

Benign Neoplasms of the Gallbladder: *

Diagnosis and Surgical Implications

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CHOLECYSTOGRAPHIC discovery of benign tumors of the gallbladder is becoming more common. Modern roentgenographic technic may disclose them when they are only 2 or 3 mm. in diameter. Such small tumors may pose complex problems in management, because of the relatively sparse knowledge about their pathologic features and potentialities, and because of the uncertainty about the necessity for prompt excision. This analysis was undertaken to study the features of 45 cases of benign tumors encountered at the Ochsner Clinic in the hope of finding an answer to these problems.

Incidence

During the 15-year period ending October 1959, 200,000 new patients were seen at the Ochsner Clinic. Among these 1,523 had cholecystectomies, 45 (3%) of whom had benign tumors of the gallbladder. During this same period, malignant tumors of the gallbladder were diagnosed in 20 patients (1.3%). Two other varieties of polypoid mucosal lesions were not included because they were not considered true neoplasms of the gallbladder: cholesterol polyps (21 cases) and inflammatory polyps (4 cases). Increased recognition of benign tumors of the gallbladder is indicated by the fact that 35 (78%) of these were diagnosed in the past four years.

Pathologic Data

The 45 benign tumors were classified into five types: adenoma, papillary adenoma

(papilloma), adenomyoma, adenoma with noninvasive carcinoma (carcinoma-in-situ) and fibroadenoma (Table 1). As previously pointed out,² the term, adenoma, implies a true benign neoplasm. These growths may be sessile or pedunculated.⁵ Associated inflammatory changes are usually minimal. Cholesterol deposits may be present in some areas. Fourteen of our patients (33%) had multiple lesions (Fig. 1). Gallstones were present in 47 per cent of our patients (Table 2) and the wall of the gallbladder showed chronic cholecystitis in 34 (Table 3).

Adenoma (18 cases). Nonpapillary or glandular adenomas contain numerous glandular structures, some of which may be dilated in cystic fashion. The glands are separated by scanty vascular stroma which blends with the submucosal layer of the gallbladder (Fig. 2).

Papillary Adenoma (15 cases). These papillomas are somewhat like glandular adenomas, but grossly their surfaces appear more velvet-like. Microscopically, one sees delicate, finger-like projections lined by the same type of columnar cells as found in the glandular structures (Fig. 3).

Adenomyoma (9 cases). These tumors are usually sessile, and in all nine cases (20%) in this series the tumor was in the tip of the fundus of the gallbladder.¹¹ The lesion involves the submucosal and muscular layers as well as the mucosa. The distinguishing feature is the presence of a distinct nodule containing interlacing bundles of smooth muscle fibers in the stroma which separates the glandular structures. The latter are often cystically dilated.

* Presented before the Southern Surgical Association, Hot Springs, Virginia, December 8-10, 1959.

TABLE 1. *Distribution of 45 Benign Neoplasms of the Gallbladder According to Histologic Type and Multiplicity of Lesions*

Type	Cases	Multiple Lesions
Adenoma	18	6
Papillary adenoma	15	6
Adenomyoma	9	1
Noninvasive carcinoma	2	1
Fibroadenoma	1	0
Total	45	14 (33%)

Noninvasive Carcinoma (2 cases). One of these two cases of carcinoma-in-situ, which was in a papillary adenoma, was previously reported.¹³ The other was found more recently in a nonpapillary adenoma. The occurrence of cellular malignant degeneration in an otherwise apparently benign adenoma is widely recognized in other organs, and its occurrence in the gallbladder is not surprising. The literature contains increasing reports of similar cases.^{7, 8, 14, 15}

Fibroadenoma (1 case). The one case of fibroadenoma in this series was previously reported.¹² The basic structure in this case was similar to a glandular adenoma, but there was an abundant fibrous component which in places compressed the glands into slit-like spaces.

Clinical Manifestations

Benign neoplasms of the gallbladder produce no specific manifestations. The most frequent symptoms in our patients, gaseous

TABLE 2. *Incidence of Associated Gallstones in 45 Patients with Benign Neoplasms of the Gallbladder*

Type	Cases	Gallstones
Adenoma	18	11
Papillary adenoma	15	5
Adenomyoma	9	3
Noninvasive carcinoma	2	2
Fibroadenoma	1	0
Total	45	21 (48%)

TABLE 3. *Incidence of Associated Cholecystitis in 45 Patients with Benign Neoplasms of the Gallbladder*

Type	Cases	Chronic Cholecystitis
Adenoma	18	13
Papillary Adenoma	15	12
Adenomyoma	9	7
Noninvasive Carcinoma	2	1
Fibroadenoma	1	1
Total	45	34 (76%)

indigestion and upper abdominal pain (Table 4), are so common that they are difficult to evaluate. Associated gallstones may lead to pain in the right upper abdominal quadrant or episodes of biliary colic. In the absence of proved stones, one may postulate that some tumors become detached and cause pain in passing through the ducts. The pedicle of some of these tumors is extremely filamentous and readily broken. Lund and Burman¹⁰ reported a case in which a pedunculated papilloma passed into the cystic duct, and Henry⁶ reported papillomatous implants in the cystic duct. In several instances, we have found detached adenomas floating in the bile when the gallbladder was opened after excision.

Roentgenologic Observations

In 1931, Kirklin⁹ recorded the first case in which a roentgenologic diagnosis of mucosal tumor of the gallbladder was made.

TABLE 4. *Clinical Manifestations in 45 Patients with Benign Neoplasms of the Gallbladder*

Type	Number	Commonest Symptoms	
		Indigestion	Abd. Pain
Adenoma	18	12	11
Papillary adenoma	15	11	8
Adenomyoma	9	6	3
Noninvasive carcinoma	2	2	1
Fibroadenoma	1	1	1
Total	45	32	24

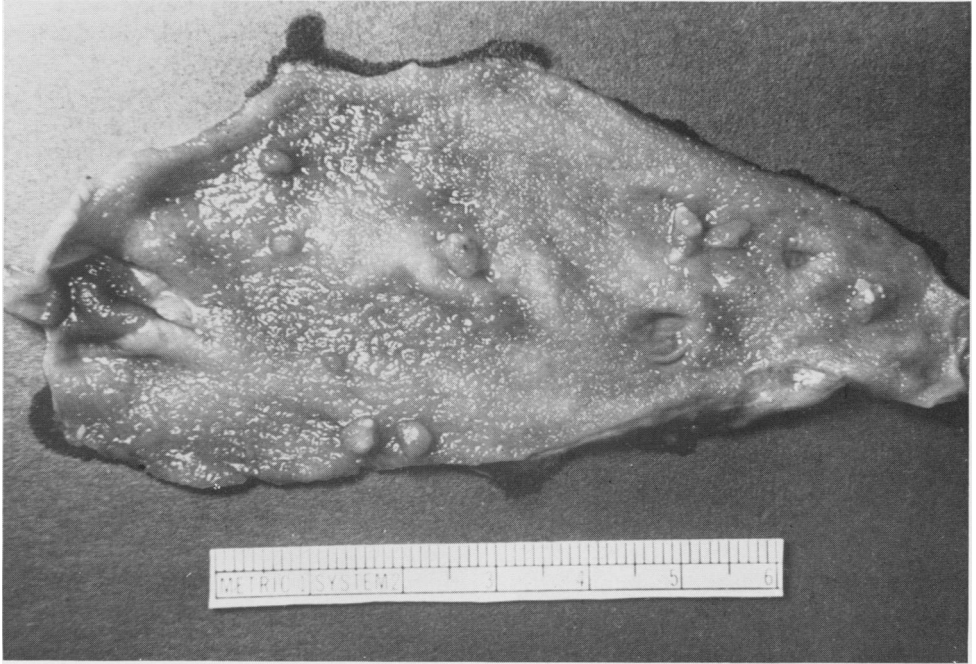


FIG. 1. Photograph of resected gallbladder containing multiple adenomas.

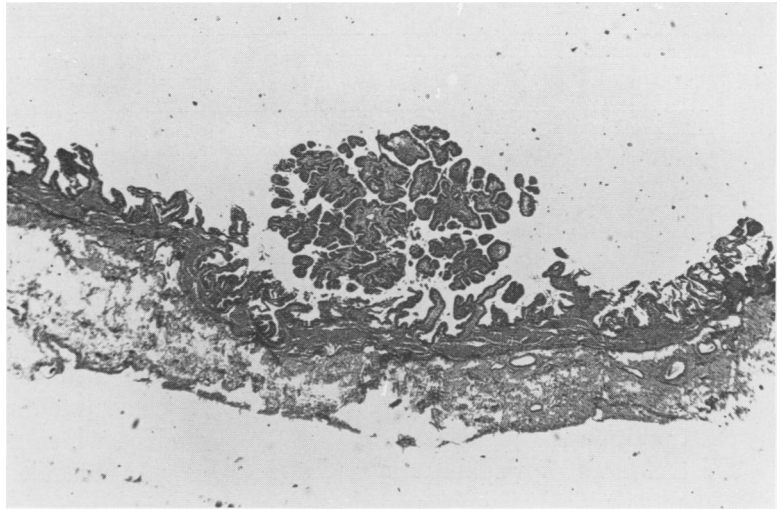
Additional reports appeared infrequently until the past several years. Improved contrast media for visualization of the gallbladder have increased the number of successful cholecystographic examinations being performed. The increased use of the examination, the better contrast provided,

and a broader knowledge of roentgenologic technic have resulted in more diagnoses of mucosal tumors. In our institution, an increased interest in this specific disease has also contributed to the increasing incidence of diagnosis, both radiologically and pathologically.



FIG. 2. Photomicrograph of glandular, non-papillary, pedunculated adenoma.

FIG. 3. Photomicrograph of papillary adenoma of polypoid type.



The essential roentgenographic observation is the presence of a fixed radiolucent defect in the opacified gallbladder. Usually the shadow is small, varying from 2 to 10 mm. in diameter. It may mimic a radiolucent gallstone, but its constant position in the gallbladder is the feature that alerts one to the diagnosis (Fig. 4). A gallstone usually moves around in the gallbladder and this is especially noticeable if roentgenograms are made with the patient in up-

right or decubitus positions. A sessile tumor may produce a marginal indentation in the opaque medium if it is seen in profile view. Benign tumors may be multiple, as occurred in 14 of our 45 cases (Fig. 5). The presence of associated gallstones may prevent the specific diagnosis of tumor, either by producing other movable radiolucent shadows or by producing (with cholecystitis) a nonvisualized gallbladder. A second cholecystographic examination is

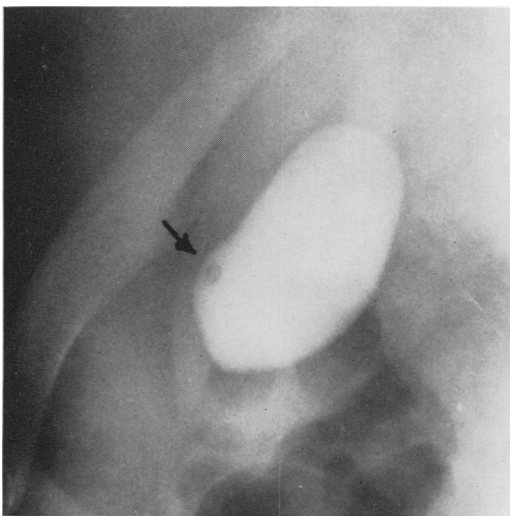


FIG. 4. Roentgenogram shows radiolucent shadow of adenoma of gallbladder.



FIG. 5. Roentgenogram reveals multiple papillary adenomas of the gallbladder.

TABLE 5. Roentgenologic Observations in 45 Cases of Benign Neoplasms of the Gallbladder

Tumor	Cases	Gallbladder Visualized	Radiolucent Shadow	Called Tumor	Called Stone
Adenoma	18	16	10	7	3
Papillary adenoma	15	14	14	8	6
Adenomyoma	9	6	6	3	3
Noninvasive carcinoma	2	0	(No function in either case)		0
Fibroadenoma	1	1	1	1	0
Total	45	37 (82%)	31 (84%)	19 (61%)	12 (39%)

valuable if there is doubt about a small radiolucent shadow, or if evidence about its fixed position is equivocal.

The incidence of visualization and specific roentgenologic diagnosis is shown in Table 5. A diagnosis of a polypoid mucosal lesion will be made more often if all small radiolucent shadows are evaluated with this possibility in mind (Fig. 6).

Surgical Features

The primary dilemma facing the patient with a suspected benign tumor of the gallbladder is whether to have the gallbladder removed. The opinion must be rendered usually by the surgical consultant who sees the patient because of clinical manifesta-

tions, which may be vague, or because of cholecystographic demonstration of a shadow, which may be extremely small. It may be difficult to convince a patient that a major surgical procedure is necessary, and it may be equally difficult to justify cholecystectomy to a doubtful internist or roentgenologist.

Our present opinion is that cholecystectomy should be recommended. The evidence in favor of this is partly indirect and partly direct. The indirect evidence comes from a consideration of benign polypoid tumors arising from mucosal surfaces of other organs. With our current knowledge, we are forced to accept the concept that malignant tumors may arise from tumors that were once benign. For this reason, removal of benign tumors is as desirable from the gallbladder as from the stomach or colon.

The direct evidence in favor of removal is found in the two of our 45 patients with noninvasive carcinoma, which represents an incidence of approximately 4.5 per cent. This type of lesion, the carcinoma-in-situ, is almost universally accepted as having grave potentialities. Advanced carcinoma of the gallbladder is such a uniformly fatal disease¹ that, by contrast, resection in noninvasive cases seems a joyful experience.

Additional factors favoring excision of suspected benign tumors may be cited. If the cholecystographic shadow proves to be a gallstone instead of a tumor, we believe that the patient has been properly treated, because we agree with others that removal

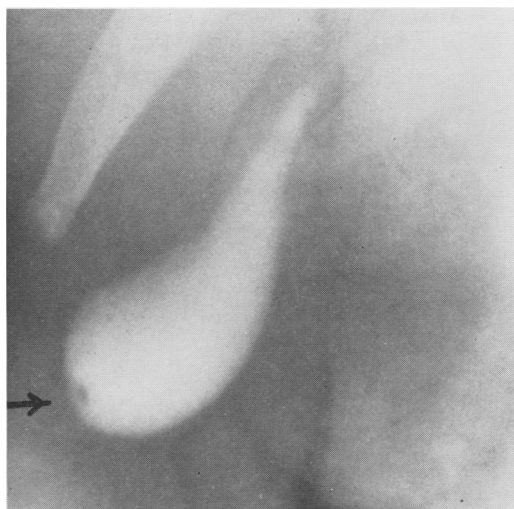


FIG. 6. Roentgenogram of gallbladder in contracted phase shows defect in fundus due to adenomyoma of gallbladder.

of gallstones is desirable. Because of the possible danger of acute cholecystitis with its attended high morbidity and mortality rates, resulting from blockage of the cystic duct by the calculus, and the fact that frank carcinoma of the gallbladder is almost invariably associated with and probably caused by gallstones, cholecystectomy should be done unless an operative procedure is otherwise contraindicated. Relief of symptoms is a factor which is difficult to evaluate.⁴ It has been gratifying, even if a little surprising, that several patients have stated that their symptoms were relieved.

An interesting technical consideration is that these tumors usually are small and quite soft. They may be readily overlooked by the surgeon in casual palpation of the gallbladder. We have learned that sometimes they cannot be felt when one carefully palpates the gallbladder during laparotomy. In these cases we have resected the gallbladder "on trust," so to speak, realizing that a firm roentgenologic diagnosis is sufficient justification for the procedure. In the seven cases in which this was done the roentgenologic opinion proved to be correct.

All gallbladders in this series were removed without difficulty, which is a great contrast to the technical problems involved in resecting invasive malignant tumors. There were no operative deaths and no significant postoperative morbidity.

Discussion

Aside from gallstones, several lesions may be mistaken for benign tumors. The commonest of these is the cholesterol polyp, which cannot be differentiated from benign tumors in roentgenograms. Often they cannot be differentiated by gross inspection but require microscopic study for verification. Inflammatory polyps are less common. Usually they are associated with gallstones and a more significant degree of cholecystitis. In our cases cholecystographic visualization has been less successful. When seen, the in-

flamatory polyp cannot be differentiated from cholesterol polyps.

Ten Eyck^{1,6} and Feldman and associates³ reported rare instances of vascular lesions of the gallbladder which mimicked benign tumors, by producing a mucosal mass which resulted in a fixed radiolucent defect in the cholecystograms.

Summary

Benign neoplasms of the gallbladder are being discovered with increasing frequency. Basically, they are adenomas of the mucosa, and histologically, they may be classified into five types. Forty-five have been diagnosed at the Ochsner Clinic during a period of 15 years. In two of these noninvasive carcinoma was present, and 21 were associated with gallstones. Indigestion and mild abdominal pain are the most frequent symptoms. Many of them can be visualized by cholecystography, and a specific diagnosis may be suspected because of a fixed radiolucent shadow in the opacified gallbladder. Our current belief is that cholecystectomy is the treatment of choice when there is no contraindication to the operative procedure.

References

1. Arminski, T. C.: Primary Carcinoma of Gallbladder; Collective Review with Addition of 25 Cases from Grace Hospital, Detroit, Michigan. *Cancer*, 2:379, 1949.
2. Carrera, G. M. and S. F. Ochsner: Polypoid Mucosal Lesions of Gallbladder. *J. A. M. A.*, 166:888, 1958.
3. Feldman, M., J. E. Goodman and T. Weinberg: Varices of the Gallbladder Associated with a Mucosal Cyst; Report of Case. *Am. J. Digest. Dis.*, 9:399, 1942.
4. Gagliardi, R. A. and P. D. Gelbach: Papilloma of the Gallbladder. *Gastroenterology*, 32:666, 1957.
5. Halpert, B.: Gall Bladder Neoplasms, in "Pathology," edited by W. A. D. Anderson, ed. 2, St. Louis, C. V. Mosby Company, 1953, pp. 844.
6. Henry, C. K. P.: Benign Papillomata of Gallbladder and Biliary Ducts. *Canad. M. A. J.*, 28:300, 1933.
7. Jones, H. W. and J. H. Walker: Correlation of the Pathologic and Radiographic Findings

- in Tumors and Pseudotumors of the Gallbladder. *Surg., Gynec. & Obst.*, **105**:599, 1957.
8. Kerr, A. B. and A. C. Lendrum: Chloride-secreting Papilloma in Gallbladder; Tumor of Heterotopic Intestinal Epithelium Containing Paneth cells and Enterochromaffine Cells and Associated with Massive Chloride Loss; with Critical Review of Papilloma of Gallbladder. *Brit. J. Surg.*, **23**:615, 1936.
 9. Kirklin, B. R.: Cholecystographic Diagnosis of Papillomas of Gallbladder. *Am. J. Roentgenol.*, **25**:46, 1931.
 10. Lund, N. M. and C. E. L. Burman: Case of Acute Cholecystitis and Obstruction due to Pedunculated Papilloma, Identical with Attack of Acute Cholecystitis and Gallstones. *Brit. J. Surg.*, **38**:390, 1951.
 11. Ochsner, S. F.: Adenomyoma of Gallbladder; a Specific Cholecystographic Picture? (To be published.)
 12. Ochsner, S. F. and G. M. Carrera: Fibroadenoma of the Gallbladder. *Arch. Path.*, **68**: 676, 1959.
 13. Ochsner, S. and M. Gage: Papilloma of Gallbladder with Carcinoma-in-situ. *Ochsner Clin. Rep.*, **2**:27, 1956.
 14. Shepard, V. D., W. Walters and M. B. Dockerty: Benign Neoplasms of Gallbladder. *Arch. Surg.*, **45**:1, 1942.
 15. Tabah, E. J. and G. McNeer: Papilloma of Gallbladder with *in situ* Carcinoma. *Surgery*, **34**:57, 1953.
 16. Ten Eyck, E. A.: Fixed Defects in the Gallbladder Wall. *Radiology*, **71**:840, 1958.

DISCUSSION

DR. ROBERT S. SPARKMAN: I wish to show two slides which will merely serve to emphasize what Dr. Ochsner has said concerning the difficulty of differentiation between polyp of the gallbladder and stone.

(Slide) The first of these slides shows multiple radiolucencies which were interpreted by our radiologist to represent polyps, since they did not move with change of position of the patient. At operation they proved to be polyps.

(Slide) The second slide shows a similar radiolucency which was seen on two separate oral cholecystograms and which remained constant in position. It was thought to be a polyp, but proved at operation to be a stone adherent to the mucosa of the gallbladder.

This demonstrates the difficulty of differentiation between these two conditions, as pointed out by Dr. Ochsner.

DR. DUNCAN SHEPARD: I enjoyed Dr. Ochsner's paper particularly since I've been interested in the same subject for several years.

We went over a large series of removed gallbladders and we found *in toto*, 45 polyps and 103 tumors which we classified as adenomyomas. It was interesting that the incidence of these in surgically removed gallbladders (these were not autopsy specimens, but gallbladders which were removed for cholecytic disease) was about the same; about one in each 100 gallbladders removed.

The sex incidence of polyps was about 1:1 for men and women, whereas the adenomyomas had a definite sex incidence of three women to every one man.

We found that our polyps were single, sometimes multiple, and we had five cases which we

classified as polyposis; grossly, it looked very much like the polyposis of the colon and in one patient we found two localized carcinomas in the polyps which could be diagnosed only microscopically.

The adenomyomas were almost invariably located at the fundus of the gallbladder and showed no malignancy but we did have the interesting complication of three cases which had intramural gallstones. Also 14% of our adenomyomas had microscopic intramural abscesses.

It has been pointed out that this may be a fatal source of generalized peritonitis in these patients in that the intramural microscopic abscess may perforate, not into the gallbladder but into the free peritoneal cavity and result in generalized peritonitis.

DR. J. W. BAKER: I wish to thank Dr. Ochsner for this clinically valuable contribution. Several years ago Drs. Jones and Walker of our clinic became interested in the subject and reviewed the findings in 1,000 surgical cholecystectomies, and published at that time an evaluation of focal elevated structures in the gallbladder based upon a combined radiologic and pathologic study.

(Slide) In this tabulation you will notice that there was less than 1% incidence of true epithelial papilloma, 1.2% carcinoma, diversely 1.6% cholesterol polyps and 0.5% inflammatory polyps. There were three cases of an anomaly of development of the tip of the gallbladder, commonly referred to in the past as adenomyoma, which Drs. Jones and Walker would prefer to term myo-epithelial hamartoma. (Slide) Because they arise in the fundus which is a frequent site of primary carcinoma, they may be mistaken radiographically for cancer. The lesion is strictly benign and gives this characteristic x-ray deformity in the tip of the gallbladder, an x-ray