Topics: Cancer of pappilla of Vater

Neoplastic diseases of the papilla of Vater

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Abstract
Although it is quite small, the papilla of Vater is an important part of the body. Carcinoma of the papilla may be one of the smallest cancers that can cause death. The 5-year survival rate after resection was 51%, which is not satisfactory. In this article, the topics discussed are (1) pathogenesis, (2) histological characteristics, and (3) the molecular biological characteristics of carcinoma of the papilla of Vater. From results obtained by the investigation of 576 autopsied and 51 resected cases, atypical epithelium was found most frequently in the common channel, where pancreatic juice and bile mix physiologically. Atypical epithelia may be a precursor of carcinoma of the papilla of Vater. Carcinoma of the papilla of Vater could be classified into two types histologically, an intestinal type and a pancreaticobiliary type. The prognosis of patients with the intestinal type was much better than that of patients with the pancreaticobiliary type. These two types of carcinoma should be treated by different operative procedures or adjuvant therapies. Regarding the molecular biological characteristics of carcinoma of the papilla of Vater; (1) K-ras mutation is mainly associated with the intestinal type, and carcinomas of the intestinal and pancreaticobiliary types may develop via different mechanisms; (2) p53 overexpression may play a role in tumor ulceration; and (3) p21/Waf1 overexpression was significantly correlated with a poor prognosis.

Key words Pathogenesis·Intestinal type·Pancreaticobiliary type

Introduction
Although it is quite small, the papilla of Vater is an important part of the body. Carcinoma of the papilla may be one of the smallest cancers that can cause death. Therefore, the pathogenesis of carcinoma of the papilla has drawn the attention of many pathologists, as well as surgeons.

In the Japanese experience from 1988 to 1994, carcinoma of the papilla of Vater was found in 939 cases, representing 12.7% of extrahepatic biliary tract carcinomas (7380 cases) (Fig. 1). In the same period, extrahepatic bile duct carcinoma was found in 3294 cases and gallbladder carcinoma was found in about 3147 cases.

As shown in the survival curves for patients with resected carcinoma of the papilla of Vater (Fig. 1), the 5-year survival rate was 51%, which is not satisfactory. If the carcinoma was not resected, most of the patients died within 2 years.

Topics discussed in this article are (1) the pathogenesis (2), the histological characteristics, and (3) the molecular biological characteristics of carcinoma of the papilla of Vater.

Pathogenesis of carcinoma of the papilla of Vater

Sites of origin
With regard to the adenoma-carcinoma sequence, Sobol and Cooperman reviewed the literature and analyzed 45 cases of adenoma of the papilla of Vater, and found carcinoma in 12 cases (27%). With regard to the incidence of “adenoma” surrounding carcinoma of the papilla of Vater, the values have been reported to be 82% by Kozuka et al. and 91% by Baczako et al. Therefore, the adenoma-carcinoma sequence is very important in the pathogenesis of carcinoma of the papilla of Vater.

However, some authors have insisted that some carcinomas of the papilla of Vater arise de novo, because adenoma is very rare compared to carcinoma in this region.
In Fig. 2, a schematic drawing of the papilla of Vater, the papilla is defined as the area surrounded by the broken line. The papilla of Vater is composed of the common channel, the intraduodenal portion of the common bile duct, the intraduodenal portion of the pancreatic duct, and the duodenal mucosa.

When considering the pathogenesis of carcinoma, it is very important to investigate the site of development. In 1913, Outerbridge reported that carcinoma of the papilla of Vater can theoretically originate from the following sites:

1. Epithelia of the common pancreatico-biliary channel (the common channel; Ac)
2. Epithelia of the common bile duct at its lower end (Ab)
3. Epithelia of the pancreatic duct at its lower end (Ap)
4. Duodenal mucosa covering the papilla (Ad)
5. The glands of Brunner
6. Aberrant pancreatic acini in the wall of the common duct

We histologically investigated the papilla of Vater in 576 autopsy cases of elderly people. Special attention was paid to the presence of epithelial atypism. After fixation with formalin, serial sections were obtained, as shown in Fig. 3. When the papilla is cut along line A (in Fig. 3), the epithelia of the common channel can be investigated. When the papilla is cut along line B, the epithelia of the intraduodenal bile duct and intraduodenal pancreatic duct can be investigated.

The criteria for epithelial atypism of the papilla of Vater were classified into the following five groups, according to cellular and structural atypism:

- **Group 1; normal (Fig. 4a)**
- **Group 2; mild atypism (Fig. 4b)**
- **Group 3; moderate atypism (Fig. 5)**
- **Group 4; severe atypism (Fig. 6)**
- **Group 5; unequivocal carcinoma (Fig. 7)**

Table 1 shows that group 1 epithelia accounted for 71% of the epithelia of the common channel in 451 cases, while group 2 accounted for 25% of the epithelia of the common channel in 451 cases. Group 3 epithelia accounted for 2.9% of the common channel, 1.7% of the intraduodenal portion of the common bile duct, and 0.6% of the intraduodenal portion of the pancreatic duct. The incidences of group 3 and 4 epithelia in the common channel were significantly higher than those in the intraduodenal portion of the bile duct, pancreatic duct; P, Pancreas; Sm, Submucosa; Pm, Muscularis propria.