

Brunner's Gland Adenoma with High-Grade Dysplasia

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ABSTRACT

Brunner's gland adenoma is a rare, benign, small-bowel neoplasm. In a few reported cases, it can cause gastrointestinal hemorrhage and can be associated with cellular atypia. We report an 84-year-old woman with a 12-mm Brunner's gland adenoma in the second part of the duodenum that was successfully removed with a saline injection-lift technique using a hot snare, followed by placement of clips to prevent postpolypectomy bleeding. Pathological examination revealed Brunner's gland adenoma with high-grade dysplasia and oncocyctic features with negative resection margins. The patient recovered uneventfully. Brunner's gland adenoma is traditionally considered a benign lesion, and few cases in the published literature have reported Brunner's gland adenoma with dysplasia or neoplasia. This suggests a dysplastic stage in the natural history of Brunner's gland adenoma and questions the malignant potential of such lesions.

INTRODUCTION

Brunner's gland adenoma is an extremely rare, benign, small-bowel neoplasm. The first case was described by Cruveilhier in 1835.¹ Brunner's glands are submucosal mucin-secreting glands and are predominantly located in the duodenal bulb and proximal duodenum. The glands secrete an alkaline fluid composed of mucin to help protect the duodenal epithelium from acidic chyme of the stomach. Brunner's gland adenomas comprise less than 5% of benign duodenal tumors. Although commonly an incidental finding, Brunner's gland adenoma can cause clinically significant symptoms including gastrointestinal hemorrhage, abdominal pain, as well as intestinal obstruction; in a few reported cases, Brunner's gland adenoma can be associated with cellular atypia or neoplasia.^{2,3}

CASE REPORT

An 84-year-old woman with a history of chronic renal insufficiency presented with severe iron-deficiency anemia. The patient had a long history of chronic anemia requiring transfusions, and she was previously admitted with severe anemia resulting in a pulseless electrical activity arrest and non-ST segment elevation myocardial infarction. She fully recovered from this event. She denied melena or hematemesis. Prior esophagogastroduodenoscopy (EGD) in the community setting showed angioectasias, which were treated with argon plasma coagulation; EGD also revealed a duodenal adenoma, for which she was referred to our institution for further management. Prior endoscopic evaluation for her anemia also included a colonoscopy and capsule endoscopy.

EGD after admission was notable for a 12-mm sessile polyp with a central depression in the second portion of the duodenum, opposite the major papilla (Figure 1). Angioectasias were not noted during this EGD. The duodenal polyp was successfully removed with a saline injection-lift technique using a hot snare, followed by placement of 2 clips to prevent postpolypectomy bleeding. Pathological examination revealed Brunner's gland adenoma with oncocyctic features and focal high grade dysplasia (HGD) characterized by increased mitoses and cytological atypia, with negative resection margins for HGD and no evidence of submucosal invasion (Figure 2). The diagnosis was

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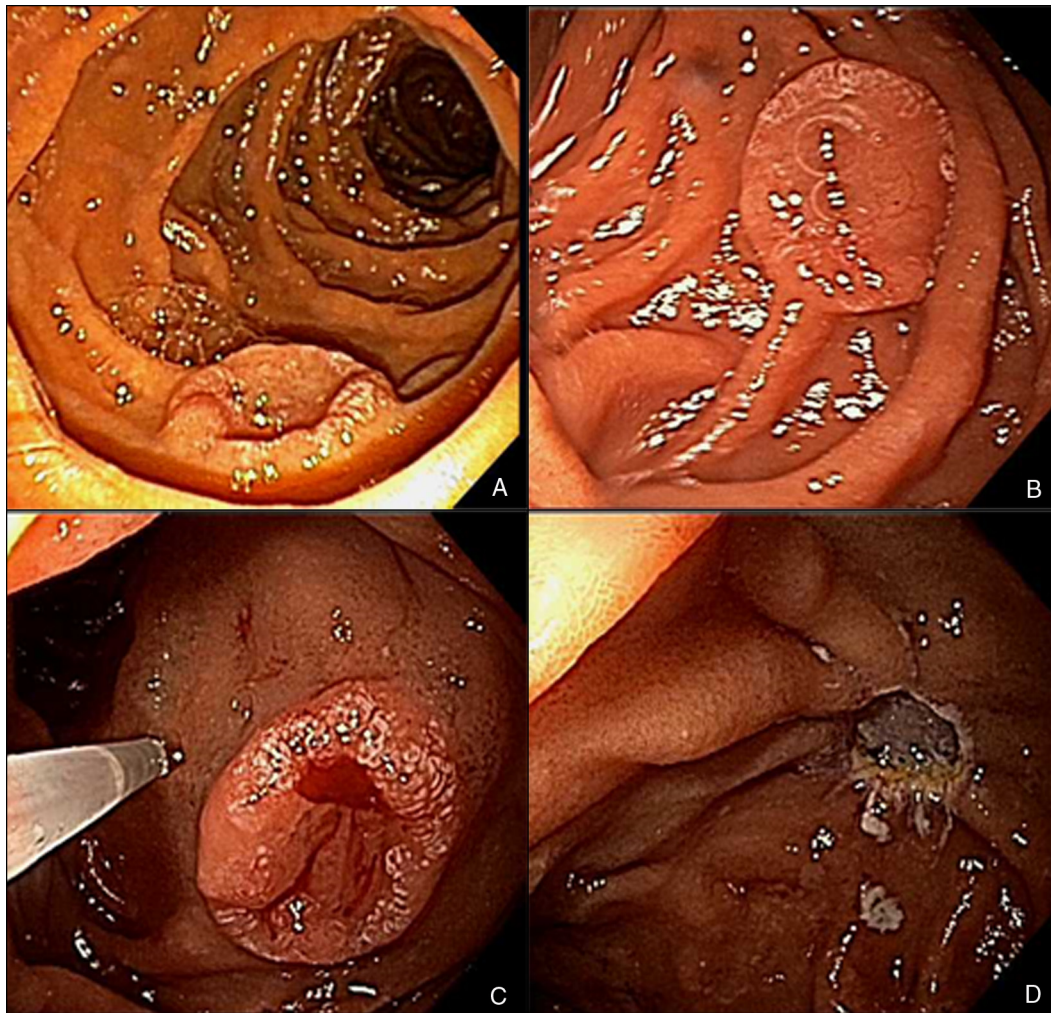


Figure 1. (A and B) Esophagogastroduodenoscopy of the second part of the duodenum showing a sessile polyp with a central depression. (C) Snare polypectomy of lesion. (D) Site after successful polypectomy.

based on the hematoxylin and eosin morphology, which was consistent with Brunner's gland origin. This was confirmed with review by an expert in gastroenterologist pathology at our institution. *Helicobacter pylori* immunostain was negative. The patient recovered uneventfully and was offered surveillance endoscopy for follow-up after resection, but she declined given her age and comorbid conditions. The patient is otherwise doing well.

DISCUSSION

While Brunner's gland adenoma is traditionally considered a benign, small-bowel neoplasm, we report a case with focal HGD. Only a few cases in the literature have reported Brunner's gland adenoma with cellular atypia or neoplasia, with 1 study reporting dysplastic changes in 2.1% and invasive carcinoma in 0.3% of all Brunner's gland hyperplasia.²⁻⁹ Of 722 cases of Brunner's gland hyperplasia examined for hyperplastic changes culminating in dysplasia and carcinoma, 15 cases

were found to have some degree of cellular atypia and 2 cases were found to have invasive carcinoma. Six cases were found in the duodenal bulb, and 9 cases were found in the second portion of the duodenum.⁹ Of note, dysplastic changes were frequently associated with a central depression (9 cases), as was seen in our patient's lesion. A central depression is an unusual finding for Brunner's gland hyperplasia. In the same study, immunohistochemical testing supported the concept of a continuous spectrum in carcinogenesis from hyperplasia to atypical hyperplasia or dysplasia and eventually to adenocarcinoma.⁹ These findings suggest that dysplastic or carcinomatous change does occur in Brunner's gland hyperplasia, and metaplasia may be a precursor lesion in the process of carcinogenesis in Brunner's gland adenoma.

The mechanism behind the development of dysplasia and neoplasia in Brunner's gland adenoma is unclear. It is likely the result of repeated mucosal damage resulting from mechanical stimuli, *H. pylori* infection, and a hyperacidic environment in

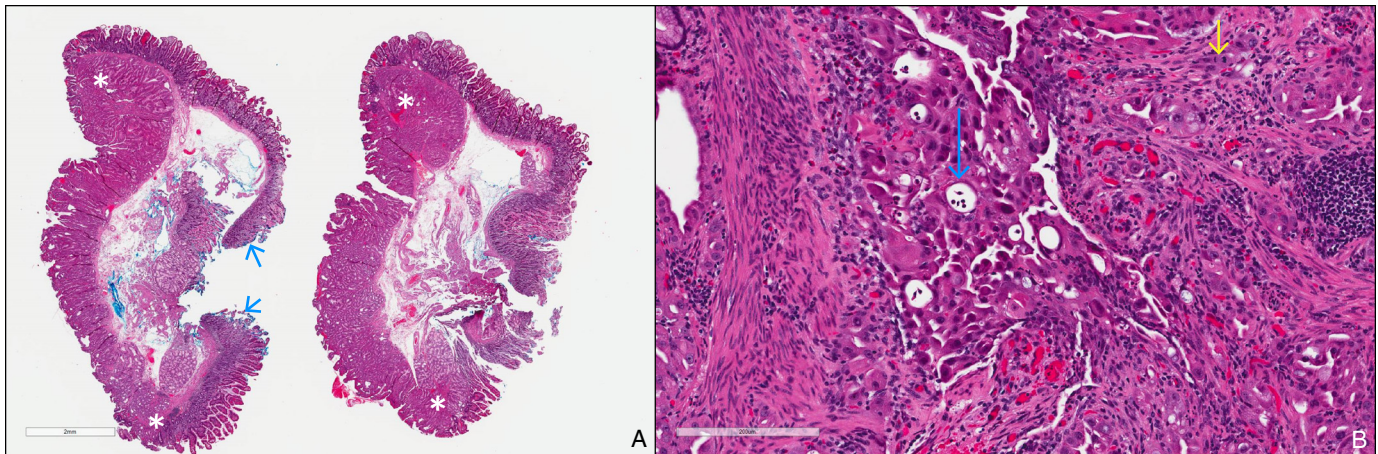


Figure 2. Histological images of Brunner's gland hyperplasia in the duodenum. (A) Low-power view showing the adenoma between the asterisks * and the clear margins (arrows). (B) High-power view showing prominent mitoses (yellow arrow), increased apoptosis (blue arrow), and cytological atypia.

the duodenum that activates the mucosal repair mechanism and facilitates the proliferation of Brunner's glands.^{10,11} It has been speculated that the increase in size of Brunner's gland hyperplasia induces ulceration of the surface mucosa, and the subsequent repair with gastric foveolar metaplasia with papillary architecture in turn evokes dysplastic and neoplastic changes.⁹ Of note, the relationship with *H. pylori* infection is unclear; in our case, *H. pylori* immunostain was negative.

Brunner's gland adenoma is often an incidental finding during EGD or imaging. These lesions can also cause gastrointestinal bleeding.^{12,13} Several cases in the literature report Brunner's gland adenoma with dysplasia or neoplasia, which suggests a dysplastic stage in the natural history of Brunner's gland hyperplasia and questions the overtly malignant potential of such lesions.^{2,3,6-8} In one case, primary duodenal adenocarcinoma arising from Brunner's gland was reported after 17 years of observation.³ It remains controversial whether a small, asymptomatic Brunner's gland adenoma found incidentally during EGD should be removed; some suggest that Brunner's gland adenomas should be followed sequentially and removed if their shape or size changes significantly.^{3,11,14} In the case of a symptomatic Brunner's gland adenoma, polypectomy or resection is generally recommended. Endoscopic polypectomy or resection of these lesions not only allows for confirmation of the diagnosis and excludes underlying dysplasia or malignancy, but can also be curative such as in this patient.

There are no data on recurrence or recommendations regarding endoscopic surveillance after resection of a Brunner's gland adenoma with dysplasia or neoplasia. We recommend surveillance endoscopy after endoscopic polypectomy or resection for follow-up. Our patient declined surveillance

endoscopy given her advanced age and comorbid conditions, and she is otherwise doing well.

In conclusion, this case illustrates the potential for dysplasia in Brunner's gland adenoma, previously felt to be benign lesions, and raises the question of potential malignant transformation. The pathophysiology of the development of dysplasia and malignant transformation in these lesions is not completely understood. Given the presence of HGD in Brunner's gland adenoma in this case, and considering prior reports with cellular atypia or neoplasia, it is judicious to avoid presuming that all Brunner's gland adenomas are benign.²⁻⁹ Endoscopic polypectomy or resection of Brunner's gland adenomas can allow for diagnosis and exclusion of underlying dysplasia or malignancy; it can also be curative, as was the case for our patient.

DISCLOSURES

Author contributions: FH Ramay wrote the manuscript. JC Papadimitriou provided the histological images. PE Darwin revised the manuscript and is the article guarantor.

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Informed consent was obtained for the case report.

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REFERENCES

1. Cruveilhier J. Anatomie Pathologique Du Corps Humain. Paris: J.B. Ballière, 1829-1842.
2. Itsuno M, Makiyama K, Omagari K, et al. Carcinoma of duodenal bulb arising from the Brunner's gland. *Gastroenterol Jpn*. 1993;28(1):18-25.
3. Koizumi M, Sata N, Yoshizawa K, Kurihara K, Yasuda Y. Carcinoma arising from Brunner's gland in the duodenum after 17 years of observation: A case report and literature review. *Case Rep Gastroenterol*. 2007;1(1):3-9.
4. Brookes MJ, Manjunatha S, Allen CA, Cox M. Malignant potential in a Brunner's gland hamartoma. *Postgrad Med J*. 2003;79(933):6-7.
5. Faller G, Kirchner T. Low-grade intraepithelial neoplasia of Brunner's gland. *Histopathology*. 2005;47(1):8-9.
6. Ohta Y, Saitoh K, Akai T, et al. Early primary duodenal carcinoma arising from Brunner's glands synchronously occurring with sigmoid colon carcinoma: Report of a case. *Surg Today*. 2008;38(8):56-60.
7. Akino K, Kondo Y, Ueno A, et al. Carcinoma of duodenum arising from Brunner's gland. *J Gastroenterol*. 2002;37(4):3-6.
8. Kamei K, Yasuda T, Nakai T, Takeyama Y. A case of adenocarcinoma of the duodenum arising from Brunner's gland. *Case Rep Gastroenterol*. 2013;7(3):3-7.
9. Sakurai T, Sakashita H, Honjo G, Kasyu I, Manabe T. Gastric foveolar metaplasia with dysplastic changes in Brunner gland hyperplasia: Possible precursor lesions for Brunner gland adenocarcinoma. *Am J Surg Pathol*. 2005;29(11):2-8.
10. Akaki M, Taniguchi S, Hatakeyama K, Kushima R, Kataoka H. Duodenal mucosal damage is associated with proliferative activity of Brunner's gland hamartoma: A case report. *BMC Gastroenterol*. 2014;14:14.
11. Lu L, Li R, Zhang G, et al. Brunner's gland adenoma of duodenum: Report of two cases. *Int J Clin Exp Pathol*. 2015;8(6):5-9.
12. Meltser E, Federici M, Cooper R 2nd, Capanescu C, Behling KC. Fatal gastrointestinal hemorrhage in a patient with Brunner's gland hyperplasia. *Case Rep Gastroenterol*. 2017;11(2):1-5.
13. Sorleto M, Timmer-Stranghöner A, Wuttig H, Engelhard O, Gartung C. Brunner's gland adenoma: A rare cause of gastrointestinal bleeding: Case report and systematic review. *Case Rep Gastroenterol*. 2017;11(1):1-8.
14. Gao YP, Zhu JS, Zheng WJ. Brunner's gland adenoma of duodenum: A case report and literature review. *World J Gastroenterol*. 2004;10(17):6-7.