

CASE REPORT

# Giant Brunner glands hyperplasia of the duodenum: Case report of an uncommon malignancy mimicker

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**Introduction:** Brunner's glands hyperplasia (BGH) is an uncommon benign proliferative lesion found in the proximal duodenum. It is typically discovered incidentally during surgery or endoscopic examinations, and it can often be mistaken for a malignant process.

**Case presentation:** We report the case of a 59 years-old man who presented in the surgical department with a 5-days history of upper gastrointestinal tract symptoms associated with mild increase in serum amylase level. An esophagogastroduodenoscopy was performed, which showed a large infiltrating-type mass located in the proximal duodenum rising the suspicion for a pancreatic head tumor with duodenal wall involvement. Consequently, Whipple procedure was conducted. The resection specimen was further sent and processed in the Pathology department of Mureș County Clinical Hospital. On macroscopy a large polypoid-sessile mass located in the proximal duodenum was described, while the adjacent pancreatic tissue exhibited areas of extensive necrosis and hemorrhage. Microscopic evaluation revealed a benign proliferation composed of closely packed clusters of Brunner's glands separated by thin fibrous septa located in the duodenal submucosa, with no evidence of atypia or mitotic figures.

**Conclusions:** Large diffuse BGH is a rare benign condition that poses diagnostic challenges due to its potential to mimic malignant processes. Given the indolent character of the lesion, it is crucial to consider BGH as part of the differential diagnosis in routine pathological activity when evaluating lesions of the duodeno-pancreatic region.

**Keywords:** malignancy, duodenum, mimicker, Brunner's glands

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## Introduction

The small intestine represents about two-thirds of the overall length of the gastrointestinal tract. However, only less than 2% of the primary digestive tract neoplasms develop from this segment [1,2]. Brunner's gland hyperplasia (BGH) is a rare benign proliferative lesion of the small intestine, accounting for up to 10% of benign duodenal lesions [3], with an estimated incidence of 0.008% [4,5].

BGH was first described in 1872 by Salvioli [6]. Since then, only few cases have been reported in the literature. BGH is usually an incidental finding during routine endoscopy and in most cases, it is clinically silent.

In this paper we report an unusual case of large BGH, diffuse nodular type, associated with symptoms of upper abdominal pain, bleeding, nausea and vomiting, which was difficult to differentiate from a malignant process.

## Case presentation

A 59 years-old male patient was admitted to the Surgery Department, complaining of diffuse abdominal pain, hematemesis, nausea, vomiting and weight loss (approximately 10 kilograms in the last 4 months). In his medical history, the patient had a previous episode of acute pancreatitis in 2019. Complementary investigations were performed to establish an accurate diagnosis and treatment. Serologic investigations showed normal hemoglobin lev-

els (12.81 g/dL; normal range: 12-16 g/dL), leukocytosis ( $17.73 \times 10^3/\mu\text{L}$ ; normal range:  $4 - 10 \times 10^3/\mu\text{L}$ ) particularly with increased neutrophils count (78%; normal range: 50% - 70%), high C-reactive protein (13.33 mg/dL; normal range: <0.5 mg/dL) and a slight elevation of amylase levels (162 U/L; normal range: 28-100 U/L).

Computed tomography (CT) scan revealed inhomogeneous areas with central necrosis withing the head of the pancreas, associated with a diffuse thickening of the duodenal wall (Figure 1). Suspicion was raised for a pancreatic head tumor with duodenal involvement. Subsequently, an esophagogastroduodenoscopy was performed which revealed a large infiltrating-like mass located in the first and second part of the duodenum. Taking into consideration both clinical presentation and radiologic findings, the patient was referred for surgery. A cephalic duodenopancreatotomy was performed, since a malignant process could not be completely excluded.

The resected specimen was sent and further processed in the Pathology Department, Mureș County Clinical Hospital. For histological analysis, tissue samples were fixed in 10% neutral-buffered formalin, followed by dehydration and paraffin embedding. Paraffin-embedded tissues were sectioned at 5  $\mu\text{m}$  thickness, then mounted on glass slides. For general histological examination, tissue sections were stained with Hematoxylin and Eosin.

On macroscopy, in the first and second portion of the duodenum we described a large circumferential polypoid-sessile lesion measuring 55x50x15 mm, while

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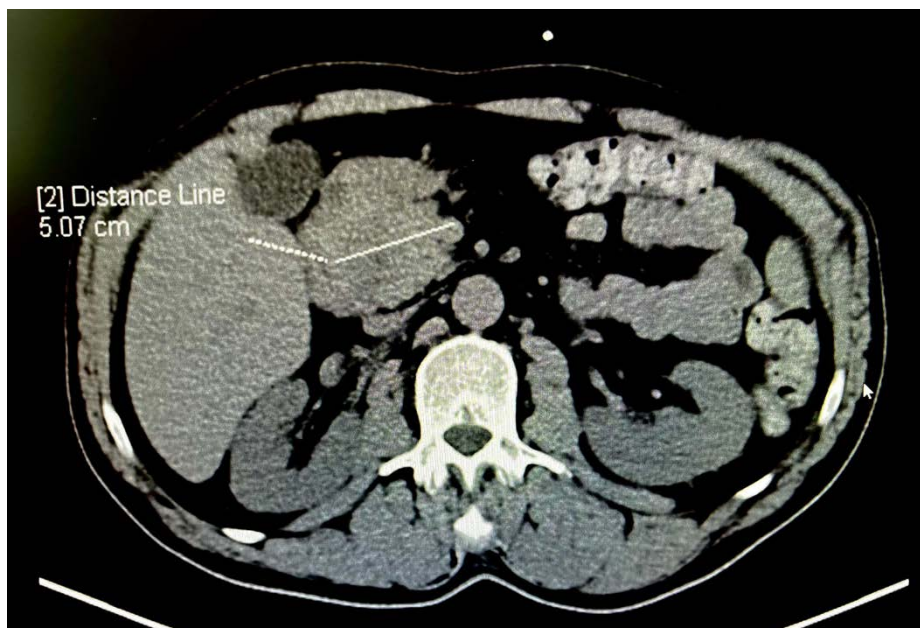


Fig. 1. Computed tomography examination – Large well-defined hypodense lesion in the duodeno-pancreatic region and left side of the liver.

the duodenal wall was diffusely thickened. The adjacent pancreatic head exhibited tan areas of fibrosis mainly in the pancreatic groove, alongside extensive dark-brown areas of necrosis and hemorrhage (Figure 2).

The histological examination showed a diffuse proliferation of Brunner glands located in the duodenal submucosa, separated in lobules by thin fibrous septa. The glands were lined by a single layer of cuboidal to columnar cells with basally located nuclei, lacking atypia or mitotic figures (Figure 3). The pancreatic tissue presented areas of fibro-adipose degeneration (highlighted using Van Gieson staining (Figure 4. C,D,F), abundant acute inflammatory

infiltrates (neutrophils, lymphocytes, plasma cells), marked hemorrhage and panlobular necrosis (Figure 4. A,B,E).

Finally, the patient was diagnosed with a diffuse nodular type Brunner's gland hyperplasia associated with acute hemorrhagic necrotizing pancreatitis.

The post-operative period was uneventful, and the patient was discharged 8 days after the surgical intervention without any complications.

## Discussions

Due to its anatomic, embryologic, and histologic complexity, duodenum can be involved in a heterogeneous group

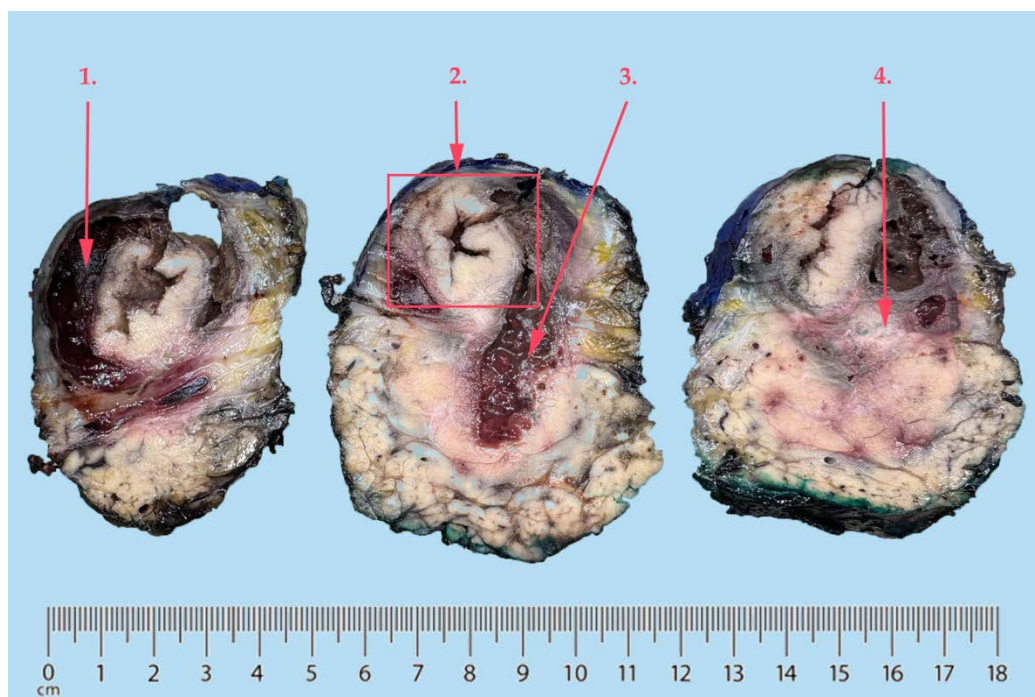


Fig. 2. Resection specimen; (1) paraduodenal hematoma; (2) diffuse thickening of the duodenal wall; (3) areas of hemorrhage and necrosis within the pancreatic head and duodeno-pancreatic groove; (4) fibrosis



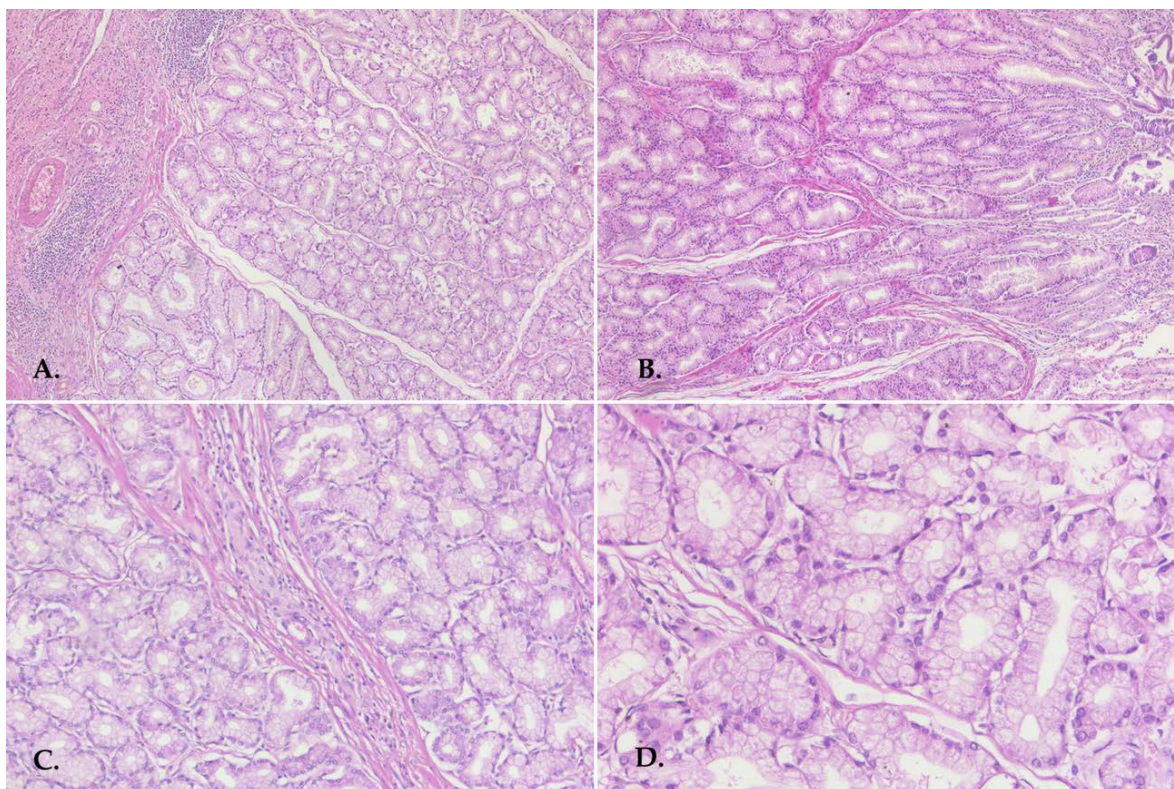


Fig. 3. BGH Hematoxylin & Eosin - closely packed groups of mucin-secreting glands separated by thin fibrous septa, located in the submucosal layer of the duodenum (A, B – 5x objective; C – 10x objective; D – 20x objective)

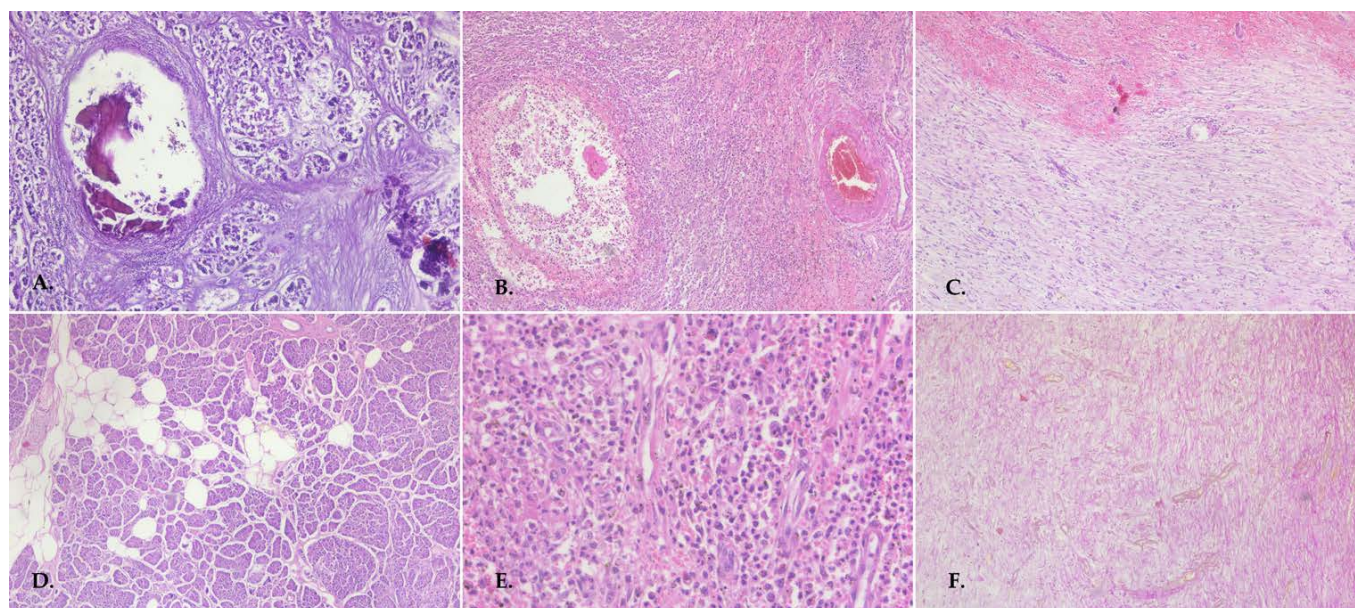


Fig. 4. Pancreas Hematoxylin & Eosin– A. lobular necrosis (10x objective); B,E – acute inflammation (5x objective; 20x objective); C. – fibrosis and hemorrhage within the duodeno-pancreatic groove (10x objective); D.- adipose degeneration (5x objective); F. – fibrosis (Van Gieson staining; 10x objective)

of benign tumors and tumor-like lesions potentially mimicking malignant conditions of the duodeno-pancreatic region. Furthermore, given its unique position, any lesion originating from the duodenal wall can interfere with the normal gastric, pancreatic or biliary flow [7,8].

Brunner glands are branched acinotubular glands predominantly located in the submucosal layer of the duodenum [9]. These glands are arranged in small lobules composed of cuboidal to columnar cells with basally located

nuclei. Their main function is to secrete alkaline substances and bicarbonate to protect the duodenal lining from the harsh gastric acid, as well as to provide a proper environment for the action of intestinal enzymes.

Histologically, BGH is composed of closely packed groups of mucin-secreting glands lacking cellular atypia, separated by thin fibrous septa, which sometimes extend into the muscularis propria [10]. However, because Brunner's gland proliferations are submucosal lesions, they are



often covered by intact mucosa and routine endoscopic biopsy specimens may sometimes fail to establish the diagnosis [11].

The complexity of this rare entity stands in its non-specific clinical presentation in relation to other neoplastic lesions and inflammatory conditions of the duodenum. Most common symptoms of Brunner's gland lesions include abdominal pain, nausea, vomiting or anemia [12], while weight loss was reported in just a few cases [13,14]. On rare occasions, BGH was associated with obstruction of the ampulla of Vater leading to consequent pancreatitis [15], a phenomenon also documented in the current presented case.

Regarding diagnostic workflow, CT scan and endoscopic studies reveal nonspecific findings, sometimes being difficult to differentiate BGH from other benign lesions, inflammatory conditions or malignancies [16]. Therefore, recent studies suggest that endoscopic ultrasound (EUS) may represent the best procedure for the diagnosis of submucosal lesions of the small intestine [13]. Unfortunately, in our case EUS was not available. In terms of dimensions, most BGH present as small lesions, rarely being larger than 5 cm [9]. Literature data favors endoscopic polypectomy as treatment of choice when dealing with small tumors [5,11,17], while surgical excision is preferred in case of large lesions or whenever there is uncertainty regarding the malignant nature of the proliferation [12]. In this case, the patient exhibited a large polypoid duodenal mass, which is a particularly uncommon variant of BGH. Furthermore, due to concerns raised by the clinical presentation about a potential malignant process, surgical excision was recommended to achieve a definitive histopathological diagnosis.

The differential diagnosis of BGH includes both epithelial lesions (Brunner gland hamartoma, duodenal adenocarcinoma, pancreatic ductal adenocarcinoma, neuroendocrine tumors) and mesenchymal proliferations (leiomyoma, lipoma, gastrointestinal stromal tumors) [10]. Our patient was diagnosed with BGH of the duodenum based on the above radiological and endoscopic findings together with detailed histological examination of the resected specimen.

Even though the exact cause of this rare entity is still unknown, it has been postulated that chronic pancreatitis, *H. pylori* infection, gastric acid hypersecretion and mucosal injury may play an important role in the pathogenesis of BGH [6,16,18]. In our case, the patient's history of acute pancreatitis 5 years before the current presentation was, most probably, the leading event in the pathophysiological chain of events, while no data regarding *H. pylori* infection were available.

Malignant transformation of BGH is particularly rare, and it is mostly associated with gastric foveolar metaplasia of the duodenal mucosa [19].

The spectrum of Brunner's gland proliferations includes lesions with distinct molecular profiles, which are not yet fully understood. LRIG1 (Leucine-rich repeats and immunoglobulin-like domains 1) maintains the normal activity

of progenitor cells in Brunner's glands and duodenal epithelium by suppressing ErbB signaling pathway, therefore the loss of LRIG1 was linked to Brunner's glands expansion in mice and intestinal adenomas in humans [20]. In addition, Ortega et al. suggests that G12D point mutation in the KRAS (Kirsten rat sarcoma) gene plays a key role in the development of Brunner's gland adenoma and duodenal carcinogenesis sequence [21]. Some other germline mutations (SMAD4/DPC4, PTEN) have also been reported [22,23]. These genetic alterations may cumulatively promote Brunner's gland neoplasia, however further validation is needed.

Feyter classifies BGH into three main subtypes: diffuse nodular hyperplasia (type 1); circumscribed nodular hyperplasia (type 2) and adenomatous hyperplasia (type 3) [16,24]. Out of these three categories, type 2 is the most common one, being mostly located in the duodenal bulb. The diffuse nodular type, which was also the histological type of BGH found in the case herein presented, can frequently mimic a malignant process [24]. The duodenal bulb accounts for 57% of BGH, while postbulbar regions of the duodenum are less frequently affected by Brunner glands proliferations [17,24].

BGH represents a unique and uncommon lesion of the duodenum, therefore the integration of data regarding patients' history, radiological studies, histological features and more recently molecular data, play a vital role in understanding Brunner's glands proliferations. Consequently, this case illustrates the importance of a multidisciplinary approach when dealing with difficult cases.

## Conclusion

Large diffuse BGH associated with upper gastrointestinal tract symptoms is a rare entity, with only few cases reported in the literature. By presenting this rare, unusual case, our goal was to highlight the specific diagnostic criteria as well as difficulties when setting the pathological diagnosis of BGH. Although BGH is a benign condition, the diagnosis in routine pathological activity might be challenging, as it can mimic a malignant process from the duodeno-pancreatic region.

## Authors' contributions

GNR (Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Visualization, Software)

ANB (Writing – review & editing, Supervision, Formal Analysis, Validation)

EAS (Conceptualization, Visualization, Supervision)

## Conflict of interest

None to declare.

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