CLINICAL CASE

THE CHALLENGES OF DIFFERENTIAL DIAGNOSIS IN ADENOMYOMATOSIS - A CASE REPORT

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Abstract

Gallbladder adenomyomatosis (GAM) is a type of hyperplastic cholecystopathy, characterized by benign gallbladder thickening, determined by excessive proliferation of the surface epithelium into a thickened muscularis propria. It is an incidental finding in approximately 9% of cholecystectomies, GAM being an asymptomatic entity. Its prevalence rises with age, while having a female predilection. From all forms of GAM (focal, segmental and diffuse), the segmental form is considered the most difficult to distinguish from gallbladder carcinoma. D.L., a 44-year-old male was admitted for further investigations and treatment of a suspected gallbladder malignancy. The patient reported right hypochondrium colicative pain and nausea. An abdominal ultrasound performed prior to his admission, had shown a gallbladder with irregular thickened wall, without lithiasis. Clinical examination revealed pain in the right hypochondriac region, no peritoneal irritation and negative Murphy maneuver. Abdominal ultrasound revealed numerous small hyperechoic images , segmental mural thickening with double-contour and discontinuity of the wall and uneven caliber of the common bile duct. Abdominal computed tomography showed rosary sign (a suggestive aspect of GAM). The therapeutic approach consisted in laparoscopic cholecystectomy,. On gross evaluation, the gallbladder had lithiasic aspect and a thickened wall. The pathological examination revealed adenomyomatosis of the gallbladder, chronic cholecystitis and microlithiasis. The patient's evolution was uneventful. In conclusion, we present a case of GAM in a 44-year-old male. The particularity of this report consists in the initial diagnosis of cancer and the low rate of incidence of the disease (9% of cholecystectomy specimens). Furthermore, the age and gender of the patient are not characteristic for this illness.

Keywords*: gallbladder, adenomyomatosis, hyperplastic cholecystopathy*

Introduction

Gallbladder adenomyomatosis (GAM) is a type of hyperplastic cholecystosischole-cystopathy, characterized by benign, diffused or localized gallbladder thickening. It is considered that in approximately 9% of cholecistectomiescholecystectomies, the gall-bladder presents foci of adenomyomatosis, these being discovered mostly accidentally. GAM is an asymptomatic entity, but it can be frequently associated with chronic biliary inflammation, development of gallstones, cholesterolosis or pancreatitis [1,2].

Its prevalence raises with age (frequently found after the 5th decade of life), with a female predilection (M:F 1:3). It is found more often in gallbladders that present chronical inflammation (entity that predisposes to a higher risk of adenocarcinoma). However, it is considered that adenomyomatosis of the gallbladder as the sole finding in a patient does not predispose to malignancy [1].

Pathologically, it is defined by acquired hyperplasia of the gallbladder wall, of unknown etiology, determined by excessive proliferation of the surface epithelium and associated with invaginations of the Rokitansky-Aschoff sinuses into a thickened layer of muscularis propria. The bile is trapped in the sinuses and therefore precipitation of cholesterol crystals may occur.
Based on the imagistic findings, GAM can be classified as focal, segmental (with an annular appearance), or a diffuse, generalized form [1,3]. The segmental form is considered the most difficult to distinguish from a gallbladder carcinoma, the differential diagnosis being often problematic. The differential diagnosis also includes polyps of the gallbladder, cholelithiasis and congenital anatomic variants of the gallbladder [4].

Case presentation

D.L., a 44-year-old male known smoker was referred to our hospital for further investigations and treatment of a suspected gallbladder malignancy. The patient reported right hypochondriac colicative pain and nausea. His past medical history included appendectomy, allergic asthma – with last documented attack two years previous admission, chronic obstructive pulmonary disease and hiatal gastric hernia. Home treatment included montelukast, albuterol and budesonide/formoterol fumarate for his allergic asthma. An abdominal ultrasound performed prior to his admission, had shown a gallbladder with irregular thickened wall, without lithiasis raising the suspicion of cancer.

Clinical examination revealed flat and mobile with respiration abdomen, spontaneous and provoked pain in the right hypochondriac region, no signs of peritoneal irritation and negative Murphy maneuver. Examination of his cardiovascular, respiratory and urinary systems was unremarkable.

Standard blood test results showed mild thrombocytopenia, however white blood cell count was within normal limits.

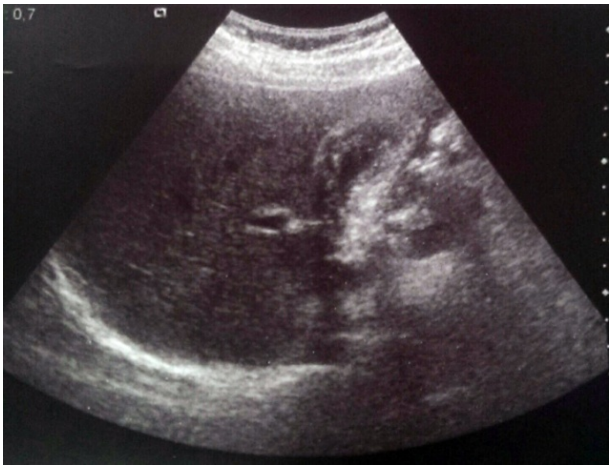

Figure 1 - Abdominal ultrasound - hyperechoic images with arciform pattern, segmental mural thickening with double-contour and discontinuity of the wall

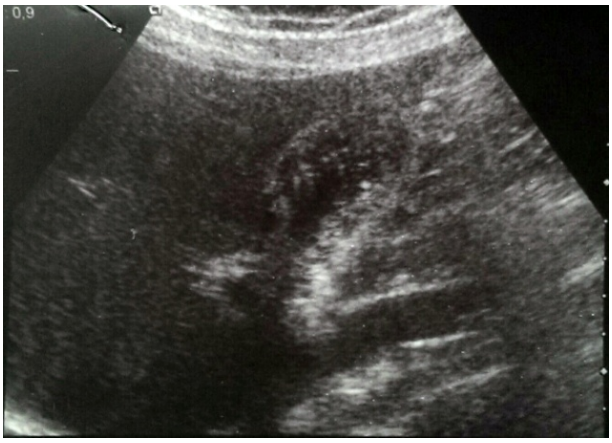

Figure 2 - Abdominal ultrasound - hyperechoic images with arciform pattern, segmental mural thickening with double-contour and discontinuity of the wall

Abdominal ultrasound revealed gallbladder changes: numerous small hyperechoic images, segmental mural thickening with double-contour and discontinuity of the wall – maximum thickening of 7 mm (normal value under 3 mm) (Figures 1,2.) There was ultrasound evidence of uneven caliber of the common bile duct with a maximum diameter of 6 mm (normal value less than 6 mm). Further investigations was required and we have performed an abdominal computed tomography which showed a suggestive aspect of GAM – rosary sign which is formed by the enhanced

proliferative mucosal epithelium, with the intramural diverticula surrounded by the unenhanced hypertrophied muscle coat of the gallbladder (Figures 3 and 4) [3].

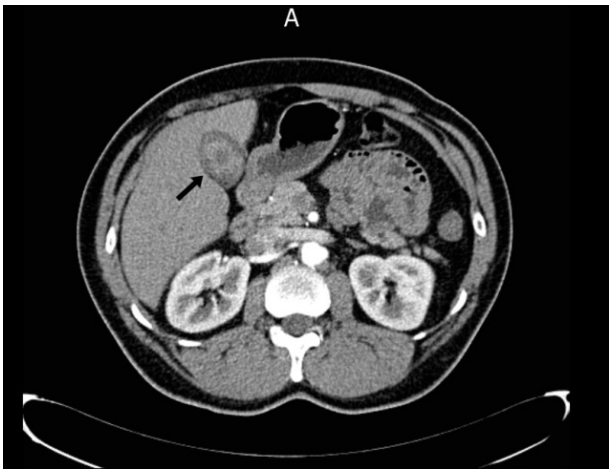

Figure 3 - Abdominal computed tomography - rosary sign - enhanced proliferative mucosal epithelium, with the intramural diverticula surrounded by the unenhanced hypertrophied muscle coat of the gallbladder

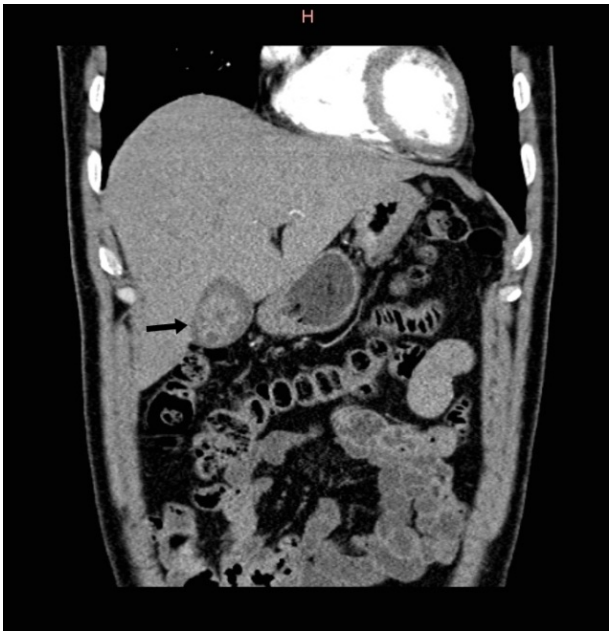

Figure 4 - Abdominal computed tomography - rosary sign

The therapeutic approach of the disease consists in cholecystectomy which was performed subsequently in our clinic. The chosen technique was laparoscopic retrograde cholecystectomy. With the patient in a reverse Trendelenburg position with the right side up to allow the small bowel and colon to fall away from the operative field, the optic trocar was placed through a supraumbilical incision to inspect the abdominal organs. The working trocars were placed in standard positions. The gallbladder was identified and described as adherent to the liver bed and with thickened fundus wall. Adhesiolysis was performed and the gallbladder pedicle was identified and dissected: the cystic duct - thickened, the cystic artery - short anatomic variant, common bile duct - with normal aspect. The pedicle was clipped and cut, while the cholecyst was dissected from the liver bed and afterwards removed. On gross evaluation, the gallbladder had lithiasic aspect and a thick wall.

The pathological examination offered the final diagnosis of adenomyomatosis of the gallbladder, chronic cholecystitis and microlithiasis. The patient's evolution was uneventful and he was discharged two days following the intervention with lifestyle recommendations. He will be monitored furthermore through his regular follow-ups.

Discussions

Gallbladder adenomyomatosis is a degenerative and proliferative disease of the gallbladder.

It was previously termed cholecystitis glandularis proliferans, cystic cholecystitis, intramural diverticulosis, adenomyoma, adenofibromyoma, hamartoma and diverticular disease of the gallbladder. The majority of patients diagnosed with this disease have been reported to be females in their 50s.[5] The rate of incidence, determined on the basis of cholecystectomy specimens, is 9%.

The common symptoms of GAM are pain in the right upper quadrant of the abdomen (intermittent and mostly self-limiting)[5,6], dyspepsia, fatty food intolerance, nausea and vomiting. These manifestations persist for a long time. Nevertheless, there are asymptomatic cases with incidental discovery.[7,8] The manifestations in our patient's case consisted of right hypochondriac region colicative pain (spontaneous and provoked) with nausea, while blood test results were unremarkable. Thus he was suspected of cholecystitis.

The pathogenesis of GAM is yet to be understood. Neurogenic dysfunction of the gallbladder may create an increased intracystic

pressure that is thought to be responsible for the formation of the Rokitansky-Aschoff sinuses.[5] Moreover, there is an association between GAM and gallstones in 36%-95% of cases.[9] Chronic inflammation of the gallbladder may cause GAM. The pathological findings in our patient included multiple lithogenic foci, with signs of chronic inflammation.

Ultrasonography is an adequate, noninvasive diagnostic technique for GAM. Intramural cystic formation (anechoic diverticula) with echogenic foci and/or reverberation artifacts together with full or partial thickening of the gallbladder wall are considered to be diagnostic findings on ultrasonographic examination.[3] However, this imaging technique is highly operator-dependent. While the first ultrasound rised the suspicion of gallbladder cancer, a second ultrasound on our patient's abdomen showed numerous hyperechoic images with arciform pattern, segmental mural thickening with double-contour and discontinuity of the wall associated with an uneven caliber of the common bile duct. Therefore, in our patient the differential diagnosis was between gallblader cancer and acute cholecystitis. Because the treatment and prognosis was completely different, a computed tomography scan was performed. The test revealed the rosary sign, thus establishing the final diagnosis of GAM. Recently, it has been suggested that magnetic resonance imaging is the most accurate diagnostic technique, while positron emission tomography (5-fluorodeoxyglucose) can be used to distinguish GAM from malignancy.

The relationship between gallbladder carcinoma and GAM has long been questioned. It is unclear whether GAM is a pre-malignancy lesion. Ootani et al. determined, through their retrospective study, the existence of a strong association between gallbladder carcinoma and segmental-type GAM.[9] However, the pathological examination excluded malignancy in our case.

The treatment of choice 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 the differential diagnosis with carcinoma.[10] We opted for a laparoscopic retrograde cholecystectomy.

Conclusion

In conclusion, we present a case of GAM in a 44-year-old male. The particularity of this report consists in the initial diagnosis of cancer and the low rate of incidence of the disease (9% of cholecystectomy specimens). Furthermore, the age and gender of the patient are not characteristic for this illness (M:F=1:3; age over 50 years), while the multiple associated comorbidities stand as a potential risk factor in the evolution of the patient.

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