**Name of journal: World Journal of Gastrointestinal Endoscopy**

**ESPS Manuscript NO: 2382**

**Columns:** **CASE REPORT**

Serrated adenoma of the stomach: Case report and literature review

**Rubio CA *et al*.** Gastric serrated adenoma

Carlos A Rubio, Jan Björk

**Carlos A Rubio**, Gastrointestinal and Liver Pathology Research Laboratory, Department of Pathology, Karolinska Institute and University Hospital, Stockholm, 17176, Sweden

**Jan Björk**, Department of Gastroenterology, Karolinska University Hospital, Stockholm, 17176, Sweden

**Author contributions**: Rubio CA performed the pathological examination, designed and wrote the paper; Björk J was the attending doctor for the patient, provided the clinical data and the endoscopic illustration; Both authors critically revised the draft and approved the final version to be published.

**Correspondence to: Dr. Carlos A Rubio**, Gastrointestinal and Liver Pathology Research Laboratory, Department of Pathology, Karolinska Institute and University Hospital, Hälsovägen, Flemingsberg, 17176 Stockholm, Sweden. carlos.rubio@ki.se

**Telephone**: +46-8-51774527 **Fax:** +46-8-51774524

**Received:** February 18, 2013 **Revised:** April 9, 2013

**Accepted:** April 17, 2013

**Published online:**

**Abstract**

Gastric serrated adenomas are histologically characterized by protruding glands with lateral saw tooth-like indentations lined with stratified dysplastic cells containing abundant eosinophilic cytoplasm. Since the first case of gastric serrated adenoma foundin 2001,18 additional cases have been reported. Gastric serrated adenomas have a particular proclivity to progress to invasive carcinoma; 75% or 15 of the 20 cases now in record -including the present one - exhibited invasive carcinoma. The 20th case of gastric serrated adenoma reported here differs from the preceding ones in as much as it evolved in a patient with Lynch syndrome, implying that this adenoma phenotype may develop not only sporadically but also in patients with hereditary traits.

© 2013 Baishideng. All rights reserved

**Key words:** Gastric; Serrated; Neoplasia; Lynch syndrome

**Core tip:** Gastric serrated adenomas have a particular proclivity to progress to invasive carcinoma; 75% or 15% of the 20 cases that are now in record - including the present one - exhibited invasive carcinoma.

Carlos A Rubio, Jan Björk. Serrated adenoma of the stomach: Case report and literature review.

Available from: URL:

DOI:

**INTRODUCTION**

Ninety years ago Konjetzny[1] described mucosal polyps in gastric specimens. Six years later Stewart[2] found among 11000 necropsies, 47 gastric polypoid lesions with mucosal aberrations that he called adenomas. Since then, much attention has been centred on gastric adenomas due to their propensity to evolve into invasive carcinoma[3-11].

 Throughout the years several classifications of gastric polyps have been proposed[12-15]. Based on the endoscopic appearance, endoscopists have classified gastric polyps (adenomas being a histologic diagnosis) as flat[16] (also called non-polypoid or non-protruding) and polypoid[11] (also called protruding). Non-protruding polyps that appear thinner than the surrounding mucosa are called, depressed lesions[17]. This endoscopic classification was subsequently confirmed at the histological level[18]. Based on the gross appearance, Goldstein and Lewin[19] classified gastric polyps into flat topped, villiform, and pedunculated and Ming and Goldman[12] into flat and papillary. Based on their histological configuration, gastric polyps were classified by Elster[14] into focal foveolar hyperplasia, hyperplasiogenic polyps, tubular and villous adenomas, and by Appelman[20] into non-neoplastic (focal foveolar hyperplasia and hyperplastic polyps), non-neoplastic possibly hamartomatous (Peutz-Jehgers-type polyps), and neoplastic adenomas (with or without invasive carcinoma). Nakamura[7] grouped gastric polyps into types I and II (hyperplastic polyps), and types III and IV (adenomas), and Kozuka[10] grouped them into common type (hyperplastic, adenomatous, and carcinomatous polyps), special-type hamartoma (Peutz-Jehgers polyps, juvenile polyps, polyps in Cronkhite-Canada syndrome, and fundic gland cyst polyps), polypoid lesions (inflammatory polyps and polypoid carcinoma), and polyps resulting from a submucosal mass.

 In 2001 we reported a novel histologic phenotype of gastric adenoma characterized by protruding glands with lateral saw tooth-like notches due to scalloped epithelial indentations[21]. The serrated elongations were lined with stratified dysplastic cells containing abundant eosinophilic cytoplasm; it was called gastric serrated adenoma since it mimicked other serrated adenomas evolving in the colon[22] the appendix[23], the duodenum[24], the pancreatic duct[25] and the Barretts's esophagus[26]. Remarkably, this adenoma phenotype was not included in any of the aforementioned classifications of gastric polyps[11,18,20-22]. One possible explanation could be that gastric serrated adenomas were classified together with gastric villous adenomas. Another possible explanation could be that this type of lesion is very rare in the stomach. In this context, it should be mentioned that no case of serrated adenoma was recorded in a survey of 67 consecutive gastric adenomas[18], nor in larger series of gastric adenomas in the literature[5,6,10-14].

 Subsequently, we reported six additional cases of gastric serrated adenoma[27,28]. More recently, cases with gastric serrated adenomas were reported from such disparate countries as Tunisia[29], Japan[30], Turkey[31] and Korea[32].

 The purpose of the present communication is to report another case of gastric serrated adenoma, this time occurring in a patient with Lynch syndrome, an [autosomal dominant](http://en.wikipedia.org/wiki/Autosomal_dominant) genetic condition with an increased risk to develop cancer in various organs, including the stomach.

**CASE REPORT**

The patient is a 57 year-old male with confirmed *MSH2* mutation Lynch syndrome. His mother was treated for endometrial cancer and an uncle for colorectal cancer. In 1995 the patient was operated for cancer in the right colon. In 2007, a second colon cancer was found at surveillance colonoscopy, this time in the transverse colon. A total colectomy with ileo-rectal anastomosis was performed. In 2009 he was operated for a metastasis in the small bowel. Histology revealed a metastasis from colon cancer.

 A gastro-esophagoscopy was done in October 2012, because of protracted gastro-esophageal reflux. Histology showed short Barrett´s esophagus with low-grade dysplasia. During the same séance, a 10 mm in diameter polypoid lesion was detected in the stomach (Figure 1). The polyp was endoscopically excised. No complications occurred during or after the procedure. The histological examination of the gastric polypoid lesion revealed a serrated adenoma showing protruding glands with lateral saw tooth-like notches due to scalloped epithelial indentations with high-grade dysplasia (Figure 2). In addition, an adenocarcinoma invading the submucosal tissues was demonstrated (Figure 3). The invasive carcinoma component retained the serrated configuration and the cytological features of the adenoma (Figure 4).

**DISCUSSION**

Despite decreasing incidence, gastric carcinoma continues to be one of the most common cancers world wide[33]. It is generally assumed that the histogenesis of gastric carcinoma of intestinal type follows the atrophic gastritis-intestinal metaplasia-dysplasia-pathway[34]. On the other hand, the histogenesis of gastric carcinomas of diffuse type remains elusive. Thus, the histogenesis in the majority of the gastric carcinomas has not yet being disclosed.

 It is known that gastric tubular or villous adenomas may progress to gastric carcinoma of intestinal type[9,10,12,35]. The same fate seems to apply to gastric serrated adenomas, since of the 20 gastric serrated adenomas now in record (including the one reported here), 75% had evolved into invasive carcinoma (Table 1).

 Recently, Kwon *et al*[32] reported 9 cases of gastric serrated adenomas. These authors found that MUC5AC expression was present in 66.7% (6/9) of the gastric serrated adenomas, in 71.4% (5/7) of the serrated adenocarcinomas, and *KRAS* mutations in 33.3% (3/9) of the cases. Kwon *et al*[32] concluded that the high frequencies of malignant transformation and *KRAS* mutations suggested that gastric serrated adenomas might be precursors of gastric mucin-phenotype adenocarcinoma.

Here, we report the first case of serrated adenoma of the stomach in a patient with Lynch syndrome. Lynch syndrome is an [autosomal dominant](http://en.wikipedia.org/wiki/Autosomal_dominant%22%20%5Co%20%22Autosomal%20dominant) genetic condition which has a high risk of [colon cancer](http://en.wikipedia.org/wiki/Colon_cancer%22%20%5Co%20%22Colon%20cancer) as well as other cancers including [endometrium](http://en.wikipedia.org/wiki/Endometrial_cancer%22%20%5Co%20%22Endometrial%20cancer), [ovary](http://en.wikipedia.org/wiki/Ovarian_cancer), [stomach](http://en.wikipedia.org/wiki/Stomach_cancer), [small intestine](http://en.wikipedia.org/wiki/Gastrointestinal_cancer), [hepatobiliary tract](http://en.wikipedia.org/wiki/Gallbladder_cancer), upper [urinary tract](http://en.wikipedia.org/wiki/Urinary_tract%22%20%5Co%20%22Urinary%20tract), [brain](http://en.wikipedia.org/wiki/Brain_tumor), and [skin](http://en.wikipedia.org/wiki/Skin_cancer%22%20%5Co%20%22Skin%20cancer). The increased risk for these cancers is due to inherited mutations that impair [DNA mismatch repair](http://en.wikipedia.org/wiki/DNA_mismatch_repair%22%20%5Co%20%22DNA%20mismatch%20repair). The occurrence of this case of gastric serrated adenoma in a patient with Lynch syndrome implies that this adenoma phenotype may develop not only sporadically but also in patients with hereditary traits.

Paradoxically, eight out of 20 cases of serrated adenoma of the stomach now in record (including present case) have been reported from a single Institution[21,27,28]. The increased awareness of the existence of these gastric aggressive adenomas may result in more cases being reported from other Institutions in the future.

**REFERENCES**

**1 Konjetzny GE.** Die entzündliche Grundlage der typischen Geschwursbildungen im Magen und Duodenum. *Zieglers Beit* 1923; ***20***: 321-345

2 **Stewart MJ**. Brit Med J, ii: 567-572, 1929 (cited by Hurst AF). Precursors of carcinoma of the stomach. Lancet 1929; **217**: 1023-1028

3 **Bone GE**, McClelland RN. Management of gastric polyps. *Surg Gynecol Obstet* 1976; **142**: 933-938 [PMID: 936039]

4 **Ito H**, Hata J, Yokozaki H, Nakatani H, Oda N, Tahara E. Tubular adenoma of the human stomach. An immunohistochemical analysis of gut hormones, serotonin, carcinoembryonic antigen, secretory component, and lysozyme. *Cancer* 1986; **58**: 2264-2272 [PMID: 3530427 DOI: 3.0.CO; 2-F']

5 **Johansen A**. Elevated early gastric carcinoma. Differential diagnosis as regards adenomatous polyps. *Pathol Res Pract* 1979; **164**: 316-330 [PMID: 223135 DOI: 10.1016/S0344-0338(79)80052-7]

6 **Kato Y**, Yanagisawa A, Sugano H. Biopsy interpretation in diagnosis of gastric carcinoma In: Gastric Cancer Nishi M., Ichikawa H. Nakajima T, Maruyama K and Tahara E (ed). Tokyo, Springer Verlag, 1993: 133-150

7 **Nakamura T**. [Patho-histological classification of gastric polyps with specific reference to their malignant degeneration]. *Chirurg* 1970; **41**: 122-130 [PMID: 5515840]

8 **Rubio CA**, Auer GU, Kato Y, Liu FS. DNA profiles in dysplasia and carcinoma of the human esophagus. *Anal Quant Cytol Histol* 1988; **10**: 207-210 [PMID: 3408547]

9 **Kamiya T**, Morishita T, Asakura H, Miura S, Munakata Y, Tsuchiya M. Long-term follow-up study on gastric adenoma and its relation to gastric protruded carcinoma. *Cancer* 1982; **50**: 2496-2503 [PMID: 7139542 DOI: 3.0.CO; 2-1']

10 **Kozuka S.** Gastric polyps. In: Gastric carcinoma. Filipe M, Jass J (eds). Edingburgh. Churchill Livingstone, 1986: 132-151

11 **Laxén F**, Sipponen P, Ihamäki T, Hakkiluoto A, Dortscheva Z. Gastric polyps; their morphological and endoscopical characteristics and relation to gastric carcinoma. *Acta Pathol Microbiol Immunol Scand A* 1982; **90**: 221-228 [PMID: 7102316]

12 **MING SC**, GOLDMAN H. GASTRIC POLYPS; A HISTOGENETIC CLASSIFICATION AND ITS RELATION TO CARCINOMA. *Cancer* 1965; **18**: 721-726 [PMID: 14297468]

13 **Tomasulo J**. Gastric polyps. Histologic types and their relationship to gastric carcinoma. *Cancer* 1971; **27**: 1346-1355 [PMID: 5088211]

14 **Elster K**. Histologic classification of gastric polyps. *Curr Top Pathol* 1976; **63**: 77-93 [PMID: 795617]

15 **Park do Y**, Lauwers GY. Gastric polyps: classification and management. *Arch Pathol Lab Med* 2008; **132**: 633-640 [PMID: 18384215 DOI: 10.1055/s-2005-870126]

16 **Fucuchi S**, Hiyama M, Machizuki T. Endoscopical diagnosis of IIa-like borderline lesions (IIa subtype) of stomach. Stomach Intestine1975; **10**: 1487- 1494

17 **Nakamura K**, Sakaguchi H, Enjoji M. Depressed adenoma of the stomach. *Cancer* 1988; **62**: 2197-2202 [PMID: 3179932]

18 **Rubio CA**, Kato Y, Jònasson JG. Protruding and non-protruding adenomas of the stomach. *Anticancer Res* 2001; **21**: 3037-3040 [PMID: 11712807]

19 **Goldstein NS**, Lewin KJ. Gastric epithelial dysplasia and adenoma: historical review and histological criteria for grading. *Hum Pathol* 1997; **28**: 127-133 [PMID: 9023391 DOI: 10.1016/S0046-8177(97)90095-2]

20 **Appelman HD**. Pathology of the Esophagus, Stomach and Duodenum. Churchill Livingstone, London 1984: 94-100.

21 **Rubio CA**. Serrated neoplasia of the stomach: a new entity. *J Clin Pathol* 2001; **54**: 849-853 [PMID: 11684719 DOI: 10.1136/jcp.54.11.849]

22 **Rubio CA**, Nesi G, Messerini L, Zampi GC, Mandai K, Itabashi M, Takubo K. The Vienna classification applied to colorectal adenomas. *J Gastroenterol Hepatol* 2006; **21**: 1697-1703 [PMID: 16984592 DOI: 10.1111/j.1440-1746]

23 **Rubio CA**. Serrated adenomas of the appendix. *J Clin Pathol* 2004; **57**: 946-949 [PMID: 15333655 DOI: 10.1136/jcp.2004]

24 **Rubio CA**. Serrated adenoma of the duodenum. *J Clin Pathol* 2004; **57**: 1219-1221 [PMID: 15509689 DOI: 10.1136/jcp.2004.016360]

25 **Rubio CA**, Grimelius L, Von Sivers K, Höög A. Intraductal serrated adenoma of the pancreas. A case report. *Anticancer Res* 2005; **25**: 3099-3102 [PMID: 16080572]

26 **Rubio CA**, Befrits R, Ericsson J. Serrated adenoma of the esophagus (Anticancer Res, in press, 2013).

27 **Rubio CA**, Lagergren J. Serrated adenomas of the cardia. *Anticancer Res* 2004; **24**: 2113-2116 [PMID: 15274410]

28 **Rubio CA**, Petersson F, Höög A, Jónasson JG, Nesi G, Chandanos E, Lindblad M. Further studies on serrated neoplasias of the cardia: a review and case report. *Anticancer Res* 2007; **27**: 4431-4434 [PMID: 18214056]

29 **M'sakni I**, Rommani SR, Ben Kahla S, Najjar T, Ben Jilani S, Zermani R. Another case of serrated adenoma of the stomach. *J Clin Pathol* 2007; **60**: 580-581 [PMID: 17513520 DOI: 10.1136/jcp.2006.037960]

30 **Hasuo T**, Semba S, Satake S, Shirasaka D, Aoyama N, Yokozaki H. Superficially elevated-type serrated hyperplastic lesion of the stomach with minute adenocarcinoma. *Dig Endosc* 2009; **21**: 101-105 [PMID: 19691783 DOI: 10.1111/j.1443-1661.2009.00831.x]

31 **Köklü S**, Başar O, Akbal E, Ibiş M. Gastric serrated adenoma polyp treated with endoscopic band ligation (with video). *Surg Laparosc Endosc Percutan Tech* 2010; **20**: e204-e205 [PMID: 21150403 DOI: 10.1097/SLE.0b013e3181fd27ab]

32 **Kwon MJ**, Min BH, Lee SM, Park H Y, Kang SY, Ha SY, Lee JH, Kim J J, Park CK. Serrated adenoma of the stomach: A clinicopathologic, immunohistochemical, and molecular study of nine cases. Histol Histopathol (personal communication, in press), 2013.

33 **McColl KE**, Watabe H, Derakhshan MH. Sporadic gastric cancer; a complex interaction of genetic and environmental risk factors. *Am J Gastroenterol* 2007; **102**: 1893-1895 [PMID: 17727430 DOI: 10.1111/j.1572-0241.2007.01417.x]

34 **Correa P**, Houghton J. Carcinogenesis of Helicobacter pylori. *Gastroenterology* 2007; **133**: 659-672 [PMID: 17681184]

35 **Lee WA**. Gastric extremely well differentiated adenocarcinoma of gastric phenotype: as a gastric counterpart of adenoma malignum of the uterine cervix. *World J Surg Oncol* 2005; **3**: 28 [PMID: 15907218 DOI: 10.1186/1477-7819-3-28]

**P-Reviewers** Zullo A, Phull PS **S-Editor** Wen LL

**L-Editor**  **E-Editor**

**Figure 1 Endoscopic view.** A: Gastric polyp; B: Gastric polyp after indigocarmine staining.

**Figure 2 The histological examination of the gastric polypoid lesion revealed a serrated adenoma showing protruding glands with lateral saw tooth-like notches due to scalloped epithelial indentations with high-grade dysplasia.** A: Adenoma showing serrated glands lined with high-grade dysplasia [Hematoxylin and eosin (H and E) × 10]; B: High power view of the adenomatous component showing serrated glands with indentations lined with high-grade dysplasia (H and E × 20); C: View of a single elongated gland with saw-tooth-like configuration lined with high-grade dysplasia (H and E × 20).

**Figure 3 Low-power view of serrated adenoma with invasive carcinoma (H and E × 10).**

**Figure 4 High power view of the invasive component with retained serrated configuration (H and E × 10).**

**Table 1 Gastric serrated adenomas case reports**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|

|  |  |  |  |
| --- | --- | --- | --- |
| Ref. | Year of publication | No. of cases | No. cases with invasive carcinoma |

 |

|  |  |  |  |
| --- | --- | --- | --- |
| Rubio *et al*[21] | 2001 | 1 | 1 |
| Rubio *et al*[27] | 2004 | 5 | 4 |
| Rubio *et al*[28] | 2007 | 1 | 1 |
| M'sakni *et al*[29] | 2007 | 1 | 0 |
| Hasuo *et al*[30] | 2009 | 1 | 1 |
| Köklü *et al*[31] | 2010 | 1 | 0 |
| Kwon *et al* [32] | 2013 | 9 | 7 |
| Rubio, Björk1 | 2013 | 1 | 1 |

 1Present communication.