Brunner's gland cyst in combination with gastrointestinal stromal tumor: A case report

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Received February 21, 2015; Accepted February 1, 2016

DOI: 10.3892/ol.2016.4382

Abstract. Brunner's gland cysts are rare benign lesions that are mainly observed in the first and the second regions of the duodenum. Patients with Brunner's gland cyst demonstrate no specific symptoms. The present study reports the case of a patient with Brunner's gland cyst located in the duodenum in combination with a gastrointestinal stromal tumor (GIST) in the same region. To the best of our knowledge, the present study reports the first case of Brunner's gland cyst with GIST. A 58-year-old female patient was referred to Tianchang Hospital of Traditional Chinese Medicine (Tianchang, China) with a one-month history of upper abdominal discomfort, diarrhea and recurrent vomiting following the intake of food. Upper gastrointestinal endoscopy and a computed tomography scan revealed the presence of a round, cystic-like lesion with internal low density located within the duodenum. Pathological examination revealed that the cyst measured 0.3 cm in diameter and was consistent with a diagnosis of Brunner's gland cyst. Histopathology revealed that the cyst possessed characteristics of GIST. The patient underwent surgical exploration and tumor resection, and was discharged 2 weeks post-surgery. During the 12 month post-operative follow-up period, the outcome of the patient was good. This case study of Brunner's gland cyst combined with GIST enriches the present literature and promotes better understanding of the two diseases. Further investigation is required to explain the mechanism and association between the two rare diseases.

Introduction

Brunner's glands are submucosal mucin-secreting glands that were first characterized by Brunner in 1688. The glands have been observed between the pylorus and the jejunum (1), mainly in the first and second regions of the duodenum, usually in individuals aged 40-60 years (2).

Brunner's gland cysts are rare, benign polypoid, nodular mass lesions arising from Brunner's glands, with no associated underlying malignancy (3-5). Only 13 cases have been reported in the literature (6,7). Certain cases appear to present as a cystic dilatation of the Brunner's gland ducts in association with hamartoma (8). Brunner's gland cysts are detected incidentally and are usually asymptomatic (9,10). Brunner's gland cyst of the duodenum may be removed by endoscopy, and is one of the most cost-effective approaches of resection (11). Furthermore, surgical resection via a laparoscopic approach or laparotomy is required for complete resection in cases where the tumor is too large to be resected by endoscopy or if malignancy is suspected (12).

Gastrointestinal stromal tumor (GIST) is a rare stromal tumor that accounts for 0.1-3.0% of all gastrointestinal tumors arising from the interstitial cells of Cajal or the common intestinal mesenchymal precursor cells (13). GISTs are observed in adults >40 years old (range, 55-60 years), but rarely in children. The majority of GISTs are located in the stomach (55.6%) and small intestine (31.8%), and 1 in 5 GISTs are detected incidentally (14,15). The most common symptoms of the disease are abdominal pain, gastrointestinal bleeding and obstruction, together with other non-specific presentation (14). The treatment of GIST includes molecularly targeted therapy and surgery. Although immunotherapy has had profound effects on the management of these type of tumors, surgery remains the optimal treatment approach for GIST based on expert consensus, with optimistic outcomes following surgery (16-19).

The present study reports the case of a patient with Brunner's gland cyst in combination with a GIST and reviews the clinical presentations, pathological features and therapy.

Case report

A 58-year-old female was admitted to Tianchang Hospital of Traditional Chinese Medicine (Tianchang, China) on 19 July, 2014, with a one-month history of epigastric abdominal discomfort, diarrhea and recurrent vomiting following the intake of food. The feces of the patient occasionally appeared similar to yellow jelly. A review of the body's systems and past medical history of the patient, and the

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Key words: Brunner's gland cyst, gastrointestinal stromal tumor

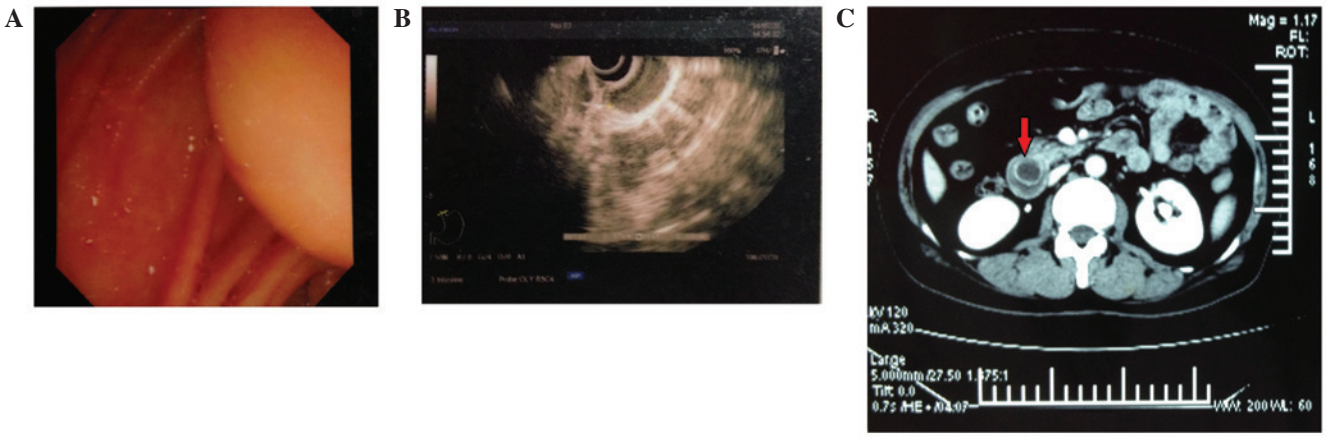

Figure 1. (A) Gastroduodenoscopic examination revealed the presence of a 2.37x1.20-cm half-globular, submucosal mass located in the descending region of the duodenum. (B) Endoscopic ultrasound revealed that a submucosal, low-echo conglomeration, which originated from the muscle layer, was located in the wall of the duodenum near the duodenum bulb. (C) An axial portal arterial-phase computed tomography scan revealed the presence of a spherical low-density mass (arrow), which possessed a thick wall abutting the duodenal bulb, and the presence of a cyst in right lobe of the liver.

findings of physical examination and routine laboratory tests performed were not notable. The body temperature of the patient was 37.2˚C (normal range, 36-37˚C), blood pressure was 130/77 mmHg (normal range, 90-140/60-90 mmHg) and radial pulse rate was 70 beats/min and regular (normal range, 60-100 beats/min). A complete blood count revealed a red blood cell count of $321x10^4$ cells/μl (normal range, 350-500x10^4 cells/μl), hemoglobin concentration of 9.1 g/dl (normal range, 13.5-17.6 g/dl), and mean corpuscular volume of 87 fl (normal range, 80-100 fl).

Upper gastrointestinal endoscopy was performed on 19 July 2014 and revealed the presence of a cap mass at the descending region of the duodenum (Fig. 1A). A computed tomography (CT) scan revealed a round, cystic-like lesion with low internal density located within the duodenum (Fig. 1C). The patient underwent treatment with norfloxacin (0.3 g, administered orally 2 times a day for 3 days) and support treatment (500 ml of 5% glucose normal saline, 500 ml Sodium Lactate Ringer's Injection, 30 ml of 10% KCl and 20 ml of 10% NaCl mixed into a single infusion bag, and administered every day for 2 days by intravenous infusion). Following administration, the diarrhea, nausea and vomiting stopped, but the abdominal pain remained. The patient underwent endoscopic ultrasound, which revealed the presence of a half-globular, submucosal, low-echo cystic conglomeration in the wall of the duodenum, near the duodenal bulb (Fig. 1B). The cyst originated from the muscle layer and its cross-sectional size was 2.37x1.20 cm. A differential diagnosis of GIST was provided, and the patient was admitted to the First Affiliated Hospital of Nanjing Medical University (Nanjing, Jiangsu, China) on 12 August, 2014, to confirm the diagnosis and receive treatment. Considering the size and position of the mass, the patient underwent surgical exploration and tumor resection instead of endoscopic management. The surgery was performed on 14 August 2014. During surgery, a submucosal cyst was identified and transduodenal local resection was performed. The specimen was histopathologically examined.

The mass was surgically resected and the specimen was histopathologically examined using a OLYMPUS BX43 microscope (Olympus Corporation, Tokyo, Japan) subsequent to staining with hematoxylin and eosin (Fuzhou Maixin Biotech Co., Ltd., Fuzhou, China). The typical appearance of the mass was a soft, submucosal cyst measuring 3.0x2.0x2.0 cm in size that ruptured during biopsy. The mass was full of fluid and flocculent precipitate. Microscopy revealed that the tumor was composed of Brunner's glands. The surface epithelium of the duodenum was normal. Chronic duodenal mucosal inflammation with lymphoid tissue hyperplasia was observed in the mass, but no dysplasia or malignancy was observed.

Adenomatous hyperplasia of the spindle cells was identified inside a small nidus, which was extremely close to the cyst and measured ~0.3 cm in diameter. The small nidus was resected with the cyst during surgery. Additional immunohistochemistry was performed using the following antibodies: Monoclonal rabbit cluster of differentiation (CD)117 (catalog no., RMA-0632), mouse CD34 (catalog no., Kit-0004), rabbit discovered on GIST-1 (DOG-1; catalog no., Kit-0035), mouse S-100 (catalog no., Kit-0007), mouse desmin (catalog no., Kit-0023), mouse α-smooth muscle actin (SMA; catalog no., Kit-0006), and mouse Ki-67 (catalog no., Kit-0005), which were all purchased from Fuzhou Maixin Biotech Co., Ltd.. All antibodies were ready-to-use products and did not require further dilution. Succinate dehydrogenase complex iron-sulfur subunit B (SDHB) was used for immunostaining. The mass clearly expressed CD34 (Fig. 2C), while DOG-1, S-100, desmin and SMA were not expressed. A final diagnosis of extremely low-risk type GIST was provided, which was based on the mitotic index, tumor size, location and peritoneal deposits. The mitotic index was calculated according to a mitosis count of 50 high-power field (HPF) (20). The mitosis count of the current patient was 2-3/50 HPFs, indicating a low risk of aggressive behavior. Therefore, the lesion was diagnosed as a Brunner's gland adenoma in combination with a GIST. The patient received norfloxacin as an anti-infective therapy, and was administered glucose and sodium chloride solution with electrolytes as a support treatment (using same dose and duration as initial treatment). The patient was discharged 2 weeks post-surgery, and during the 12 month follow-up period, the outcome was good.

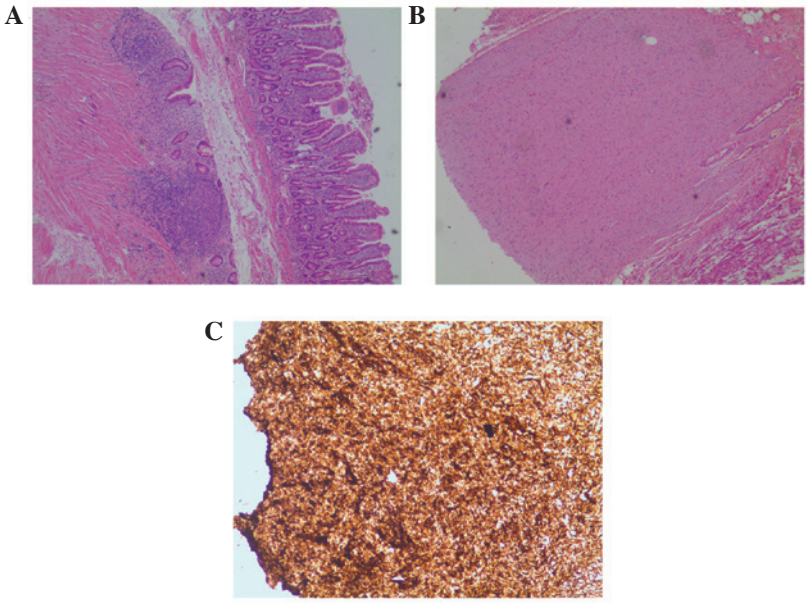

Figure 2. (A) Pathological examination of the oral side of the tumor demonstrated that the tumor appearance was consistent with normal Brunner's glands. The cyst was confined to the submucosa and consisted of a single layer of epithelial cells and connective tissue. The epithelial cells were composed of an orderly array of tall columnar cells containing basal round nuclei and fine granular cytoplasms (H&E staining; magnification, x40). (B) Histopathology revealed that the cyst was a gastrointestinal stromal tumor measuring 0.3 cm in diameter (H&E staining; magnification, x40). (C) Immunohistochemical staining, using specific markers, revealed that the glands were positive for cluster of differentiation 34. H&E, hematoxylin and eosin.

Discussion

Brunner's glands were first characterized by Brunner in 1688, and are alkaline-secreting glands located in the submucosal layer of the duodenum (21). The glands have been observed in ectopic locations, such as the pylorus and jejunum, but the majority of Brunner's glands are located in the first region of the duodenum (1). Brunner's gland cysts have also been termed cyst of Brunner's glands (22), Brunner's gland cystadenoma (23), Brunner's cyst (24), cystic hamartoma of Brunner's glands (25), mucocele of Brunner's glands (26) and cystic Brunner's gland hamartoma (27).

Brunner's gland cysts are usually detected incidentally (2,28), including in the case reported in the present study. The etiology of Brunner's gland cyst has not been fully elucidated; however, the cysts are hypothesized to arise as a result of obstruction to a major Brunner's gland duct (29). In Brunner's gland cysts, Brunner's glands may be mildly dilated, but predominantly the cysts consist of hyperplastic lobules of Brunner's gland acini, without cystically dilated spaces. By contrast, hyperplasia of the Brunner's glands is not often observed in Brunner's gland cysts (30,31). The cysts typically appear as soft, submucosal lesions that rupture during biopsy (32). These cysts are not composed of solid aggregates of Brunner's glands, and are occasionally mixed with fibromuscular, adipose and lymphoid tissues, unlike classic Brunner's gland hamartoma (6,33). Brunner's gland cysts are benign, with no associated underlying malignancy, and may be excised endoscopically or surgically, depending on the size and location of the cyst (11,12). Although Brunner's gland cysts are often identified incidentally, in symptomatic patients the most common symptoms are gastrointestinal hemorrhage and obstructive symptoms (6,32).

Diagnosing Brunner's gland cyst is challenging. It should be distinguished from other duodenal lesions, including Brunner's gland hamartoma, duplication cysts, pancreatic pseudocysts, cystic dystrophy arising in heterotopic pancreatic tissue, aberrant pancreatic tissue, leiomyoma, polypoid adenoma of the superficial mucosal glands and malignant tumors (10,33-35). The soft and submucosal appearance and the rupture or flattening of the lesions following endoscopic biopsies may aid in diagnosing Brunner's gland cyst. However, a final diagnosis of Brunner's gland cyst is based on pathological findings of resected lesions obtained by endoscopic mucosal resection, polypectomy or surgical treatment (10,36). Pathologically, Brunner's gland cysts are typically confined to the submucosa and consist of a single layer of connective tissue and epithelial cells, which are composed of columnar cells containing basal round nuclei and granular cytoplasm (37). Cystic configuration of a solitary duodenal mass should allow differentiation of Brunner's gland cysts from other duodenal lesions (37).

Endoscopic or surgical removal of Brunner's gland cyst may prevent the development of complications (38,39). Endoscopic tumorectomy is the ideal surgical procedure for Brunner's gland cyst and Brunner's gland adenoma resection, depending on the region and size of the mass and the presence of a peduncle (40). In the present study, considering the size and distal location of the mass, a tumorectomy was performed.

GISTs are rare stromal tumors that account for 0.1-3.0% of all gastrointestinal tumors, which are hypothesized to arise from the interstitial cells of Cajal or the common intestinal mesenchymal precursor cells (41).

In 95% of GISTs, positive immunohistochemical staining is observed for CD117 and DOG-1, whilst 70% are positive for CD34 (18,42). Patients with GISTs may present in various forms and GISTs are often diagnosed incidentally. Symptomatic patients tend to possess large tumors with a mean size of 6.0 cm, compared with 2.0-cm masses in asymptomatic

patients and 1.5-cm masses in patients that are diagnosed with GIST at autopsy (43).

In conclusion, the present study reports a case of a Brunner's gland cyst of the duodenum in combination with a GIST at the same position, which, to the best of our knowledge, has not previously been reported. Brunner's gland cyst should be considered as a differential diagnosis of duodenal masses. The existence of Brunner's gland cyst is not yet known to be associated with the presence of GISTs. Consequently, considering the possible causes of mucosal damage, including mechanical stimuli, *Helicobacter pylori* infection and hyper acidic environment in the duodenum, the mechanism and association of Brunner's gland cyst with GIST require additional investigation.

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