Differences between images of large adenoma and protruding type of gallbladder carcinoma

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Abstract. The aim of this study was to investigate the differences between images of large adenoma of the gallbladder and the protruding type carcinoma of the gallbladder. A retrospective study was performed on 130 patients who underwent cholecystectomy or biopsy for gallbladder polypoid lesions larger than 10 mm; among them, 20 patients were malignant and 110 patients were benign. Patients' details including ultrasonography (US), computed tomography (CT) and magnetic resonance (MR) findings were analyzed. All patients whose lesions were >15 mm by US, had CT or MR scans to further determine the nature of the lesion; two patients who were suspected to have a malignant lesion due to their large tumor size were benign by histological examination. Distinct differences were found between large adenoma and protruding type of gallbladder carcinoma. There were distinct differences between adenomas and the protruding gallbladder cancers, and there was a pathological basis for the differences. Benign tumors had a more homogeneous texture, had spaces between the tumor and the gallbladder wall and a relatively normal configuration of the gallbladder wall. Based on these findings, certain lesions could be definitively diagnosed as benign adenomas and could help in treatment strategy.

Introduction

The detection of polypoid lesions of the gallbladder (PLGs) has increased significantly due to the widespread use of ultrasonography (US) imaging techniques (1-3). US is the first choice in the diagnosis of this disease and enhanced computed tomography (CT) and magnetic resonance imaging (MRI) confirm its nature (4-8). Many studies have indicated that the size of tumor is vital for diagnosis. A diameter >10 mm is regarded as the threshold for malignancy (3,9-11). In this study, a large tumor size did not necessarily mean that the lesion was malignant; the configuration of the tumor and the gallbladder wall and the existence of space between the two were the main indicators of the nature of the lesion. This knowledge will enable optimal management of this type of patient. In this article, a retrospective analysis of clinical data of PLG patients over a 5-year time period was performed.

Materials and methods

Patients. The study was approved by the Ethics Committee of Zhejiang Provincial People's Hospital, Hangzhou, China. The study was retrospective so consent was not required. Two qualified radiologists reviewed images from 130 patients from 2005 to 2011 with PLGs larger than 10 mm who consented to the removal of the gallbladder or biopsy. All patients were pathologically diagnosed by routine postoperative examination; the age of patients ranged from 28 to 82 years old.

CT, MR and US protocol. Patients fasted for at least 8 h before examination; no oral contrast medium or water was administered. CT examinations were performed using Philips Brilliance 16 (Philips Medical Systems, Best, Netherlands). Each patient received 100 ml of a nonionic contrast material (iopromide; Ultravist 370, Bayer HealthCare, Berlin, Germany) through an 18-gauge angiographic catheter inserted into a forearm vein. CT scans were routinely obtained with the patient in a supine position. The contrast material was injected at a rate of 3 ml/sec with an automatic power injector. Magnetic resonance cholangiopancreatography was taken using a Siemens 3.0 Tesla MR magnet (Magnetom Trio; Siemens AG, Erlangen, Germany) through an 18-gauge angiographic catheter inserted into a forearm vein. CT scans were routinely obtained with the patient in a supine position. The contrast material was injected at a rate of 3 ml/sec with an automatic power injector. Magnetic resonance cholangiopancreatography was taken using a Siemens 3.0 Tesla MR magnet (Magnetom Trio; Siemens AG, Erlangen, Germany); sonography was performed using Esaote MyLab 70 (Esaote SPA, Genova, Italy) with 1-8 MHz linear array probes or a Toshiba (Applio XG 790; Toshiba, Tokyo, Japan) with 3-6 MHz 6C1 probes. Specific attention was given to the size and the base of the lesion, and the configuration of the wall to elucidate the differences between benign and malignant lesions.

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Table I. Patients’ clinical data.

| Characteristics                  | No.   | Percentage |
|----------------------------------|-------|------------|
| Total (n=130)                    |       |            |
| Benign                           | 110/130 | 85         |
| Malignant                        | 20/130   | 15         |
| Malignant (n=20)                 |       |            |
| Platform                         | 13/20 | 65         |
| Protruding lesions               | 7/20 | 35         |
| Female                           | 16/20 | 80         |
| Male                             | 4/20 | 20         |
| Benign (n=110)                   |       |            |
| Lesion >20 mm                    | 8/110 | 7          |
| Lesion >50 mm                    | 2/110 | 1.8        |
| Laparoscopic cholecystectomy     | 102/110 | 93        |
| Open cholecystectomy             | 8/110 | 7          |

Results

**Patient characteristics.** Twenty-two patients were diagnosed as malignant by CT and 20 of them were confirmed by biopsy or postoperative pathological examination. Two patients with lesions larger than 50 mm were suspected to be malignant preoperatively but were benign on histological examination. One patient had two polyoid lesions. On pathological examination one was benign and the other was malignant (Table I).

**Differences in morphology between large adenoma and protruding type cancer.** Before the operation, 2 patients were diagnosed with gallbladder cancer due to the large size of their tumors but these were revealed to be adenoma. One was tubular adenoma and the other was rare villous adenoma. Following CT scans, the villous adenoma turned out to be akin to dendritic processes; there were spaces within the mass, the surface had no contraction and the whole shape appeared to be natural like dendritic processes in the MRI scan (Fig. 1). The CT and MRI image of the tubular adenoma was different from that of villous adenoma, the appearance was similar to a congregation of mulberries (Fig. 2). In contrast, the surface of the malignant tumor was uneven, the enhancement of the solid entity of the tumor seemed to be inhomogenous and grew in a solid mass (Fig. 3). In Fig. 4, where a benign and malignant tumor grew together in the same gallbladder, the malignant tumor became more enhanced than the benign one (Fig. 4).

**Difference in the base size of the tumor, and the space between the tumor and the gallbladder wall.** The base of the benign polypus was smaller than the malignant one and there was space between the tumor and the gallbladder wall. In the case of tubular adenoma, the CT and MR images showed that the mass had almost no contact with the gallbladder wall and the whole mass appeared to be floating in the water. Macroscopically, the mass was connected to the wall of the gallbladder with small and slender fibers and could easily be removed from the wall of the gallbladder, while the gallbladder wall remained smooth with integrity (Fig. 2). In the case where benign and malignant tumors coexisted, there was a space between the wall and the tumor, while the space disappeared between the malignant tumors and the wall (Fig. 4). In the case where the lesion was a polyoid with a slender pedicel, the CT scan showed a strip parallel with the wall resembling a trailing plant, and was separated from the wall by a narrow space (Fig. 5). In contrast, the base of the protruding carcinoma was wide, the space between the polypus and the gallbladder wall disappeared and the enhancement became more evident close to the base of the tumor (Figs. 4 and 6).

**Shape of the gallbladder wall.** The gallbladder wall with the benign tumor was smooth and soft, had the normal thickness and normal extent of enhancement, with the normal space...
between the wall and the liver. The wall of malignant lesions, however, became thicker and stiff and the space became obscure. In some cases it disappeared. In certain cases, the wall had broken and the lesion had infiltrated the liver parenchyma, which was a sign of a malignant lesion.

Discussion

Polypoid lesions of the gallbladder are an imaging feature, which indicate a wide variety of pathology. They affect ~5% of the adult population (3,12,13). Although most of these lesions are benign, some early carcinomas of the gallbladder present as polypoid lesions; malignant transformation is always a concern. The differentiation of benign and malignant lesions can be challenging. Several features, including patient age, tumor size and the speed of growth of the lesions, are important discriminating features between benign and malignant polyps. Many studies have shown that age >50 years and a polyp size >1 cm are the two most important factors predicting malignancy in polypoid lesions of the gallbladder (3,9-11).

Microscopically, malignant tumors no longer possess the normal structure of the original tissue. There is frequent necrosis and subsequent repair within the tumor; the surface of a malignant tumor is often uneven and the whole configuration is unnatural and becomes stiff (14). Growing in an infiltrative way, the malignant tumors invade neighboring tissue; thus, the demarcation between the tumor and the normal tissue is obscure. Benign tumors do not grow uncontrollably; most benign tumors have a similar structure to the tissue they originate from and do not invade neighboring tissues and spread throughout the body. Since adenoma has the structure of gland tube, which is characterized by short fibrovascular stalks that are covered by dysplastic or neoplastic cells, the CT and MR images of large adenoma have the similar shapes, akin...
to float grass. In contrast, gallbladder cancer infiltrates the base and there is necrosis on the inside of the tumor and the image appears to be inhomogenous without a natural texture. Macroscopically, the gallbladder tumors are classified into the protruding, flat or infiltrative type (15). US, CT and MR images are used to classify these types (8,16-20).

In this study, pathological differences in the shape and texture of the mass, the base of the mass, the space between the tumor and gallbladder wall, and the changes of the gallbladder wall were used to determine whether the lesion was benign or malignant. The results support the differences between large adenoma and protruding type carcinoma. In gallbladder adenoma, even though the lesions were very large there were still spaces within the tumor, indicating that the tumor was not a solid mass; in the villous adenoma, the spaces were narrow and resembled dendritic processes; in the tubular adenoma, the spaces were irregular. Microscopically, this kind of spaces exist between the fibrovascular stalks that are covered with gland. Since the malignant tumor grows in an infiltrative way and always has a wide base, there is no space between the tumor and the gallbladder wall and the gallbladder walls are always thickened and contracted; the spaces between the gallbladder wall and the liver disappear when the tumors break the gallbladder wall and invade the liver parenchyma.

Many studies have demonstrated that lesion size and patient age are strong indicators of a malignant tumor. In this study, the large size of polypoid lesions of the gallbladder did not necessarily mean the tumor was malignant. A possible reason for this may be that the cancerous change needs time and the speed of this change is relatively slow. Conversely, small adenoma does not always mean benign. According to a study conducted by Roa et al (21), adenomas associated with cancer may measure <5 mm. Using polyp size to decide surgical behavior may, therefore, be misleading. Adenoma is a precancerous disease which could transform to adenocarcinoma in an adenoma-dysplasia-cancer manner (22,23). A protruding type of gallbladder was likely the result of adenoma continuing stimuli such as gallstones or chronic inflammation. In this study, the co-existence of a benign and malignant tumor in one patient was evidence of this theory.

Although it is difficult to discriminate between large adenoma and cancer, removing the gallbladder by open laparotomy is usually the first choice of treatment for these two diseases. However, in an era of minimally invasive surgery, both doctors and patients prefer to choose laparoscopic cholecystectomy. Size may not be the key indicator to discriminate benign from malignant lesions, or the indication for a laparoscopic or open procedure. Preoperative images indicate that the feasibility of laparoscopic cholecystectomy mainly depends on the lesion's configuration; they should be confined to the lumen of the gallbladder, the wall of the gallbladder should be smooth and thin and the space between the wall and liver should be clear; this indicates that the separation of the gallbladder from the liver should be relatively simple. Many articles have reported that even PLGs with a diameter >1.5 mm, a potential early-stage cancer, could still be resected by laparoscopic cholecystectomy with full-thickness dissection (24-26). The key issue with such surgery is to maintain the integrity of the gallbladder and protect the Trocar port in order to avoid the dissemination of the cancer in case the lesion is malignant (27,28).

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