Carcinoid Tumor of the Gall Bladder

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A classical carcinoid tumor, measuring 11 x 17 mm, was found in a 41-year-old woman in the neck of the gall bladder. The lesion infiltrated the muscular layer of the gall bladder wall. Histologically, the tumor was positive for only Grimelius and chromogranin A stains. In a literature search, approximately half of the tumors reported as gall bladder carcinoid tumor appear to be actually endocrine cell carcinomas, which are completely different from classical carcinoid tumors with respect to size, metastasis and prognosis. These carcinomas should not be termed as carcinoid tumors from both the clinical and histological points of view, and should be clearly distinguished from benign lesions when reported.

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Key words: endocrine cell tumor, gall bladder, carcinoid tumor

Introduction

Recently, carcinoid tumors have been reported more frequently. The tumors arise mainly in the gastrointestinal tract or the bronchi, but rarely develop in the gall bladder. This report describes a classical carcinoid tumor found in the gall bladder of a 41-year-old woman, as well as discusses the relevant literature.

Case Report

A 41-year-old woman complained of an abnormal sensation in the pharynx and esophagus, but there were no abnormalities on gastrointestinal examination performed in December 1994. However, abdominal ultrasound revealed several gall stones and a polyp in the gall bladder. In March 1995, cholecystectomy was carried out.

The laboratory findings on admission revealed the following: Red blood cell (RBC), 420 x 10^4/μl; Hemoglobin (Hb), 13.3 g/dl; White blood cell (WBC), 10,000/μl; platelet count, 25.4 x 10^4/μl; total protein, 6.6 g/dl; total bilirubin, 0.8 mg/dl; Glutamate oxaloacetate transaminase (GOT), 26U; and Glutamate pyruvate transaminase (GPT), 15U.

Abdominal ultrasonography demonstrated several gall stones (several millimeters in diameter) in the gall bladder lumen and a protrusion showing bizarre echogenicity and an irregular surface in the neck of the same organ (Fig. 1). Abdominal CT scan showed a low-density mass in the neck of the gall bladder.

On gross inspection of the operated material, the gall bladder contained four black stones, sized approximately 3 mm in diameter. In addition, there was a fragile, cauliflower-shaped lesion measuring 11 x 7 mm in the neck of the gall bladder (Fig. 2). Histologically, the tumor cells contained small, round and uniform nuclei, formed small nodular, trabecular or acinar structures, and showed no mitotic figures. Although most tumor cells were present in the lamina propria of the gall bladder wall, some infiltrated into the muscular layer (Fig. 3). Brown granules were observed in the cytoplasm of most cells by Grimelius (Fig. 4) and chromogranin A stains (Fig. 5), but were negative for Fontana-Masson stain. In addition glucagon, insulin, ACTH, NSE, somatostatin, CEA and serotonin were immunocytochemically negative. Neither chromogranin A and Grimelius positive cells nor pyloric gland and intestinal metaplasia were observed in the surrounding mucosa of the tumor. By flow cytometry, it was found that the tumor cells showed a diploid pattern (Fig. 6).

Discussion

In 1838, Merling (1) first described the histological features of carcinoid tumor. In 1907, Oberdorfer (2) proposed the name “Karzinoide” for small benign tumors which lie in the submucosa, grow slowly, never infiltrate the surrounding tissues and never metastasize.
Figure 1. Right oblique subcostal sonogram showing a polypoid mass (arrow) in the gall bladder.

Figure 2. Gross appearance of the resected gall bladder. A yellowish-colored polyp is noted in the neck region.

Figure 3. Low-magnification view of carcinoid tumor of the gall bladder (HE stain, ×40).

Figure 4. Grimelius staining is positive in almost all the tumor cells (Grimelius stain, ×400).

Figure 5. The tumor cells are diffusely positive for Chromogranin A stain (Chromogranin A stain, ×100).

Figure 6. DNA ploidy pattern of carcinoid tumor of the gall bladder.
More recently in the endocrine cell tumors of the stomach, Gilligan et al (3) have proposed a classification in which these are divided into tumors associated with chronic atrophic gastritis or Zollinger-Ellison syndrome (classical carcinoid tumors) and sporadic lesions (endocrine cell carcinomas) which combine adenocarcinoma and probably arise from it (4). The former type of tumor shows diploidy in all tumor cells, rare metastasis, hypergastrinemia, positive reaction for both the serotonin and polypeptide stains and therefore has a favorable prognosis. On the other hand, the latter type demonstrates the nuclear atypia, mitotic figures, DNA aneuploidy, vascular invasion and a high metastatic rate, and also positive reaction for serotonin. Therefore, regarding terminology, the same pathological name should not be given to these two diseases with a completely different prognosis, based simply on the fact that both types of tumors contain endocrine granules.

Primary carcinoid tumors are generally found in the digestive tract and the bronchi, and rarely arise in the gall bladder. Sanders (5) reported only 7 tumors (0.2%) in the gall bladder among 3,633 digestive tract carcinoids. Godwin (6) reported only one tumor (0.04%) in the gall bladder among 2,837 carcinoids.

Primary carcinoid tumor of the gall bladder was first reported by Joel in 1929 (7). We found a total of 39 cases (8–42) reported to date indicated that 12 were classical carcinoid tumors (7, 9, 31, 35, 36, 38, 39, 40, 41, 42, 43) and another 12 were endocrine cell carcinomas (10, 13, 20, 21, 25, 27, 28, 29, 32, 33, 34, 37). The size of the former tumors ranged from 3 mm to 20 x 20 mm, and only one was associated with metastasis. In addition, none of the 12 patients died of their tumors. On the other hand, the latter tumors ranged in size from 80 x 80 x 15 mm to 20 x 20 mm, metastasis was found in 8 patients, and 8 patients died within 10 months. These facts also support the concept that the two diseases are completely different.

A detailed histological review of the gall bladder carcinoids reported to date indicated that 12 were classical carcinoid tumors (7, 9, 31, 35, 36, 38, 39, 40, 41, 42, 43) and another 12 were endocrine cell carcinomas (10, 13, 20, 21, 25, 27, 28, 29, 32, 33, 34, 37). The size of the former tumors ranged from 3 mm to 20 x 30 mm, and only one was associated with metastasis. In addition, none of the 12 patients died of their tumors. On the other hand, the latter tumors ranged in size from 80 x 80 x 15 mm to 20 x 20 mm, metastasis was found in 8 patients, and 8 patients died within 10 months. These facts also support the concept that the two diseases are completely different.

The origin of gall bladder carcinoid tumors is a matter of great interest in relation to intestinal metaplasia. Endocrine cells generally do not exist in the mucous membrane of the normal gall bladder and are only rarely observed in the gall bladder neck (44). Thus, endocrine cells developing in the body and fundus of the gall bladder are generally thought to appear, associated with intestinal metaplasia (45). In the present patient, the tumor was localized in the neck of the gall bladder and no intestinal metaplasia was detected, so the lesion was considered to have arisen from endocrine cells in the mucous membrane. Gall bladder carcinoids that were reported previously included tumors in the neck, body, and fundus of the gall bladder, and intestinal metaplasia was found around mucosal carcinoids localized in any of these 3 sites (45). These findings indicated that gall bladder carcinoid tumors may develop from endocrine cells induced by intestinal metaplasia of the body and fundus, as well as from pre-existing endocrine cells in the neck of the gall bladder.

References

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