

Prevalence of adenoma of gallbladder, ultrasonographic and histological assessment in a retrospective series of 450 cholecystectomy



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Prevalence of adenomyoma of gallbladder, ultrasonographic and histological assessment in a retrospective series of 450 cholecystectomies

BACKGROUND: Adenomyomas of the gallbladder are difficult to examine during standard ultrasound examination of the abdomen. They sometimes undergo malignant transformation and their optimal management still remains a problem. The authors have aimed to investigate the ultrasonographic and histopathological prevalence of gallbladder adenomyomas focusing on the diagnostic performance of ultrasound examination.

MATERIALS AND METHODS: A retrospective series of 450 consecutive patients who underwent cholecystectomy is reported. Data regarding characteristics of the patients, US and histology examination of the gallbladder were collected. Sensitivity, specificity, positive and negative predictive values of ultrasound scan were calculated with respect to histological examination of the gallbladder.

RESULTS: The study group consisted of 261 female and 189 male. Ultrasound scan detected adenomyomas in 22 patients, confirmed by histopathology in 13 and found to be not present in 9. Incidental adenomyomas were found in 16 patients of 428 who underwent cholecystectomy for gallstones. Prevalence was 4.9% and 6.4% for ultrasound scan and histopathology respectively. Ultrasound scan showed sensitivity of 43.3% (c.i.:25.4%-62.5%), specificity of 97.8% (c.i.:95.9%-99%) with a positive predictive value of 59% (c.i.:36.3%-79.2%) and with a negative predictive value of 96.2% (c.i.:93.7%-97.6%). On histopathology, adenomyomas localized in the fundus were predominant. Two female patients with adenomyomas of the fundus (diameter 5 mm) and single stone showed intestinal metaplasia with high-grade dysplasia.

CONCLUSIONS: The diagnosis of gallbladder adenomyomas by ultrasound scan still remains a problem because of its low sensitivity, which is mainly due to the association with gallstones. Histopathological findings in the perilesional mucosa confirm the hypothesis of a metaplasia-dysplasia-carcinoma sequence already shown in the colon-rectum. At present, the selection of patients requiring cholecystectomy is still controversial.

KEY WORDS: Adenomyomas, Cholecystectomy, Gallbladder polyps, Ultrasound scan

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Introduction

Polypoid lesions of the gallbladder are usually diagnosed incidentally and may present malignant features¹⁻⁶. Factors predictive of malignancy are reported in Table I⁷⁻²².

Incidence of gallbladder adenomyomas (GA) ranges from 2.8% to 5% with respect to all polypoid lesions. GA account for 40% of all benign tumours with prevalent localization in the gallbladder fundus²³⁻²⁵. Diffuse, localized and segmental patterns are associated with a different risk of malignancy²³⁻²⁸.

The majority of patients are asymptomatic²⁸. Some subjects present with abdominal pain similar to symptomatic cholelithiasis^{4,29}.

Diagnosis of gallbladder polyps with conventional trans-abdominal ultrasound scan (US) is very difficult^{5,15,17}. The sensitivity of different imaging techniques is reported in Table II^{19,30-32}. Positron emission tomography may be useful in some cases to indicate malignancy³³.

The aim of the present study is to assess the performance of US and histological examination to diagnose GA in a consecutive series of patients submitted to cholecystectomy.

Material and methods

From January 2008 to February 2011, 450 patients underwent cholecystectomy in the Department of Surgery in the Hospital "A. Fiorini", Terracina, Italy. Data regarding characteristics of the patients, US and histology examination of the gallbladder were collected. Pearson χ^2 test and Fisher exact test were used for categorical data; Student t test was used for continuous data. Sensitivity, specificity, positive and negative predictive values with relative confidence intervals (c.i.) were calculated with the Wilson method. All tests were two-tailed, and the level of significance was 0.05. All data were analyzed using STATA (v.11.0, Texas, USA).

Results

The study group consisted of 450 patients (189 male and 261 female, mean age 54 years, range 16-88 years), who underwent laparoscopic cholecystectomy in 334 (74.2%) cases and conventional cholecystectomy in 116 (25.8%).

Pre-operative US showed the presence of gallbladder stones in 428 (95.1%) patients (179 male and 249 female; mean age 54 years, range 16-88 years); GA were detected in 22 (4.9%) subjects (10 male and 12 female; mean age 42.5, range 21-85 years). GA were solitary in 19 (86.3%) cases, multiple in 1 (4.5%), and associated with gallstones in 2 (9.0%). All patients with GA were asymptomatic at presentation. Laparoscopic cholecystectomy was performed in 86.3% of patients affected by gallbladder stones and in 73.5% of subjects with GA (difference 12.8%, 95% c.i.: -3.9-35.9; $p=0.174$).

Histological examination of the gallbladder showed the presence of GA in 29 (6.4%) patients (Fig. 1). The findings at histological examination are reported in Table III.

TABLE I - Predictive factors of malignancy in gallbladder polyps.

Factors	References
<i>Epidemiological</i>	
Age > 50-60 years	(7-14)
Female sex	(7-8)
<i>Morphological</i>	
Diameter > 10 mm	(9-13,15)
Single lesions	(9-13)
Sessile polyps	(9,10,12,13)
Gallbladder fundus location	(14,16)
Dismorphic gallbladder wall	(17,18)
Thickening > 3 mm of gallbladder wall	(17,18)
Associated gallbladder stones	(10-12,15,19,20)
<i>Histopathological</i>	
Adenomatous polyps	(11,14,21,22)

TABLE II - Sensitivity of imaging methods.

Method	Sensitivity	Reference
Ultrasound scan	43%	(30)
Diameter >1cm	80%	(31)
Diameter <1cm	20%	(31)
Absence of gallstones	99%	(19)
Echo-endoscopy	86%	(32)
High-resolution ultrasound scan	90%	(32)
Computed tomography	72%	(32)
Magnetic resonance imaging	93%	(30)

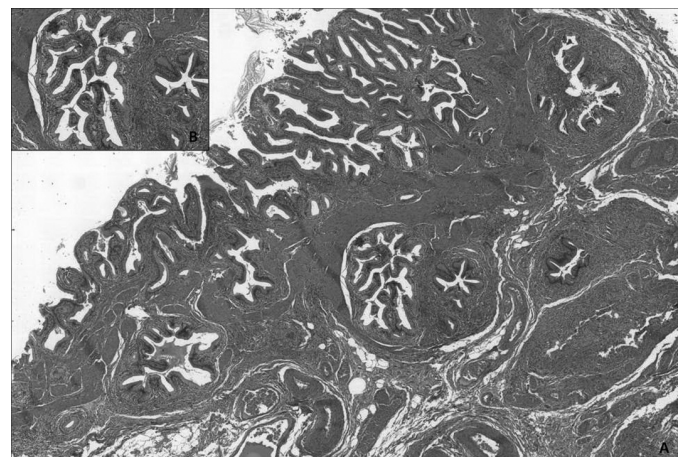


Fig .1: A) Adenomyoma of gallbladder fundus (Hematoxylin-eosin, 2X). B) Hypertrophy of the muscular layer with evidence of hyperplastic tubular structures (Hematoxylin-eosin, 10X).

TABLE III - Histological characteristics of gallbladder adenomyomas.

Characteristics	N. (%)
Localization	
Fundus	22 (75.8)
Corpus	4 (13.7)
Diffuse	3 (10.3)
Mean diameter (range)	9.6 mm (3-20)
M	12.8 mm (6-20)
F	7.6 mm (3-14)
Pyloric metaplasia	17 (58.6)
Intestinal metaplasia with high-grade dysplasia	2 (6.9)

In particular, two female patients with adenomyomas of the fundus (diameter 5 mm) and single stone showed intestinal metaplasia with high-grade dysplasia.

Prevalence of GA was 4.9% for US and 6.4% for histopathology. US detected GA in 22 patients, confirmed by histopathology in 13 and found to be not present in 9. Incidental GA was found in 16 patients of 428 who underwent cholecystectomy for gallstones. US showed sensitivity of 43.3% (95% c.i.:25.4-62.5), specificity of 97.8% (95% c.i.:95.9-99.0) with positive predictive value of 59% (95% c.i.:36.3-79.2) and negative predictive value of 96.2% (95% c.i.:93.7-97.6).

Discussion

Pre-operative diagnosis of GA is still difficult³⁴. In our retrospective series more than half of GA was incidentally diagnosed at histological examination after cholecystectomy performed for symptomatic cholelithiasis. In particular, US showed a poor sensitivity with a very good specificity, which explains the high rate of false negative results of this test. These results confirm the high variability of the diagnostic performance of US, reported in the literature^{19,31}. The present study shows that sensitivity of US is affected by the dimension of the GA and the association with cholelithiasis. When GA are small (diameter < 1 cm) and associated with gallstones, high resolution US is preferred with recommendation of computed tomography and magnetic resonance in case of doubt^{30,35}. US diagnosis of GA in the presence of gallstones is also difficult with respect to the detection of malignancy features (36). Sensitivity of US is not influenced by the location of GA³⁷.

GA are prevalent in women^{7,8}. In the literature there are few studies analysing the prevalence and the natural history of GA either isolated or associated with cholelithiasis^{4,36,37}. The association with gallstones was found in 62% of GA and many authors consider it a risk factor for malignancy^{4,10,12,19,20,37}. Diffuse adenomyomatosis is the rarest histological type of GA with the lowest malignancy potential. According to the lit-

erature, we found that precancerous lesions were more frequently localized in the gallbladder fundus¹⁶. Pyloric and intestinal metaplasia surrounding the GA may be the main factors related to malignancy evolution. This finding supports the hypothesis that the sequence metaplasia, dysplasia and cancer is valid for GA, similar to what happens in colorectal cancer^{5,13,21,22,38-43}. We found the presence of high grade dysplasia in the perilesional mucosa in 2 patients with very small (diameter < 5 mm) GA. However, this finding requires support by studies with a larger series⁴⁴.

Surgery is indicated in the presence of GA > 1 cm and if symptomatic cholelithiasis is present. With respect to polyps smaller than 1 cm the presence of diameter increase, the association of thickening (>3mm) of the gallbladder wall and the presence of dysmorphism at follow-up with US are widely considered as indications for surgery^{4,10-13,15,19,35,42,45}. According to the results of our study surgery is proposed when GA is associated with cholelithiasis in all cases because of the increased risk of malignancy development, independently from the dimension of the lesion.

Conclusion

US still remains fundamental in the diagnosis of GA. However, its unsatisfactory diagnostic performance should be considered and a larger use of high-definition US should be recommended in order to detect potentially malignant lesions.

Cholecystectomy should be also performed in every polypoid lesion of the gallbladder associated with cholelithiasis to prevent malignancy.

Riassunto

INTRODUZIONE: Gli adenomiomi della colecisti sono difficilmente identificabili all'ultrasonografia convenzionale trans-addominale (US). Possono rivelare comportamento maligno e non è stato definito un management ottimale. Scopo dello studio è stato valutare la loro prevalenza ecografica ed istologica e la sensibilità e specificità dell'US.

PAZIENTI E METODI: Studio retrospettivo su 450 pazienti consecutivi sottoposti a colecistectomia. Tutti i pazienti erano stati sottoposti preoperatoriamente a US. Sono state definite le caratteristiche dei pazienti, le caratteristiche ecografiche ed istologiche della colecisti. Sono state calcolate sensibilità, specificità, valori predittivi e intervalli di confidenza. Sono stati utilizzati i test di Pearson, di Fisher ed il t-test.

RISULTATI: Il campione era costituito da 261 femmine e 189 maschi. La US identificava adenomiomi in 22 pazienti, confermati all'esame istologico in 13 ed esclusi in 9. Adenomioma incidentale si riscontrava in 16 su

428 pazienti colecistectomizzati per litiasi. La prevalenza US era del 4.9% mentre la prevalenza istologica era del 6.4%. L'US dimostrava sensibilità del 43.3% (CI:25.4%-62.5%) con valore predittivo positivo del 59% (CI:36.3%-79.2%) e specificità del 97.8% (CI:95.9%-99%) con valore predittivo negativo del 96.2% (CI:93.7%-97.6%). All'esame istologico gli adenomiomi erano localizzati prevalentemente nel fondo. In 2 pazienti con adenomioma del fondo associato a calcolo singolo veniva riscontrata nella mucosa perilesionale metaplasia intestinale con displasia epiteliale di alto grado.

CONCLUSIONI: La diagnosi US di adenomioma della colecisti di diametro <6mm resta difficile per la bassa sensibilità della metodica, principalmente dovuta alla presenza di calcoli. Le alterazioni istologiche della mucosa perilesionale confermano l'ipotesi della progressione carcinogenetica metaplasia-displasia-carcinoma già descritta per il colon e il retto. Resta aperto il problema della selezione dei pazienti da sottoporre a colecistectomia.

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Commento e Commentary

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Dalla casistica citata nello studio retrospettivo su 450 pazienti sottoposti a colecistectomia si apprende che l'ecografia preoperatoria aveva sollevato il sospetto della diagnosi di adenomioma in 22 pazienti, pari al 4,8% del totale. Il riscontro postoperatorio e istologico aveva ridotto questo numero a 13 pazienti, indicando la reale incidenza sull'intera casistica del 2,8%.

Inoltre per quanto riguarda il numero dei sospetti (22 pazienti), la conferma al riscontro postoperatorio si era avuta su 13 pazienti, cioè nei 2/3 dei sospettati (66,2%).

Dalla stessa casistica risulta, come è esperienza di tutti gli operatori, che la localizzazione dell'adenomioma solitario predilige il fondo della colecisti, proprio là dove possono localizzarsi anche i calcoli di piccole dimensioni. Resta allora da suggerire agli ecografisti di controllare la spostabilità dell'immagine sospetta del fondo per ridurre ulteriormente l'incidenza dei sospetti in fase preoperatoria.

Sul piano operativo, che costituisce la questione lasciata aperta dagli Autori, resta la regola aurea di sottoporre a colecistectomia i pazienti sintomatici, indipendentemente dal sospetto di essere portatori di un singolo adenoma, che di per sé rappresenta un rischio prognostico minimo, ben inferiore a quello rappresentato dalla poliposi multipla¹.

Esclusa possibilmente la diagnosi di colecistosi² – oggi meno agevole per l'abolizione della colecistografia con prova di Bronner, se anche la discriminante diagnostica tra adenoma e calcolo unico della colecisti non è raggiungibile con lo studio del paziente asintomatico, è giustificato un atteggiamento conservativo, con controlli periodici ma non necessariamente assidui, per sorvegliare il volume della formazione sospetta, dato l'accertato intervallo di circa 25 anni tra insorgenza della litiasi colecistica e comparsa di incidenza del cancro della colecisti³.

L'attuale sviluppo della tecnica laparoscopica della colecistectomia tende però a vedere ampliate le indicazioni operatorie anche nei pazienti asintomatici.

* * *

From the cited retrospective study of 450 patients undergoing cholecystectomy is learned that the preoperative ultrasound raised the suspicion of the diagnosis of adenomyoma in 22 patients, or 4.8% of the total. The postoperative and histological controls had reduced this number to 13 patients, indicating the true incidence of 2.8% over the entire series. Moreover, as regards the number of suspects (22 patients), the postoperative finding of an adenomyoma had been confirmed in 13 patients, i.e. in 2/3 of the suspects (66.2%).

From the same series, as it is experienced by all the operators, results that the location of the single adenomyoma prefers the bottom of the gallbladder, right there where they can locate even small stones. As a consequence comes the obvious suggestion to sonographers to control the mobility of any suspect image, so further reducing the incidence of preoperatively suspected.

At the operational level, which is the issue left open by the authors, can be observed the golden rule to limit the indication to the cholecystectomy only in symptomatic patients, also regardless of suspicion of the existence of a single adenoma, which in itself represents a minimal prognostic risk, well below that represented by multiple polyposis¹.

Excluded possibly the diagnosis of colecistosi² - now more difficult for the abolition of the radiologic colecistography with Bronner test, if the discriminating diagnosis between adenoma and bile stone is not reached by the study of the asymptomatic patient, a conservative decision is well justified, with regular checks, but not necessarily assiduous to monitor the volume of the eventually suspected image, given the confirmed interval of about 25 years between onset and gallbladder lithiasis and incidence of gallbladder cancer³.

The actual development of the technique of laparoscopic cholecystectomy, however, tends to see extended the operative indications also in asymptomatic patients.

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