that confirms it.

On the occasion of a case in our service, we have carried out this work with the objective to review clinical aspects, diagnostic tests and therapeutic options of this disease.

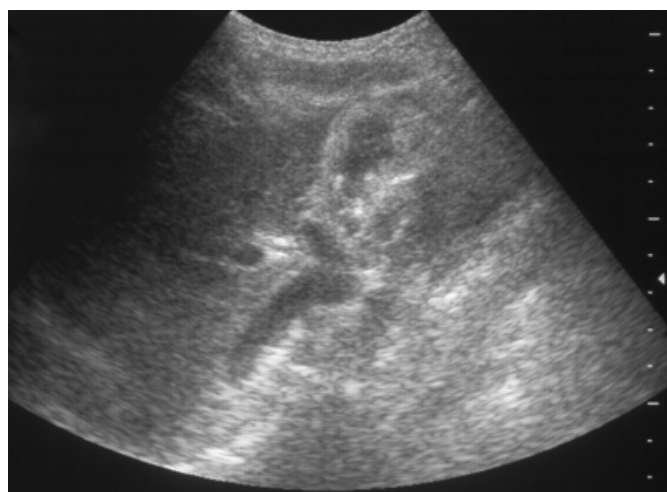
## CASE REPORT

A 35-year-old woman with antecedent of tobacco addiction and metoclopramide allergy came to the consultation with dyspepsia, inappetence, weight loss of 8 kg in 6 months and progressive deterioration of her general state. At physical

exploration, she presented with extreme thinness and paleness. The abdomen was soft without masses but painful in the right hypochondrium. Laboratory data showed the following: hemoglobin 12.2g/dl, hematocrit 35.3%, red blood count 3,700.000/ $\mu$ L, platelets 175.000/ $\mu$ L, white blood count 7.300/ $\mu$ L, partial thromboplastin time 32 seconds, prothrombin time 13.9 seconds, blood urea nitrogen 13mg/dl, creatinine 9.4mg/dl, aspartate aminotransferase 34 IU/l, alanine aminotransferase 45 IU/l, total bilirubin 0.8mg/dl, sodium 140 mEq/l and potassium 4.5 mEq/L. Serum carbohydrate antigen 19-9, carcinoembryonic antigen and alpha-fetoprotein antigen were normal. Breathe test for *Helicobacter pylori* was normal. Abdominal ultrasonography (Fig. 1) revealed a gallbladder with very thick wall due to acute cholecystitis containing multiple stones.

**Figure 1**

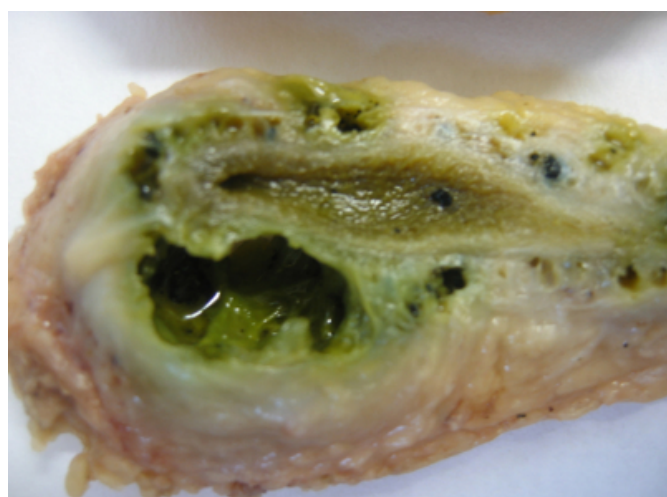
Figure 1: Abdominal ultrasonography showing reduction of the gallbladder lumen with irregular enlargement of the wall containing multiple stones.



The patient underwent programmed laparoscopic cholecystectomy. Histopathological examination showed diffuse adenomyomatosis of the gallbladder, chronic cholecystitis and multiple cholelithiasis. (Fig. 2, 3).

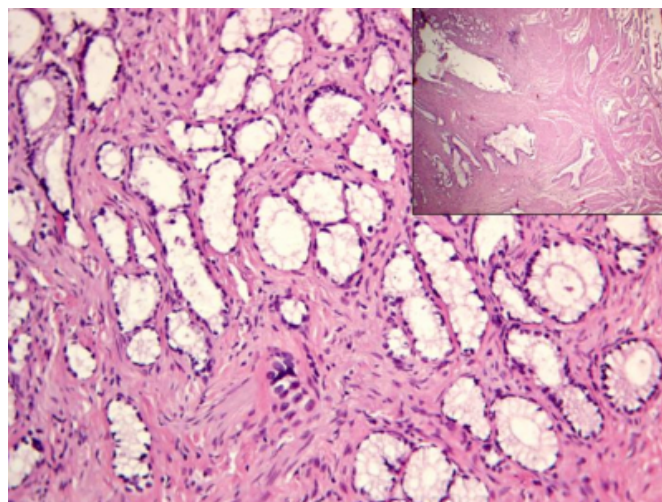
**Figure 2**

Figure 2: Longitudinally opened gallbladder with stones and diverticular enlargement of the wall.



**Figure 3**

Figure 3: Microscopical aspect of gallbladder adenomyomatosis (HE x 4 y x 20) showing cystic glandular formations in the thickened gallbladder wall surrounded by muscle fibres and lined with glandular epithelium.



The postoperative course was uneventful. There is no evidence of recurrence and the patient is asymptomatic after a follow-up of 1 year.

## DISCUSSION

GBA belongs to a heterogeneous group of alterations included in polypoid lesions of the gallbladder. Sánchez et al.<sup>2</sup> found 216 (6.5%) polypoid lesions in a total of 3.316 extirpated gallbladders: 125 (3.8%) with adenomyomatosis, 29 (0.87%) heterotopic lesions, 28 (0.84%) cholesterol polyps, 11 (0.33%) adenomas, 8 (0.24%) dysplasia lesions, 6 (0.18%) inflammatory polyps, 4 (0.12%) in situ carcinomas, 3 (0.09%) hyperplasia lesions and 2 (0.06%) hamartomas.

In the study by Cruz et al.<sup>3</sup>, nine of the eleven cases of biliary adenomyomatosis were located in the bottom of the gallbladder (82%), one in the cystic conduit and one in the distal common bile duct. In some occasions, it can be located in the right and left hepatic conduits, in the common hepatic duct and in the ampulla of Vater. Outside of the biliary conduits, adenomyomatosis has been described in stomach, duodenum, jejunum, ileum, Meckel's diverticulum, sigmoid colon, rectus muscles, navel, uterus, broad ligament, uterosacral ligament, round ligament, uterine tubes, ovary, recto-vaginal wall, abdominal cavity and also associated to Gardener syndrome.

Adenomyomatosis is an uncommon disease, characterized by slow growth, benign hyperplasia of the gallbladder mucosa forming invaginations through the muscular layer,

well-known under the name of Rokitansky-Aschoff sinus and by a very enlarged gallbladder wall, generally more than 5mm in thickness (Fig. 2). It is considered an acquired disease with a physiopathology similar to colon diverticular disease<sub>4</sub>. Microscopically, it is constituted by a proliferation of flat muscular fibres and epithelial adenomatous cells (Fig. 3). According to the distribution of this disease in the gallbladder, three forms are described: Focal (48%<sub>5</sub>-89%<sub>6</sub>), diffuse (26%) and segmental form (26%)<sub>5</sub>. There can also be mixed forms<sub>7</sub>.

Frequently (in 81%), GBA is associated to another biliary or pancreatic diseases: cholelithiasis and chronic cholecystitis in 89% of the cases, choledocholithiasis in 22% and antecedents of pancreatitis of biliary origin in 22%. Therefore, it is believed that chronic inflammation of the biliary mucosa is implied in the origin of this disease<sub>3</sub>. In some occasions, this pathology is also associated to gallbladder adenocarcinoma or leiomyosarcoma<sub>8,9,10</sub>, to anomalies of the biliary tree or to duodenal diverticula<sub>11</sub>. Nabatame et al.<sub>12</sub> found a stronger association between segmental adenomyomatosis and carcinoma (6.6%), especially in elderly patients (15.6%), with a statistically significant difference ( $p < 0.001$ ), which suggests that segmental adenomyomatosis could be a factor of high risk for carcinoma of gallbladder in elderly patients.

These tumours have been described with other names such as adenomyosis, hamartomas or hyperplastic adenomyomatosis<sub>13</sub>.

GBA affects men and women between 40 and 70 years in similar proportion. The age of maximum frequency is located around 50 years<sub>3</sub>. However, it has also been described in children as casual finding<sub>14,15</sub>.

Preoperative diagnosis is difficult as one does not suspect this disease because it can clinically show several forms in function of the localization. Qiao et al.<sub>16</sub> reported that only in 7 out of 42 cases the diagnosis was made correctly before the surgical intervention. The clinical picture can vary from asymptomatic (60%)<sub>6</sub> to symptomatic patients. These symptoms can be: dyspepsia, pain in the right hypochondrium, fever of unknown origin, acute or chronic cholecystitis<sub>17</sub>. When it affects the biliary tree, it can cause symptoms of extrahepatic cholestasis, hemobilia, cholangitis or pancreatitis. In the particular case of an adenomyoma of the cystic conduit, it is manifested with pain of colic type and gallbladder hydrops<sub>18</sub>.

Generally, there are no alterations in the laboratory analyses. However, when adenomyomatosis accompanies acute cholecystitis, it can show high leukocytes counts with deviation to the left. When adenomyomatosis affects the biliary tree, there can be alterations in hepatic and pancreatic function: Hepatic enzymes are high, alkaline phosphatase and serum amylase are altered<sub>3</sub>.

Imaging techniques constitute the tests of choice in the diagnosis of this pathology, mainly the abdominal ultrasonography (USG). Computerized tomography (CT), magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP) are of utility in the case of more complexity and in the cases of diagnostic doubt. However, in most of the cases, definitive diagnosis is made after surgical resection and histopathological study.

In the cases of diffuse adenomyomatosis of the gallbladder, ultrasonography shows an enlargement of the wall with small cystic areas representing the Rokitansky-Aschoff sinus. The segmental form has an inflammatory appearance similar to cholecystitis. Conventional ultrasound has a sensitivity oscillating between 45% and 90%. This sensitivity depends on the experience of the radiologist<sub>19</sub>. In small and flat lesions, conventional ultrasonography cannot differentiate between benign and malignant lesions<sub>20</sub>. In these cases, endoscopic ultrasonography is the method of choice<sub>21</sub>. In the opinion of Azuma et al.<sub>22</sub>, endoscopic ultrasonography has a sensitivity of 91% and a specificity of 87% in these cases.

In the conventional scanner, gallbladder adenomyomatosis appears as diverticular lesion containing gallstones<sub>23</sub>.

In MRC, gallbladder adenomyomatosis is perceived as an enlargement of the gallbladder wall with intramural diverticula indicating the presence of Rokitansky-Aschoff sinus, the specific image of this disease. This test is of great utility to differentiate gallbladder carcinoma from adenomyomatosis<sub>24,25</sub>. In the study of Haradome et al.<sub>26</sub> on 29 patients, MRC demonstrated a sensitivity of 62%, specificity of 92% and an accuracy of 74% in GBA diagnosis.

The treatment of choice of these tumours is surgical resection, both in symptomatic and asymptomatic cases, accompanied or not by cholelithiasis, due to the uncertain evolution of this disease and to the difficulty of differential

diagnosis with carcinoma, in spite of all the diagnostic tests available at present<sup>5,27</sup>. Cholecystectomy is suitable when the process is located in the gallbladder. When the tree biliary is affected surgical resection with free margins and entero-biliary derivation is indicated<sup>28,29</sup>.

## CONCLUSION

Gallbladder adenomyomatosis is an uncommon and generally asymptomatic entity and when this disease is symptomatic, it is manifested fundamentally like a cholecystopathy. Preoperative diagnosis is difficult as one does not suspect it and in most of the cases it constitutes an ultrasonography finding. The treatment of choice is cholecystectomy due to the uncertain evolution of this disease.

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