

Serrated Adenomas of the Cardia

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Abstract. Adenomas of the stomach are histologically classified into tubular and villous adenomas, mixed (tubulovillous) and papillary phenotypes being also recognized. They are localized in the antrum and the body. In a previous work we reported a case of serrated adenoma of the cardia having, at the time of diagnosis, an invasive growth. In this communication we report five newly identified cases of serrated adenomas of the cardia. The five neoplasias were characterized by serrated indentations furnished with dysplastic epithelium. Five out of six serrated adenomas – including the previously reported case – had, in addition, an invasive or a suspected invasive carcinoma. The latter case had at the time of diagnosis lung and liver metastasis. Metastases were also demonstrated in two additional cases. In similarity with other adenoma phenotypes, serrated adenomas of the cardia have a propensity to evolve into invasive carcinoma, a phenomenon that appears to be size-dependent.

Back in 1923, Konjetzny (1) reported the occurrence of polyps in the gastric mucosa. In 1926, Borrmann (2) described different types of gastric polyps and, three years later, Stewart (3) found mucosal aberrations in 47 gastric polyps that he denominated "adenomas". Gastric adenomas have attracted much interest due to the fact that they may antedate gastric carcinomas (4-23). Despite gastric adenomas being infrequent lesions, Hirota *et al.* (21) estimated that 5% of all early gastric carcinomas evolve from an adenoma.

Gastric adenomas are found more frequently in the distal and the middle portion than in the proximal part of the stomach. Several histological classifications of gastric adenomas have been proposed (11,16,18,22,23). The generally accepted microscopic structures described for gastric

adenomas are tubular or villous although mixed (tubulovillous) and papillary phenotypes have been recognized.

Recently, we reported the first case of serrated neoplasm of the stomach (cardia) in the literature (24). Its histological features mimicked those of serrated adenomas in the colon (25). Since then, five additional cases of gastric serrated adenoma in the cardia have been found at this department, four in the last two years. The fifth case – included in this report – was found while reviewing proximal gastric resections performed at this hospital (14).

The purpose of this report is to describe the clinical history and the microscopic characteristics of the five above-mentioned gastric serrated adenomas.

Materials and Methods

Clinical data. The clinical data (including follow-up) for the 5 cases to be reported below is condensed in Table I.

Histological findings

Case 1. The surgical specimen measured 14 cm in length and consisted of the distal esophagus, the cardia and the proximal fundic region. In the gastric cardia, a 5 cm in diameter exophytic tumour was found abutting the distal esophagus. Part of its luminal border was eroded and covered with fibrin. Following fixation a total of 52 blocks were obtained. The histological examination revealed a protruding neoplastic lesion composed of elongated fronds with lateral crenate, saw-tooth-like notches due to scalloped epithelial indentations (Figure 1). The nuclei covering the serrated glands were stratified, with irregular chromatin deposits. Atypical mitotic figures were present.

Ki67 (MIB1, Dako, Denmark) showed intense DNA proliferation in the dysplastic cells covering the indented fronds (Figure 2). The invasive carcinomatous glands also showed serrated structures (Figure 1). Four months later, a pelvic metastasis was detected at X-ray. A needle-biopsy revealed metastasis from an adenocarcinoma. The pelvic metastasis was treated with radiation and he received

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Table I. Clinical and follow-up data in 5 patients having a serrated neoplasia in the cardia.

	Age	Sex	Clinical data	Radiology	Endoscopy	Surgery	Follow-up
Case 1	74	M	Dysphagia (last 3 months), black faeces	Tumour in the cardia	Tumour in the cardia	Proximal esophago-gastrectomy	Pelvic metastases. Died 5 months later
Case 2	72	M	Upper abdominal pain (last 3 months)	CT: Tumour in the cardia, lymph nodes, liver and lungs	Tumour in the cardia	---	Chemotherapy
Case 3	71	M	Upper abdominal pain (last 2 months)	Tumour in the cardia	Tumour in the cardia	Proximal esophago-gastrectomy	Recurrence at esophageal-gastric anastomosis. Chemotherapy
Case 4	79	M	GI bleeding	---	Polypoid lesion in the cardia	---	Chemotherapy 8 months later: no tumour regression
Case 5	66	F	Upper abdominal pain (last 3 months)	---	Polypoid lesion in the cardia	---	New endoscopy 3 months later: cardiac arrest (no biopsies taken)

cortisone. The patient died 5 months after surgery. No post-mortem examination was performed.

Case 2. Biopsies taken from the tumour in the cardia (15 cm in diameter) revealed a serrated adenoma with high-grade dysplasia and suspected invasion. CT revealed lymph nodes, lung and liver metastasis. Because of the poor condition of the patient, no further studies were done concerning the cardia tumour. He is being treated with chemotherapy.

Case 3. The tumour was found in the cardia extending to the upper part of the lesser curvature. It measured 9 cm in diameter. Biopsies from the tumour showed a serrated adenoma with high-grade dysplasia. Ki67 showed high cellular proliferation. The gastrectomy specimen revealed a tumour built of serrated neoplastic glands, showing invasive growth. In other areas, a moderately-differentiated adenocarcinoma of intestinal type infiltrating the entire gastric wall was found. Ten of 11 regional lymph nodes had metastases. Three months later he developed a recurrence at the esophageal anastomosis, for which he is receiving chemotherapy.

Case 4. Biopsies from the tumor in the cardia (1.8 cm in diameter) were reported as serrated adenoma with high-grade dysplasia and invasive growth. The patient received chemotherapy. Biopsies taken 2 months and 8 months later, respectively, showed no tumour regression.

Case 5. Biopsies from the tumour in the cardia (1.6 cm. in diameter) showed a serrated adenoma with low-grade dysplasia. Ki67 showed basal, mid-glandular and near-the-surface proliferation in the cells that covered the indented fronds. No invasive carcinoma could be demonstrated. At a new gastroscopy performed in March 2003, the patient developed a cardiac arrest and respiratory insufficiency. Due to the poor condition of the patient, no biopsy was taken. After resuscitation she was treated at the intensive care department and discharged two weeks later with symptoms of respiratory insufficiency.

Discussion

In a previous work, we reported one case of serrated adenoma of the cardia (24). Since then, five additional cases have been found at this department. Because of its histological features and cell proliferative characteristics (*i.e.* showing cell proliferation initially at the base and mid portion of the crypts), serrated adenomas of the cardia mimic serrated adenomas of the colorectal mucosa (25).

Except for these six cases, no other case of serrated adenoma of the stomach has been reported in the literature (4-23), though it is conceivable that, in other series, similar cases have been classified as papillar adenomas. It is possible that this type of lesion is of rare occurrence in the gastric mucosa although, in a lapse of two years, we found four additional cases at routine



Figure 1. Low power view of a section from the surgical specimen showing a protruding adenoma with serrated indentations on top and invasive growth with serrated glands at the lower part (gastric cardia, H&E 2.5X).

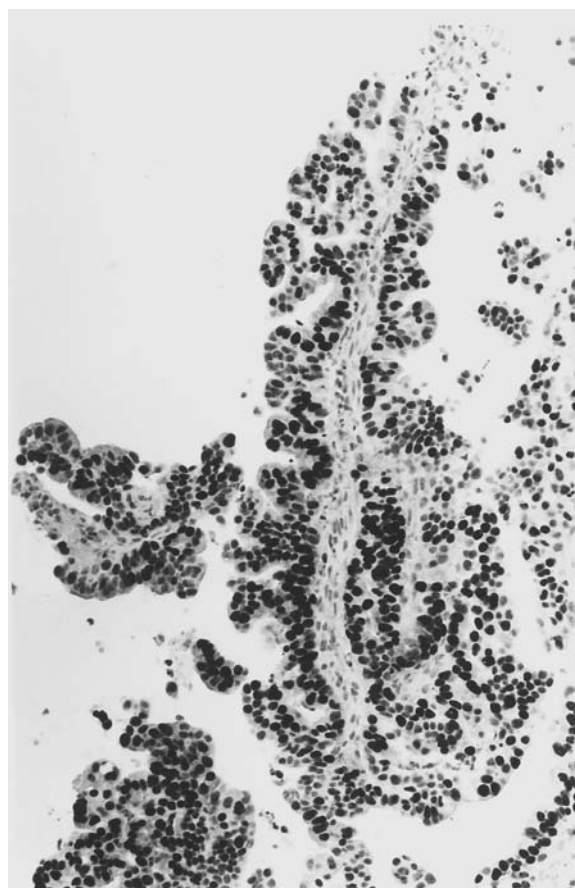


Figure 2. Detail from Figure 1 (top) showing elongated fronds bearing lateral serrated notches due to scalloped epithelial indentations with high-grade dysplasia. Note intense cell proliferation (gastric cardia, MIB1 20.5X).

gastric biopsies and the fifth case in this report was found while reviewing a series of proximal gastrectomy specimens (14).

The localization of serrated adenomas of the stomach appears to differ from that reported in tubular, villous, mixed (tubulo-villous) or papillary adenomas. Of the 167 tubular, villous or papillary gastric adenomas reported by Kozuka (16), the majority (97.6%) were localised in the antral region and corpus. On the other hand, the six serrated adenomas found at this department, (including the previous case (24)) were localised in the cardia.

Nakamura (26) studied the prevalence of cancerous changes in 2730 gastric polyps. He found cancerous changes in 8.7% of 1819 sessile elevated gastric adenomas, in 15.4% of 911 adenomas resembling colorectal adenomas and in 1.3% of 5174 hyperplastic polyps. Nakamura's report (26) summarized the opinion of 83 Japanese pathologists. We found in five of six serrated adenomas of the cardia (including our previous case (24)) that invasive or suspected

invasive carcinoma was already present at the time of first diagnoses. Thus, gastric serrated adenomas behaved in this small series of cases in an aggressive fashion.

Several series have shown that most gastric adenomas that contain an invasive carcinoma measure more than 2 cm in diameter. Recently, Vieth *et al.* (27) found, in 77 pyloric gland adenomas measuring 1.6 cm in diameter that 30% had, in addition, a well-differentiated adenocarcinoma. In the present work, two of the five adenomas were larger than 2 cm in diameter, while the previously reported case measured 4 cm in diameter. Thus, serrated adenomas of the cardia seem to have a similar proclivity to develop a malignant growth as other gastric adenoma phenotypes (4-23,27). That proclivity may be size-dependent.

In the colonic mucosa serrated adenomas may be generated through a different molecular pathway than other adenoma phenotypes (28). It remains unknown whether serrated adenomas of the cardia also evolve through an independent genetic trail.

In conclusion, serrated adenomas of the cardia appear to have distinct morphological and cell-proliferative features, at variance with other histological adenoma phenotypes (tubular, villous, mixed or papillary) reported in the literature. In similarity with other adenoma phenotypes, serrated adenomas of the cardia seem to have a propensity to evolve into invasive carcinoma, a phenomenon that appears to be size-dependent. Increased awareness of the existence of serrated neoplasm in the cardia may result in the identification of similar cases at other hospitals.

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