We report a case of a pedunculated polyp with a focus of gastric-type adenocarcinoma arising in the opposite side of the papilla Vater of the duodenal second portion. The carcinoma was surrounded by lobules of hyperplastic Brunner’s glands. Immunohistochemically the carcinoma tissue showed both gastric foveolar-type mucin (MUC5AC) and pyloric/Brunner’s gland-type mucin (MUC6), in which proliferating cells positive for MIB-1 (Ki-67) were scattered diffusely. Most of the hyperplastic Brunner’s glands were positive for MUC6, while cells toward the lumen in the superficial layer were positive for MUC5AC and MIB-1. This directional pattern of differentiation of Brunner’s glands has recently been demonstrated by our group in the histogenetic course of gastric metaplasia originating directly from Brunner’s glands. Therefore the present carcinoma is thought to have developed under induction of gastric-foveolar differentiation in a manner very similar to that of gastric metaplasia in hyperplastic Brunner’s glands.

**Keywords** Brunner’s glands · Duodenum · MUC gene · Hyperplasia · Gastric metaplasia

**Introduction**

Duodenal adenocarcinoma in the extra-ampullary region is rare, and usually consists of intestinal-type adenocarcinoma with tubular or villous adenomas akin to that of the colon. Adenocarcinomas very rarely arise in Brunner’s glands [4, 5, 8, 9, 16, 22, 23, 29], gastric metaplasia, or heterotopic gastric mucosa [3, 13, 19, 21]. Most Brunner’s gland tumors, so-called Brunner’s gland adenomas or brunnneriomas, are not true neoplasms but rather hyperplasia or hamartomas, which are composed of lobules of mature Brunner’s glands surrounded by bands of smooth muscle [18, 24, 29]. There have been only five well documented cases of carcinoma with neoplastic transformation of the underlying Brunner’s glands [5, 8, 9, 16, 29]. However, little is known about gastric-type differentiation in Brunner’s gland tumors. We have recently shown a histogenetic pathway of gastric metaplasia in close association with a reparative lineage of Brunner’s glands [12]. With special reference to MUC gene expression, this report documents an extremely rare case of adenocarcinoma that has findings relevant to the discussion of the differentiation, proliferation, and dysplastic progression of Brunner’s glands.

**Case report**

Clinical history, endoscopic, and biopsy findings

An 85-year-old woman was referred to our hospital for evaluation of Mirizzi syndrome with choledocholithiasis. Upper gastrointestinal endoscopy revealed a pedunculated and lobulated polyp on the opposite side of the papilla of Vater of the duodenal second portion (Fig. 1a). Invasive carcinoma was suspected by histological investigation of the biopsy specimens (Fig. 1b), and polypectomy was performed in March 1999. There were no signs of recurrence in August 2001.

Materials and methods

The tumor specimen (2.0×1.5×1.0 cm) was fixed in 10% formalin, sliced into three sections, and embedded in paraffin. Paraffin blocks were cut into serial sections for routine histology and im-
munohistochemical studies. In addition to hematoxylin and eosin staining, immunohistochemical staining was performed using the following monoclonal antibodies (MAbs): MUC2 (Ccp58; 1:100, Novocastra, UK); MUC5AC (CLH2; 1:100, Novocastra), MUC6 (CLH5; 1:100, Novocastra), CD10 (56C6; 1:50, Novocastra) and Ki-67 (MIB1; 1:100, Immunotech, France). More than ten distinct epithelial mucin genes (MUC1, MUC2, MUC3, MUC4, MUC5AC, MUC5B, MUC6, MUC7, MUC8, MUC11, MUC12, MUC13, and MUC16) have recently been identified [14, 26, 27, 28]. Among these, MUC5AC, MUC6, and MUC2 are specifically expressed in gastric-foveolar cells, pyloric gland cells, and intestinal goblet cells of the mature gastrointestinal tract, respectively [17]. MUC6 is also expressed in mucus neck cells of the stomach and Brunner’s gland cells [10]. MAb CD10 was used to detect the brush border of small intestinal absorptive cells [15] and MAb MIB-1 to detect proliferating cells. For immunohistochemistry the streptavidin-biotin method was performed using the Histofine-kit (Nichirei, Japan). Peroxidase binding sites were visualized using the diaminobenzidine method, and the sections were lightly counterstained with hematoxylin.

Histological findings

As the polypoid tumor consisted mostly of lobules of Brunner’s glands showing no cellular atypia, a diagnosis of Brunner’s gland hyperplasia was made. Cystically dilated glands were also noted. A severely dysplastic focus, 6 mm at the longest diameter, was discovered to be surrounded completely by the hyperplastic area (Fig. 2a). The dysplastic lesion consisted of atypical cuboidal to low columnar cells with clear cytoplasm resembling cells of Brunner’s glands. Not only prominent cellular and structural atypia but also focal invasion into the muscularis mucosae was noticed in this lesion (Fig. 2b), which was interpreted as an adenocarcinoma.

Fig. 1 a Endoscopic picture shows a pedunculated polyp with lobulation at the opposite side of the papilla of Vater of the second portion of the duodenum. b Biopsy section shows budding of glands and a trabecular pattern suggestive of invasion into the lamina propria, which is classified into “category 4.3: suspicion of invasive carcinoma” according to the Vienna classification of gastrointestinal neoplasia [20]

Fig. 2 a The tumor consists primarily of hyperplastic lobules of Brunner’s glands showing no cellular atypia. A severely dysplastic focus is seen to be adjacent to hyperplastic Brunner’s glands. b Detail of a, showing invasion into the muscularis mucosae with stromal reaction. Therefore this lesion is interpreted as adenocarcinoma.