Traditional Serrated Adenoma in a Patient with Barrett's Esophagus

CARLOS A. RUBIO[1], KYOSUKE TANAKA[2] and RAGNAR BEFRITS[2]

Departments of [1]Pathology, and [2]Gastroenterology, Karolinska Institute and University Hospital, Stockholm, Sweden

Abstract. *Background: Protruding adenomas in the Barrett's mucosa (BM) are very rare. Out of the 22 adenomas evolving in BM recorded in the literature, 21 were tubular and the remaining one, villous. Case Report: We describe a case of traditional serrated adenoma (TSA) in BM. The TSA displayed hyperplastic fronds with saw-like indentations lined with low-grade dysplasia. In addition, dysplastic cells and atypical mitoses reaching the luminal epithelial border (high-grade dysplasia) were observed in the lower part of the TSA. Cell proliferation (Ki67) mostly occurred at the bottom of the dysplastic serrations. In non-dysplastic subjacent glands with intestinal metaplasia, goblet cells contained sialomucins (alcian blue pH 2.5) and mucopolysaccharides (periodic acid Schiff). The TSA was found at the border of an invasive adenocarcinoma. Conclusion: The review of the literature indicates that this is first case of TSA in the BM ever reported. It remains unclear as to whether the TSA was an independent non-invasive neoplastic bystander, or an integral pre-cancerous remnant of the adenocarcinoma domain.*

The vast majority of the dysplasias evolving in the Barrett's mucosa (BM) retain the flat (*i.e.* non-protuding) outline of the normal mucosa (1). Protruding BM dysplasias, also called adenomas, are very rare. In 1999, Thurberg, Duray and Odze (2) described five cases of adenomas in BM, and retrieved 12 additional cases from the literature. Since then, five new cases of adenomas in BM have been reported in humans (3-7) and one in a dog (8). Thus, 22 adenomas evolving in BM in humans are on record: 21 were tubular adenomas (2-6) and the remaining one, a villous adenoma (7).

Correspondence to: C.A. Rubio, MD, Ph.D., Gastrointestinal and Liver Pathology Research Laboratory, Department of Pathology, Karolinska Institute and University Hospital, 17176, Stockholm, Sweden. Fax: +46 851774524, e-mail: Carlos.Rubio@ki.se

Key Words: Barrett's mucosa, serrated adenoma, adenocarcinoma.

Recently, we detected an adenocarcinoma in a patient with Barrett's esophagus. A biopsy obtained from a polypoid lesion, found at the margin of the tumour, revealed a traditional serrated adenoma (TSA).

The purpose of this communication is to report and illustrate this unique histological finding.

Case Report

Clinical data. A 68-year-old male with diabetes type-2, hyperlipidaemia, renal insufficiency requiring haemodialysis, hypertension, and myocardial infarction (2006), sought consultation in August 2012, for increasing dysphagia of three months' duration.

An endoscopic examination revealed a 26 cm-long Barrett's segment. Six cm proximal to the Z-line, a protruding tumor was found, measuring 3 cm in diameter, engaging approximately 75% of the esophageal circumference. On the tumour margin, a protruding lesion 4 mm in diameter was detected (Figure 1). Endosonography suggested an infiltrative carcinoma without signs of distant tumour. Because of severe co-morbidity, the patient was considered not suitable for primary surgery. At the time of writing this report, the patient is being treated with brachytherapy.

Histological findings. Biopsies obtained from the tumour revealed a moderately-differentiated adenocarcinoma. A biopsy taken from the protruding lesion at the tumor margin showed the presence of a TSA without invasive growth (Figure 2). This lesion exhibited hyperplastic fronds with saw-like indentations lined with dysplastic epithelium. Low-grade dysplasia was present in the upper part of the TSA (Figure 2). Other areas contained atypical mitotic figures (9) (Figure 3). The lower part of the TSA exhibited dysplastic cells and mitotic figures reaching the luminal border of the epithelium (Figure 4); these histological parameters were consistent with high-grade dysplasia.

Ki-67 immunostaining substantiated the identity of the non-invasive traditional serrated neoplasia, inasmuch as cell

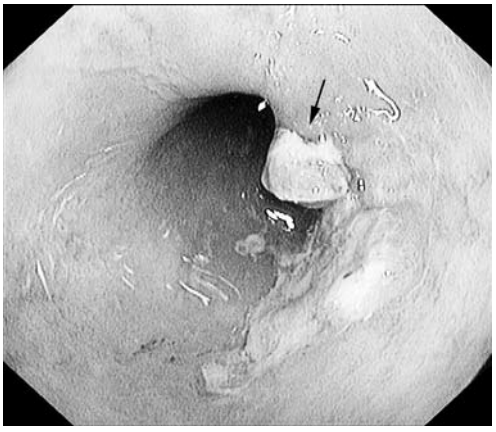

Figure 1. *Endoscopic view of a protruding lesion (arrow), at the margin of an irregular tumor with diffuse borders in a patient with Barrett's esophagus. The arrowed-protruding lesion was reported at histological examination as traditional serrated adenoma.*

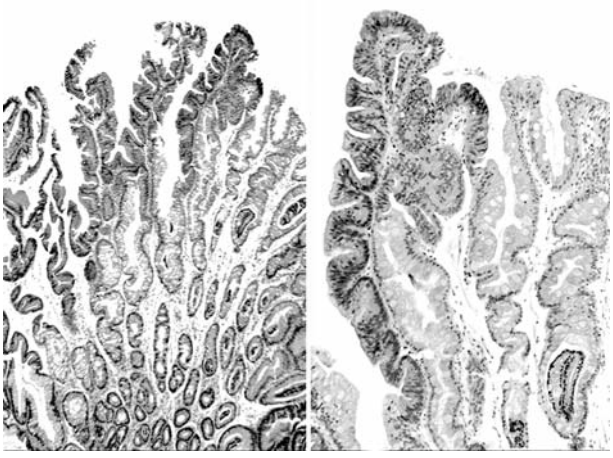

Figure 2. *Left panel: Low power view of the traditional serrated adenoma (H&E, ×4). Right panel: Detailed view of the serrated epithelium with low-grade dysplasia (H&E, ×10).*

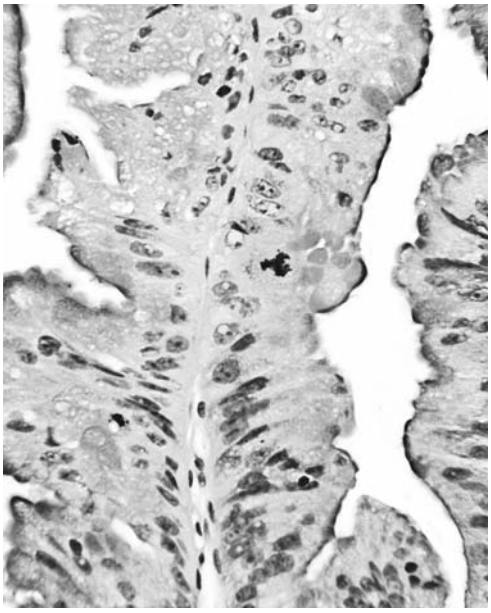

Figure 3. *Traditional serrated adenoma, with a tripolar, atypical mitosis (periodic acid Schiff stain, ×40).*

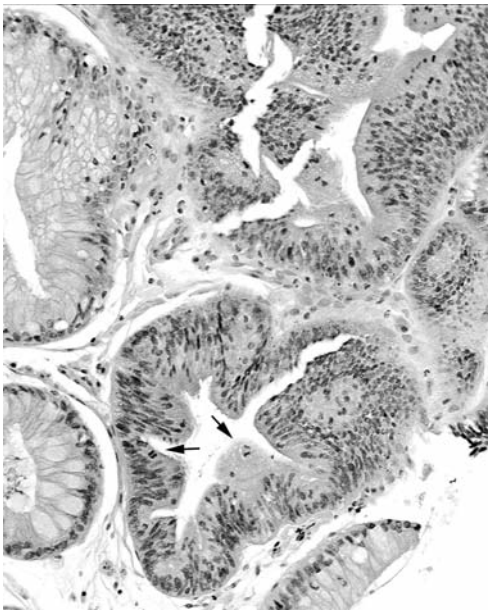

Figure 4. *Base of traditional serrated adenoma. Note high-grade dysplasia with dysplastic cells and mitotic figures (arrows) reaching the luminal border of the epithelium (H&E ×20).*

proliferation mostly occurred at the bottom of the dysplastic foveoli (10) (Figure 5).

In the subjacent non-dysplastic glands with intestinal metaplasia, the goblet cells contained mucopolysaccharides (periodic acid Schiff), and sialomucins (alcian blue pH 2.5).

Discussion

The review of the literature indicates that out of 22 adenomas evolving in BM, 21 were tubular adenomas (2-6) and the remaining one, a villous adenoma (7). Hence, ours appears to be the first case of TSA in BM in the literature.

We previously found TSA in other organs of the digestive tract: in the stomach (11), in the duodenum (12), in the pancreas (13), in the appendix (14), and in the colon and rectum, with and without ulcerative colitis (15-18).

Years ago, Vogeltein *et al.* (19) reported a series of escalating molecular cytological aberrations evolving in

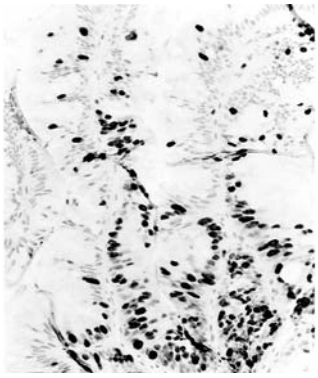

Figure 5. *Traditional serrated adenoma, showing cell proliferation mainly at the base of the lesion (Ki-67, ×10).*

colorectal tubular and villous adenomas, ranging from low-grade dysplasia to high-grade dysplasia and to invasive adenocarcinoma. TSAs were not included. In previous work, we found loss of heterozygosity (LOH) on 18q in colorectal TSA (20); this finding suggested a different genetic pathway between colorectal TSA on the one hand and colorectal tubular and villous adenomas on the other. The possibility that the same molecular pathway applied for the TSA of BM described here could not be explored.

In sum, the first case of TSA found at the border of an adenocarcinoma in a patient with Barrett's esophagus is presented. It remains unclear as to whether the TSA was an independent non-invasive bystander neoplastic lesion, or an integral pre-cancerous remnant of the adenocarcinoma domain.

References

1 Nelsen EM, Hawes RH and Lyer PG: Diagnosis and management of Barrett's esophagus. Surg Clin North Am *92*: 1135-1154, 2012.

2 Thurberg BL, Duray PH and Odze RD: Polypoid dysplasia in Barrett's esophagus: A clinicopathologic, immunohistochemical, and molecular study of five cases. Hum Pathol *30*: 745-752, 1999.

3 Wolfsen HC: Polypoid Barrett's high-grade dysplasia in a patient with familial adenomatous polyposis: A unique association. Endoscopy *37*: 280-282, 2005.

4 Kushima R, Vieth M, Mukaisho K, Sakai R, Okabe H, Hattori T, Neuhaus H, Borchard F and Stolte M: Pyloric gland adenoma arising in Barrett's esophagus with mucin immunohistochemical and molecular cytogenetic evaluation. Virchows Arch *446*: 537-541, 2005.

5 Ahlawat SK and Ozdemirli M: Polypoid dysplasia in Barrett's esophagus: Case report and qualitative systematic review of the literature. Acta Gastroenterol Belg *75*: 49-54, 2012.

6 Lindboe CF, Matre J and Nesland JM: Adenoma of the esophagus with intracytoplasmic mucoid bodies. APMIS 112: 29-33, 2004.

7 Wong WM, Shek TW, Chan CK and Kai K: Images of interest. Gastrointestinal: Villous adenoma of the esophagus. J Gastroenterol Hepatol *19*: 1213-1214, 2004.

8 Gibson CJ, Parry NM, Jakowski RM and Cooper J: Adenomatous polyp with intestinal metaplasia of the esophagus (Barrett esophagus) in a dog. Vet Pathol *47*: 116-119, 2010.

9 Rubio CA, Kato Y and Kitagawa T: Frequency of atypical mitosis in intestinal metaplasia of the gastric mucosa in Japanese patients. Jpn J Cancer Res *85*: 284-289, 1994.

10 Rubio CA and Rodensjo M: Flat serrated adenomas and flat tubular adenomas of the colorectal mucosa: Differences in the pattern of cell proliferation. Jpn J Cancer Res *186*: 756-760, 1995.

11 Rubio CA, Petersson F, Höög A, Jónasson JG, Nesi G, Chandanos E and Lindblad M: Further studies on serrated neoplasias of the cardia: A review and case report. Anticancer Res *27*: 4431-4434, 2007.

12 Rubio CA: Serrated adenoma of the duodenum. J Clin Pathol *57*: 1219-1221, 2004.

13 Rubio CA, Grimelius L, Von Sivers K and Höög A: Intraductal serrated adenoma of the pancreas. A case report. Anticancer Res *25*: 3099-3102, 2005.

14 Rubio CA: Serrated adenomas of the appendix. J Clin Pathol *57*: 946-949, 2004.

15 Rubio CA, Kato Y, Hirota T and Muto T: Flat serrated adenomas of the colorectal mucosa in Japanese patients. In Vivo *10*: 339-343, 1996.

16 Rubio CA, Nesi G, Messerini L and Zampi G: Serrated and microtubular colorectal adenomas in Italian patients. A 5-year survey. Anticancer Res *25*: 1353-1359, 2005.

17 Rubio CA, Kristjansdottir S, Thodleifsson B, Olafsdóttir E and Jonasson JG: The frequency of advanced adenoma in consulting patients: A nationwide survey in Iceland (2003-2006). Colorectal Dis *14*: 595-602, 2012.

18 Rubio CA: Serrated neoplasias and *de novo* carcinomas in ulcerative colitis: A histological study in colectomy specimens. J Gastroenterol Hepatol *22*: 1024-1031, 2007.

19 Vogelstein B, Fearon ER, Hamilton SR, Kern SE, Preisinger AC, Leppert M, Nakamura Y, White R, Smits AM and Bos JL: Genetic alterations during colorectal tumor development. N Engl J Med *319*: 525-532, 1988.

20 Yashiro M, Laghi L, Saito K, Carethers JM, Slezak P, Rubio CA, Hirakawa K, Boland CR: Serrated adenomas have a pattern of genetic alterations that distinguishes them from other colorectal polyps. Cancer Epidemiol Biomarkers Prev *14*: 2253-2256, 2005.

Received February 12, 2013
Revised March 18, 2013
Accepted March 19, 2013