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GALLBLADDER ADENOMYOMATOSIS AS AN INCIDENTAL FINDING: A REPORT OF SEVEN CASES

GALLBLADDER ADENOMYOMATOSIS AS AN INCIDENTAL FINDING: A REPORT OF SEVEN CASES

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CLINICAL CASE

ABSTRACT

Introduction: Gallbladder adenomyomatosis (GAM) is a benign condition of the gallbladder, typically asymptomatic, but with the potential to mimic or coexist with preneoplastic lesions. **Clinical case:** We report seven cases of GAM, incidentally discovered following cholecystectomies performed due to right upper quadrant pain. All patients were adults (six women and one man), with a preoperative diagnosis of cholecystitis or cholelithiasis, and no abnormalities in laboratory studies. The lesions were located in the gallbladder fundus, with thicknesses ranging from 2 to 12 mm. Histopathological analysis revealed typical features of GAM, and in one case, a single focus of low- and high-grade glandular dysplasia was identified, without evidence of invasion. **Conclusion:** The significance of this case lies in the need for thorough histological examination of the gallbladder, even when there is no clinical suspicion, due to the oncogenic potential of the dysplasia associated with GAM and the importance of differential diagnosis with gallbladder neoplasms.

Keywords: Gallbladder; Precancerous conditions; Gallbladder neoplasms. (Source: MESH-NLM)

RESUMEN

Introducción: La adenomiomatosis vesicular (AMV) es una entidad benigna de la vesícula biliar, generalmente asintomática, pero con potencial para simular o coexistir con lesiones preneoplásicas. **Caso clínico:** Se reportan siete casos de AMV, hallados incidentalmente tras colecistectomías indicadas por dolor en hipocondrio derecho. Todos los pacientes fueron adultos (seis mujeres y un hombre), con diagnóstico preoperatorio de colecistitis o colelitiasis, sin alteraciones en estudios de laboratorio. Las lesiones se localizaron en el fondo vesicular, con espesores entre 2 y 12 mm. El análisis histopatológico reveló características típicas de AMV, y en un caso se identificó un foco único de displasia glandular de bajo y alto grado, sin evidencia de invasión. **Conclusiones:** La relevancia del caso radica en la necesidad de un estudio histológico minucioso de la vesícula biliar, incluso cuando no hay sospecha clínica, dado el potencial oncogénico de la displasia asociada a AMV y la importancia de un diagnóstico diferencial con neoplasias vesiculares

Palabras clave: Vesícula biliar; Lesiones precancerosas; Neoplasia de la vesícula biliar . (Fuente: DeCS-BIREME)

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INTRODUCTION

Hyperplastic cholecystosis is a pathological entity of the gallbladder that includes two main forms: cholesterolosis and gallbladder adenomyomatosis (GAM)[1]. The latter, considered an acquired degenerative condition, is characterized by proliferation of the mucosal epithelium with deep invagination into the muscular layer, forming Rokitansky-Aschoff sinuses [2,3]. Its prevalence ranges from 1% to 9% in cholecystectomy specimens and is typically an incidental finding in patients operated on for other reasons, such as symptomatic cholelithiasis or cholecystitis [4,5]. Although mostly asymptomatic, it can cause pain in the right upper quadrant, which is clinically indistinguishable from biliary colic [6]. Laboratory tests are usually normal, and there are no specific serological markers for its detection [3]. While traditionally not considered a premalignant lesion [7], some authors have suggested a possible role as a precursor of gallbladder cancer, particularly in the segmental type[8-10].

Historically, GAM has been referred to by various names before being systematized by Jutras in 1960 [11]. Its etiology remains uncertain, although it has been linked to conditions that favor gallstone formation, such as biliary tract anomalies, inflammatory bowel disease, and obesity[12]. Three morphological patterns have been described: segmental, fundal, and diffuse [13], with the fundal type being one of the most frequent. Imaging studies may suggest the diagnosis, but in most cases it is confirmed postoperatively through histopathological examination of the gallbladder specimen.

Although GAM is often an incidental finding, its presentation may clinically mimic more serious conditions, including neoplastic lesions [5,10]. This becomes particularly relevant when atypical histological features, such as dysplasia, are identified, as they may suggest oncogenic risk, as reported in some studies [8,9]. In this context, the cases presented are clinically relevant, as all were initially diagnosed as cholecystitis or cholelithiasis, with no prior suspicion of GAM. The incidental histological finding, along with the identification of dysplasia in one case, underscores the importance of considering this entity in the preoperative differential diagnosis of gallbladder disease[3]. This report aims to describe a series of seven cases of gallbladder adenomyomatosis, highlighting their clinical presentation, histopathological findings, and potential differential diagnosis with gallbladder neoplasia.

CLINICAL CASE

We present seven cases corresponding to specimens evaluated during routine work in the Department of Pathology. In all cases, GAM was an incidental finding, identified exclusively during histopathological analysis. All patients presented with right upper quadrant pain. No symptoms beyond the typical pattern were reported. Both clinical evaluation and ultrasonography led to an initial diagnosis of cholecystitis or cholelithiasis. No additional imaging studies were performed. Preoperative laboratory tests did not show relevant abnormalities. There were no significant elevations in leukocyte count, liver enzymes, or bilirubin levels. Surgical treatment was scheduled and carried out in all patients.

The seven cases corresponded to six women and one man, all adults; two were under 50 years of age and five were older. In all cases, GAM was identified only through histopathological examination. The patients underwent cholecystectomy for typical gallbladder symptoms, with no prior detection or suspicion of GAM. The table summarizes the main clinical, morphological, and histological characteristics of the evaluated cases. All lesions were located in the gallbladder fundus, with focal wall thickening ranging from 2 mm to 12 mm. The largest lesion measured 22 × 15 mm and the smallest 4 × 4 mm. The final diagnosis was chronic cholecystitis in all seven cases, cholelithiasis in three cases, and cholesterolosis in four cases. Only two cases presented all three diagnoses, with one of them showing a focus of dysplasia (Case 1). The histopathological finding in all seven cases matched the classical description of GAM, that is, simple columnar epithelium forming multiple invaginations interspersed with hypertrophic smooth muscle bundles (Figure). In the gross image of Case 3, a lesion is seen in the gallbladder fundus, with adjacent cavity-like structures within the wall thickness (Figure).

In Case 1, a single focus of glandular dysplasia was identified, located within the muscularis propria, with no evidence of invasion (Figure). It is clearly visible in the lower left quadrant of the microphotograph due to architectural disorganization and more intense staining compared to the epithelium in the lower right quadrant (Figure).

In another microphotograph of the same case, the dysplastic focus is observed in the central lower part, beneath the muscularis propria, alongside epithelial projections to the left and right (Figure). The dysplastic focus shows both low-grade and high-grade dysplasia, alternating with patches of normal epithelium (Figure). The lesion is surrounded by isolated lymphocytes and mild fibrosis, similar to adjacent epithelial projections. In other words, the epithelial change is unlikely to be related to inflammatory injury.

Multiple sections of the gallbladder were studied, and no other dysplastic foci were found.

Table 1. Clinical, morphological, and histological characteristics of the evaluated cases.

Case	Sex	Age (years)	Location (type)	Size (mm)	Thickness (mm)	Cholecystitis	Cholelithiasis	Cholesterolosis	Dysplasia
1	Female	73	Fundus	18 × 15	12	Yes	Yes	Yes	Yes
2	Female	71	Fundus	22 × 15	5	Yes	No	No	No
3	Female	76	Fundus	18 × 10	10	Yes	No	No	No
4	Female	64	Fundus	9 × 8	8	Yes	No	Yes	No
5	Female	53	Fundus	4 × 4	2	Yes	No	Yes	No
6	Female	25	Fundus	13 × 12	6	Yes	Yes	Yes	No
7	Male	37	Fundus	12 × 10	7	Yes	Yes	No	No

Case 1 required additional histopathological evaluation after a focus of epithelial dysplasia was identified (Figure). New tissue samples from the gallbladder were obtained to rule out the presence of additional foci of dysplasia or adenocarcinoma. The initial finding of a single isolated dysplastic focus was confirmed, and the surgical margin was free of lesions. All patients had a favorable postoperative course following cholecystectomy, with complete resolution of their clinical symptoms. In the case with focal dysplasia, no further studies have been conducted to date. The described lesion is not associated with any known serological markers or elevated laboratory values.

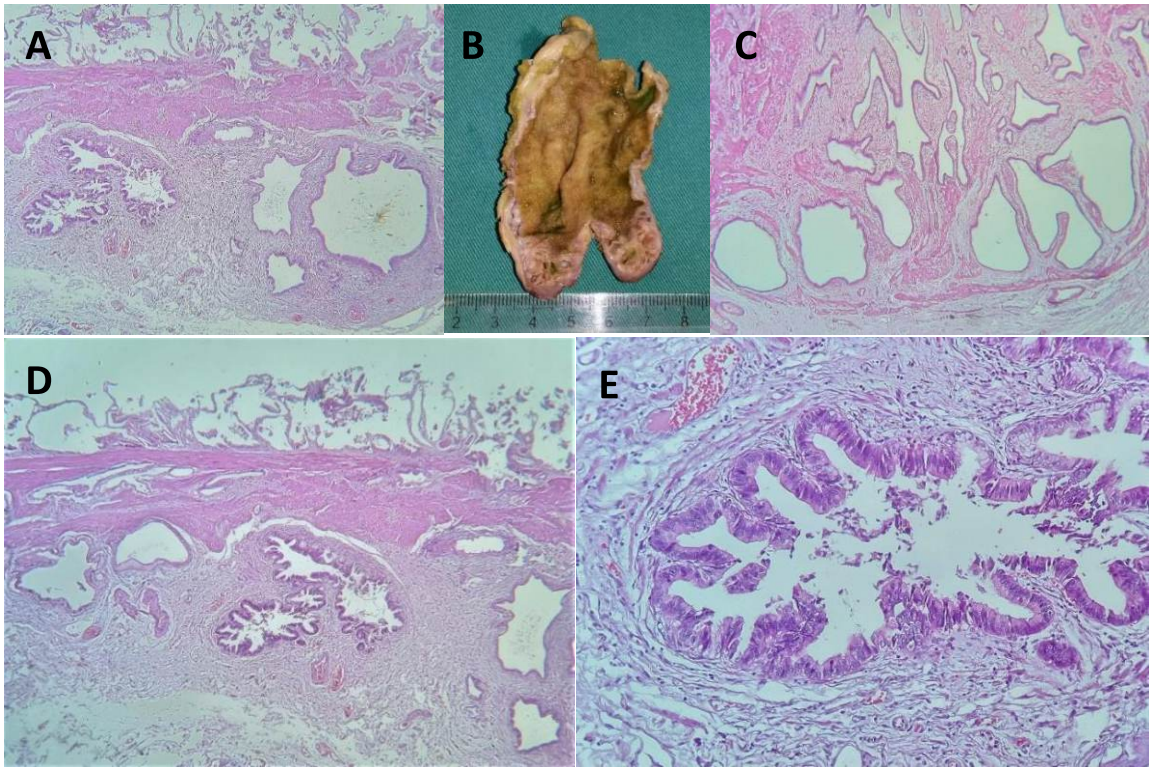

Figure. Representative macroscopic and histopathological findings from the analyzed cases. A) Microphotograph of Case 1 showing, in the lower left quadrant, a focus of glandular dysplasia identifiable by architectural distortion and more intense staining compared to the epithelium in the lower right quadrant. Dysplastic glandular focus located within the thickness of the muscularis propria, without evidence of invasion. (40×, H-E). B) Macroscopic image of Case 3, showing a lesion located in the gallbladder fundus with cavity-like appearance within the wall thickness. C) Microphotograph of Case 4, showing invagination of the hyperplastic epithelium in various forms, alternating with hypertrophic bundles of the muscular layer. (40×, H-E). D) Microphotograph of Case 1, displaying a single focus of glandular dysplasia located in the central lower area, beneath the muscularis propria. Epithelial projections can be seen on both the right and left sides. (40×, H-E). E) Microphotograph of Case 1 demonstrating both low-grade and high-grade dysplasia, alternating with patches of normal epithelium. (400×, H-E).

DISCUSSION

Various definitions of GAM can be found in the literature. In this review, we consider GAM to be an acquired degenerative disease, characterized by diffuse or localized proliferation of the mucosal epithelium, which deeply invaginates and extends into the thickness of the gallbladder muscular layer [7,14].

Characteristically, the muscular layer is hypertrophic.

It has been proposed that GAM could represent a precancerous lesion [9]; however, this remains controversial, as it would imply that gallbladder adenocarcinoma may develop from this entity. Among the seven cases reported here, one presented a microscopic epithelial focus with both low- and high-grade dysplasia. In our view, it is more likely that this dysplastic focus is not directly related to the GAM itself. In Case 1, in addition to the classic features of GAM, a definite focus of dysplasia was found alongside other transmural epithelial projections without dysplasia, all located in the subserosa, external to the hypertrophic muscularis propria (Figure 4). Dysplasia refers to a set of architectural and cytological alterations affecting epithelial tissue. It is considered a precancerous lesion that may progress from low-grade dysplasia to high-grade dysplasia, carcinoma in situ, and ultimately, invasive adenocarcinoma.

Bile has an emulsifying function and is produced by hepatocytes. It is a solution that contains, among other substances, bile acids (salts), cholesterol, pigments, various metabolites, and chemical elements. In the gallbladder, bile is not only stored temporarily but also becomes dehydrated, resulting in a proportionally higher concentration of its components. These components, theoretically, could cause progressive epithelial damage. GAM may increase epithelial exposure to the substances contained in bile, as accumulation in the deep crypts prolongs contact time. Cholecystitis and cholelithiasis may further add injurious factors to this context [15].

The presence of dysplasia in the gallbladder epithelium should be considered a multifactorial phenomenon that may evolve into gallbladder adenocarcinoma—a malignancy with a very poor prognosis and a short survival period after diagnosis. The causal relationship between GAM and gallbladder adenocarcinoma remains controversial and unproven, except for their occasional coexistence. Cases of GAM associated with gallbladder adenocarcinoma have been described in the literature; however, to the best of our knowledge, this is the first case reporting both low- and high-grade dysplasia within the characteristic context of GAM. We believe the clinical relevance of this report lies in the fact that GAM is a little-known entity, yet it affects up to 8% of adult patients. Its presence should be thoroughly evaluated, whether or not it is associated with other gallbladder diseases. This is especially important considering that adenocarcinomas have been reported to coexist predominantly with macroscopic segmental-type GAM [12].

Furthermore, recognizing this entity is important for pathologists, who must carefully examine all cholecystectomy specimens both macroscopically and microscopically, searching for GAM or dysplasia. Intraoperative pathological examination may also be helpful in certain cases. For radiologists, GAM has clinical relevance as its preoperative diagnosis depends almost exclusively on imaging studies. For surgeons, recognizing this disease and its potential relationship with dysplasia and cancer is also important, as the gallbladder is often sectioned or fragmented during surgery, which can irreparably distort its anatomy. In many cases—especially during laparoscopic cholecystectomies—the gallbladder is removed in multiple fragments, posing additional challenges for subsequent pathological evaluation. Finally, we must remember the poor prognosis of gallbladder cancer, which begins with dysplasia that typically progresses over several years.

The presence of dysplasia in the context of gallbladder adenomyomatosis reinforces the need for thorough histopathological examination of this entity, given its potential significance in the development of gallbladder neoplasms.

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