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CASE REPORT

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‘Pyloric gland-type adenoma’ arising in heterotopic gastric mucosa of the duodenum, with dysplastic progression of the gastric type

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Abstract ‘Pyloric gland-type adenoma’ is a recently described and very rare entity. We report a case of a pedunculated polyp of the duodenal bulb showing the features of pyloric gland-type adenoma. Heterotopic gastric mucosa was found adjacent to the tumour. Immunohistochemically, the tumour cells at the surface of the polyp showed foveolar-type mucin (M1) while most other tumour cells showed deep gastric mucin (M2), displaying a pattern of differentiation similar to the normal gastric mucosa. The polyp also showed villous or papillary structures with disorganization of gastric differentiation and marked increase of proliferating in foci cells. This is the first case of pyloric gland-type adenoma found to arise in heterotopic gastric mucosa of the duodenum, showing dysplastic progression of the gastric type.

Key words Pyloric gland-type adenoma · Heterotopic gastric mucosa · Duodenum · Mucin · Histogenesis

Introduction

Typical gastric adenoma usually arises in association with intestinal metaplasia and displays an intestinal type of differentiation. It is also widely considered to be a lesion with premalignant potential for development of differentiated adenocarcinoma [5, 9, 14], the so-called intestinal-type carcinoma [13]. However, we and other authors have noticed that adenomas or dysplastic lesions of the stomach may also show the gastric type of differentiation [2, 8, 11, 24].

Heterotopic or metaplastic gastric mucosa occurs through the intestinal tract, and its occurrence in the duodenum has been well documented. Neoplastic transformation of heterotopic or metaplastic gastric mucosa of the duodenum is extremely rare. To our knowledge, two cases of adenomas and three cases of adenocarcinomas probably arising in such heterotopic or metaplastic foci have been reported [6, 17–19, 26].

This study documents the first case of duodenal adenoma arising in heterotopic gastric mucosa, which had histology identical to that of pyloric gland-type adenoma as described in the recent WHO classification of gastric tumours [24]. The cellular differentiation and dysplastic progression in this peculiar tumour are discussed.

Case report

A 67-year-old woman was referred to the hospital for evaluation of tarry stool. Upper gastrointestinal endoscopy revealed a duodenal polyp that produced stenosis of the duodenal bulb. Histological investigation of biopsy specimens did not make it possible to rule out malignancy. Therefore, partial resection of the duodenal bulb was performed. There was no clinical evidence of gastrointestinal polyposis.

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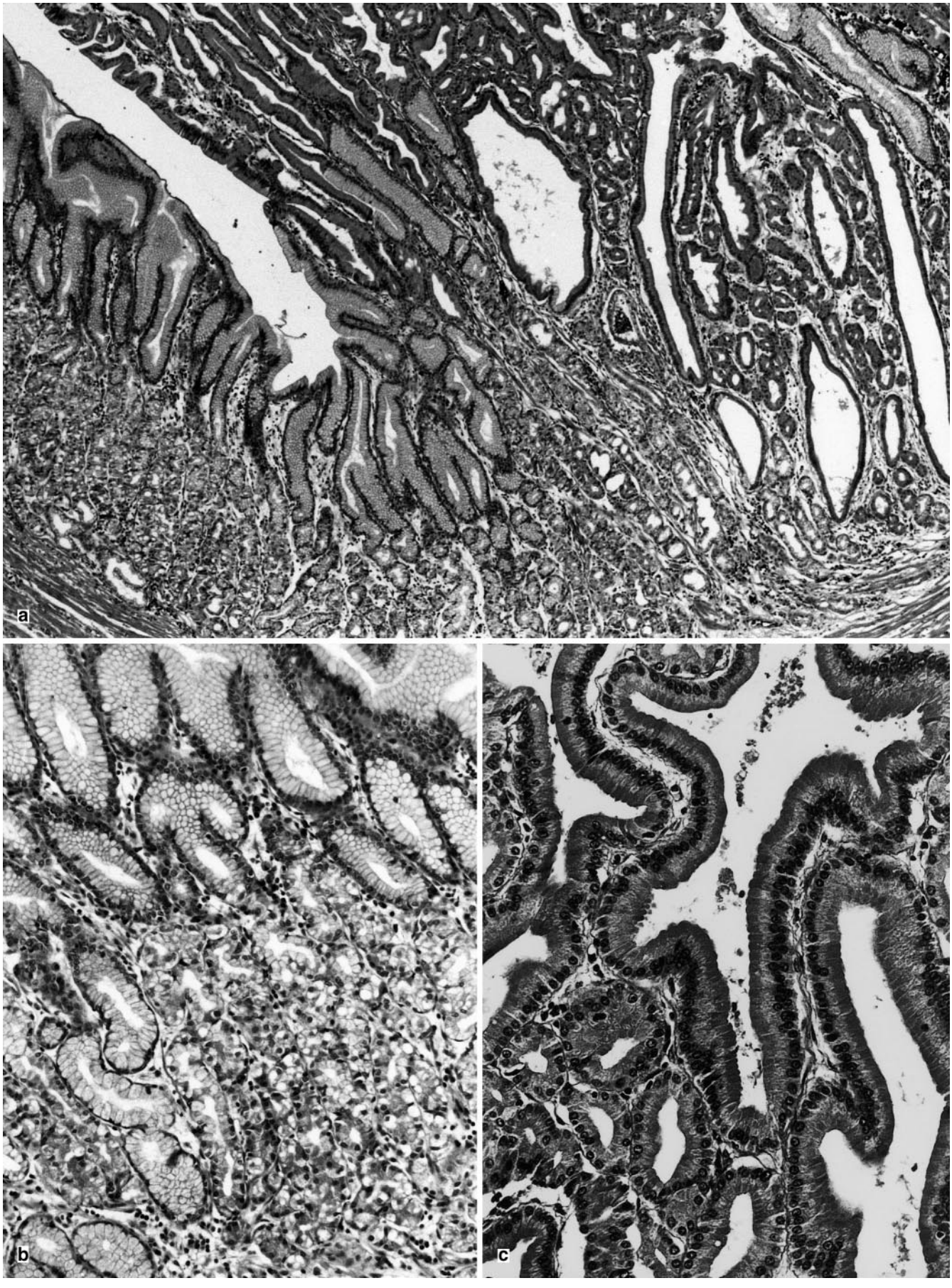
Fig. 1 a ‘Pyloric gland-type adenoma’ adjacent to heterotopic gastric mucosa. **b** Higher magnification of the heterotopic gastric mucosa. The mucosa is composed of organized fundic tissue with pseudopyloric metaplasia. **c** Higher magnification of pyloric gland-type adenoma. The tumour consists of narrow to dilated glands lined by cuboidal to columnar cells with eosinophilic cytoplasm ▶


a
b
c

Materials and methods

The specimen was fixed in 10% formalin. The tumour with surrounding normal duodenal wall was sliced into several sections and embedded in paraffin. Paraffin blocks were available for routine histology and immunohistochemical studies.

In immunohistochemistry, we employed monoclonal antibodies (MoAbs) against different mucin moieties, as defined by the classification of Bara et al. [1]: foveolar gastric mucin M1 (MoAb R3C4; 1:5) and deep gastric mucin M2 (MoAb 2B5; 1:5), which were produced in our laboratories. M1 recognizes only foveolar mucin and no other type of mucin in the mature gastrointestinal mucosa [3]. M2 stains mucous neck and pyloric gland cells of the gastric mucosa, and (pseudo)pyloric metaplasia in different parts of digestive organs [7, 12]. Furthermore, MoAb MIB-1 (DAKO; 1:100) against Ki-67 antigen was used with the aid of microwave to study proliferative activity of the tumour.

Pathological findings

In a formalin-fixed resected duodenum, a pedunculated polyp measuring 2.5×3.0×3.0 cm was found. Heterotopic gastric mucosa was found adjacent to and below the tumour. It consisted of organized fundic tissue of the stomach, although a few 'pseudopyloric glands' were found focally (Fig. 1a, b). The tumour consisted of narrow or cystically dilated glands. They were lined by cuboidal to columnar epithelial cells that contained clear or eosinophilic cytoplasm (Fig. 1a, c). The tumour cell nuclei were small and oval or round in shape, and sometimes contained small nucleoli. Mitotic figures were rare. These findings were identical to those described for 'pyloric gland-type adenoma' of the stomach in the most recent WHO classification [24]. The mucosa adjacent to the tumour was normal duodenal tissue composed of crypts and Brunner's glands, except for the focus of heterotopic gastric mucosa. Heterotopic pancreatic tissue was not found. In this tumour, villous or irregularly papillary structures were also observed, which was interpreted as severely dysplastic mucosa or intramucosal adenocarcinoma. The nuclei were slightly stratified and sometimes enlarged.

In the area of typical pyloric gland-type adenoma as shown in Fig. 1a and c, a kind of organoid growth of tumour cells was observed: that is, only superficial cells of the polyp were positive for foveolar mucin M1, while most of the lower adenomatous glands were positive for deep gastric mucin M2. These cells differentiated respectively to foveolar-type and pyloric gland-type cells (Fig. 2a, b). Tumour cells in the severely dysplastic area were also positive for M1 and/or M2, but the pattern of differentiation was deranged (Fig. 3a, b). Proliferating cells positive for MIB-1 were markedly increased in numbers in this dysplastic area, while occurring only rarely in other areas (Fig. 4a, b).

Discussion

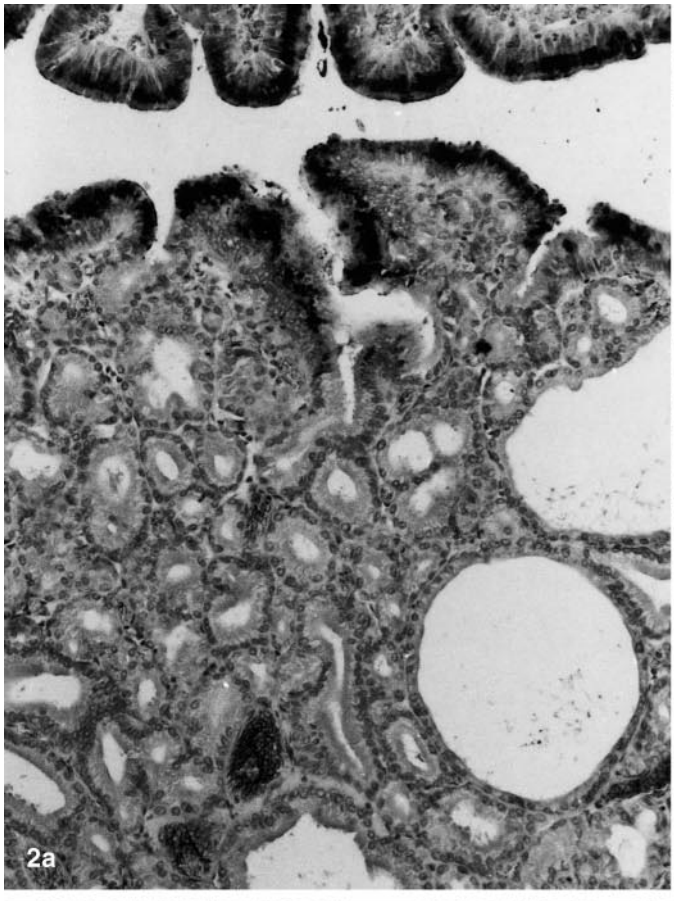
The tumour showed the histological and immunohistochemical features of pyloric gland-type adenoma. However, the present case should be distinguished from two types of benign epithelial tumours arising in the duodenum, both of which have been well documented. One is tubular or villous adenoma of conventional type, and the other is the tumour of Brunner's glands. Histologically, the tubular or villous adenoma is composed of glands of intestinal type and greatly elongated fronds lined by closely packed columnar epithelial cells that resemble those found in colonic adenomas [16]. It is considered to originate in proper duodenal mucosa and is also found in patients suffering from familial adenomatosis coli. Most Brunner's gland tumours are probably not true neoplasms but rather hyperplasia or hamartomas [21], although some glands are cystically dilated and some may show dysplastic changes [27]. Brunner's gland tumour is composed of lobules of mature Brunner's glands surrounded by bands of smooth muscle originating from the muscularis mucosae, and the tumour is covered by normal duodenal mucosa [16].

Although hyperplastic polyps of the gastric-foveolar type or fundic gland type are occasionally noted in the heterotopic gastric mucosa of the duodenum [15], only two previous reports of adenomas probably arising in gastric mucosa of the duodenum have been published [6, 17]. The polyp reported by Russin et al. [17] was composed of alternate areas of hyperplastic foveolar gastric glands and adenomatous glands. De Vita et al. [6]. found a duodenal polyp in a Billroth II resection specimen with neutral mucin- and lysozyme-containing cells. Because of these findings, they speculated that these tumours might have arisen in heterotopic gastric mucosa of the duodenum, although they could not find heterotopic gastric mucosa in the duodenal mucosa surrounding the tumour. In this connection, the term 'heterotopia' should be restricted to organized fundic tissue of the stomach as shown in Fig. 1a and b, and it should be distinguished from gastric (foveolar) metaplasia of the duodenum. Heterotopic gastric mucosa is presumed to be congenital and not associated with duodenal ulcer disease [20, 25].

The nature and biological behaviour of pyloric gland-type adenoma, which is akin to a similar lesion of the gallbladder [12, 23, 24], are unknown. Not only Fig. 1 (a, c) in the present case but also illustrations of this type of adenoma in the recent WHO classification of gastric tumours [24] might be thought to show tumours

Fig. 2a, b Immunohistochemical demonstration of gastric-type mucin in the area of typical pyloric gland-type adenoma. **a** Foveolar mucin M1 is seen in cells at the surface of polyp. **b** Deep gastric mucin M2 is seen in cells of most glands ▶

Fig. 3a, b Immunohistochemical demonstration of gastric-type mucin in the severely dysplastic area or intramucosal adenocarcinoma. **a** Foveolar mucin M1 and/or **b** deep gastric mucin M2 expression is randomly seen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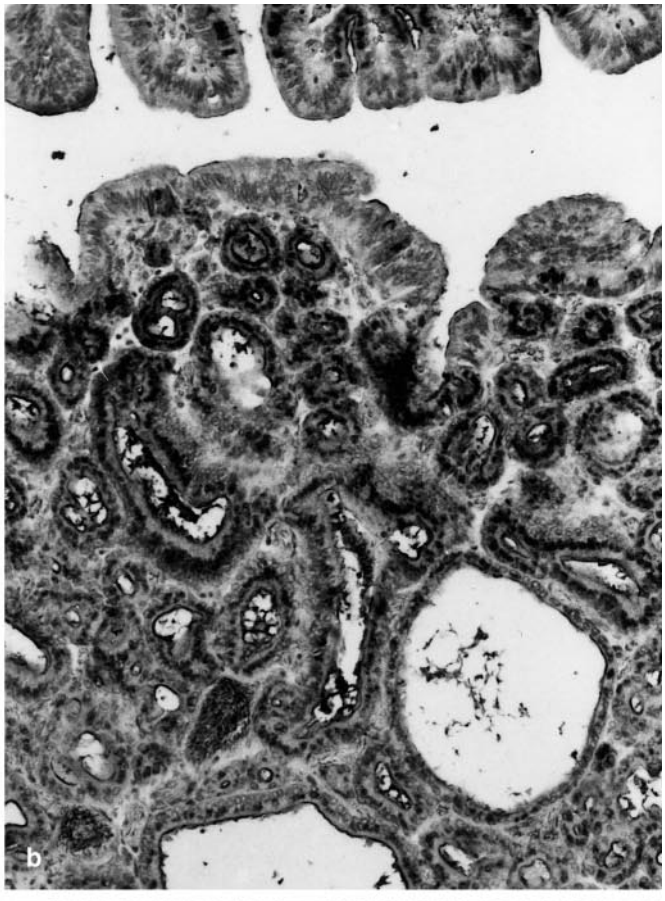
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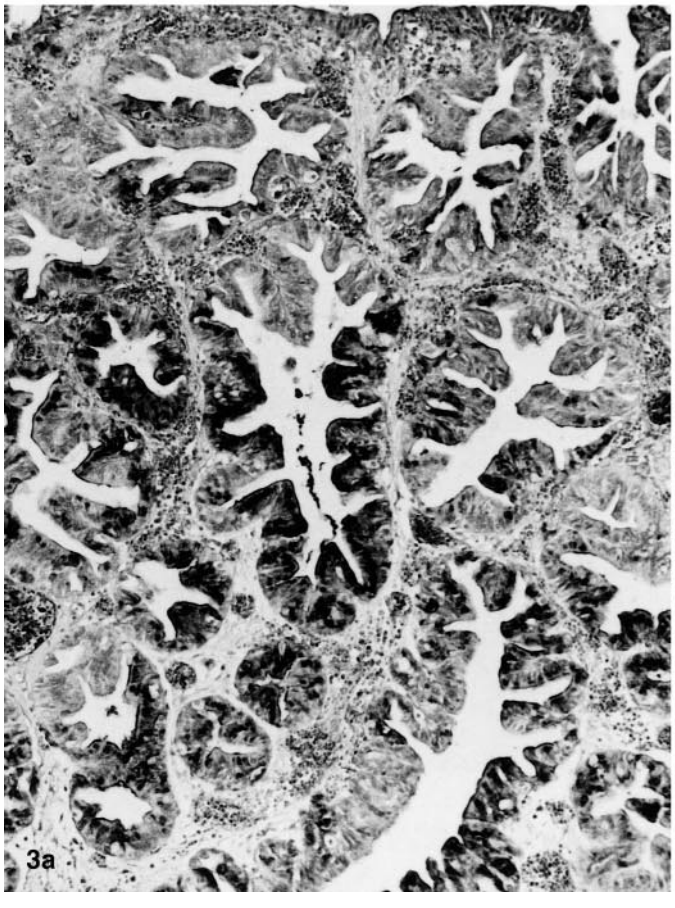
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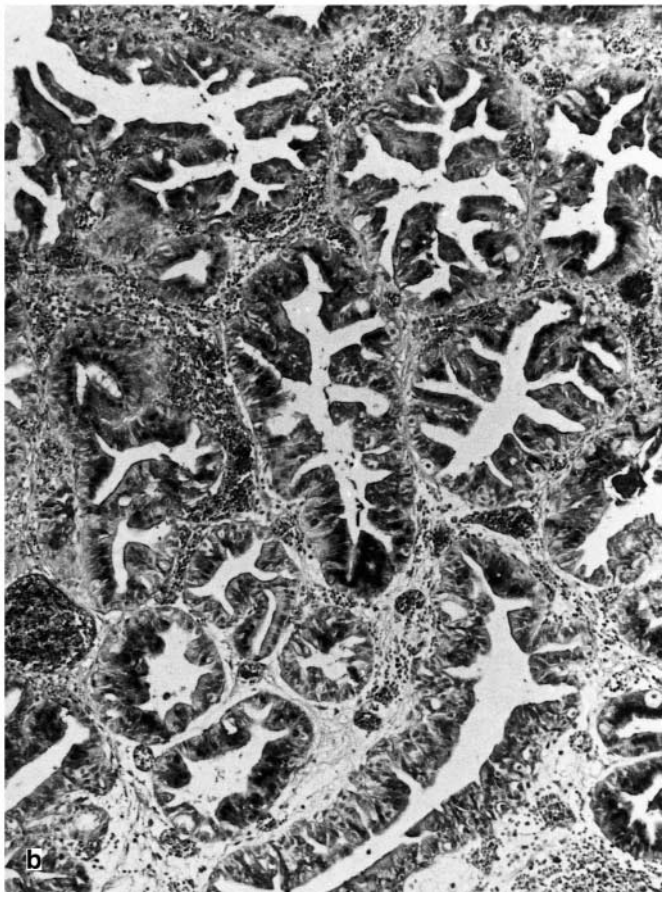
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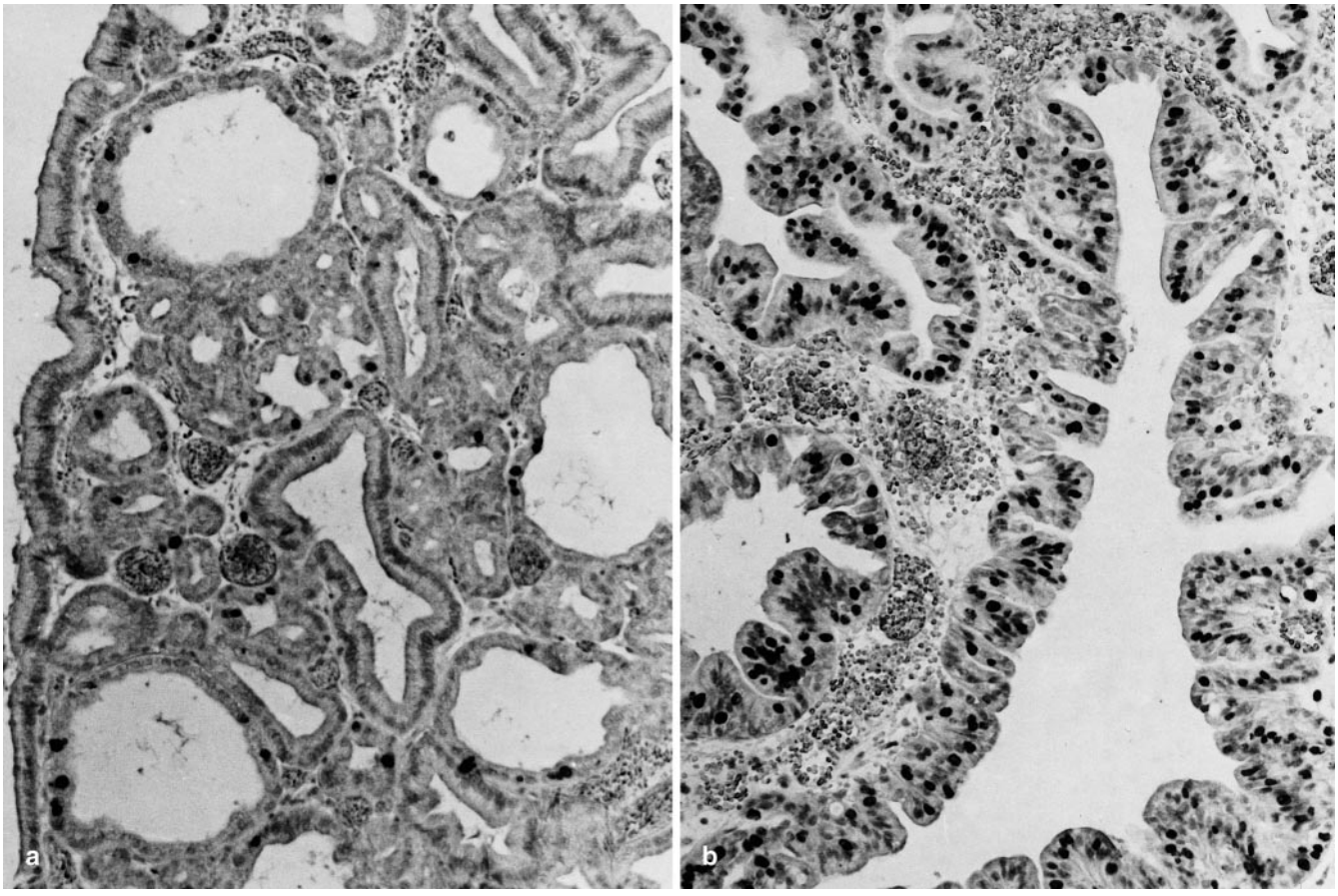

Fig. 4 Proliferating cells positive for MIB-1 are sporadically scattered in the area of typical pyloric gland-type adenoma (**a**), but they markedly increase in the severely dysplastic area or intramucosal adenocarcinoma (**b**)

not of adenomatous but of hyperplastic or hamartomatous origin, because of the minimal degree of cytological atypia. The minimal proliferative activity also seems to support this hypothesis of hyperplasia or hamartoma. The Ki-67-positive index in 'pyloric gland-type adenoma' of the gallbladder has been reported to be very low, in contrast to intestinal-type adenomas and intramucosal carcinomas (4.9±0.5%, 13.6±3.5% and 36.6±5.6%, respectively) [23]. A kind of organoid growth similar to the normal gastric mucosa also appears to support this hypothesis. However, such an organoid growth of the gastric type is often observed in both diffuse and intestinal-type carcinomas of the stomach [10, 22]. A disease entity of pyloric gland-type adenoma should be studied further.

Histogenetically, the present tumour may have originated from a committed stem cell of the heterotopic fundic gland mucosa with 'pseudopyloric glands', since the direction of differentiation to foveolar- and pyloric gland-type cells was mainly preserved in the tumour. To clarify the nature and histogenesis of this rare tumour and its relationship with morphologically similar tumours arising in different parts of digestive organs, requires examination by immunohistochemistry for pepsinogen I and II. This will indicate whether these pseudopyloric glands and tumour cells are of the mucous neck cell (transitional cell into chief cell) or the true pyloric gland cell type [4]. In gastric hyperplastic polyps of the foveolar type, in which complete-type intestinal metaplasia is rarely seen, most dysplasias and adenocarcinomas show the gastric phenotype, indicating dysplastic progression of the 'gastric' type [8, 11]. It is very likely in the present tumour that the direction of differentiation to foveolar- and pyloric gland-type cells was disoriented, with dysplastic progression of the gastric type, in which proliferative activity increased.

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