

## CASE REPORT ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

# Brunner's gland hamartoma after chemotherapy in a patient with diffuse large B-cell lymphoma

Brunner's glands are organs of the exocrine system located in the submucosal layer of the duodenum. We describe a rare case of Brunner's gland hamartoma causing almost total pyloric obstruction. The patient had been diagnosed with diffuse large B-cell lymphoma of the stomach and had been treated successfully with six cycles of immuno-chemotherapy: Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Six months later, the patient presented with symptoms of gastric obstruction. Upper endoscopy showed a mass that was later resected. The histological analysis was compatible with a Brunner's gland hamartoma. The patient has had a complete recovery. This report underscores the necessity for vigilance for secondary pathologies post-chemotherapy in the gastrointestinal tract, even following complete response of the neoplasm.

Brunner's glands are organs of the exocrine system located in the submucosal layer of the duodenum. Brunner's gland hyperplasia (BGH), also referred to as Brunner's gland adenoma, hamartoma or Brunneroma, is a rarely encountered duodenal lesion with benign and polypoid-like characteristics that comprises not more than 5% of benign duodenal tumors. Clinical symptoms are infrequent due to small size masses and are the results of blood loss and obstruction.<sup>1,2</sup>

We describe the case of a 52-year-old patient with gastrointestinal obstruction presenting after successful chemotherapy for gastric diffuse large B-cell lymphoma (DLBCL). Histological analysis of the mass causing the obstruction showed BGH not found in prior examinations. The report discusses the implications of this finding in the context of post-chemotherapy surveillance and the potential for BGH to manifest as a secondary complication.

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Αμάρτωμα των αδένων  
του Brunner μετά από  
χημειοθεραπεία σε ασθενή  
με διάχυτο Β-λέμφωμα  
από μεγάλα κύτταρα

Περίληψη στο τέλος του άρθρου

### Key words

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## CASE PRESENTATION

A 52-year-old man presented with epigastric pain and weight loss. Laboratories showed mild anemia (hemoglobin 12.5 g/dL) and mild leucocytosis (white blood cell count  $10.6 \times 10^3/\mu\text{L}$ ). Contrast enhanced computed tomography (CT) of the upper and lower abdomen, and of the retroperitoneum showed thickening of the gastric mucosal layer. Borderline-enlarged lymph nodes were also found proximal to the pylorus and at the hepatogastric ligament.

Upper endoscopy was later performed, which showed a large, ulcerated lesion with indurated margins and irregular borders in the pylorus. The lesion demonstrated signs of recent hemorrhage and was infiltrating the duodenal bulb. The second (descending) part of the duodenum showed no findings. The lesion was biopsied and histological analysis revealed tissue infiltration by neoplastic cells with diffuse pattern, negative for the pan-keratin marker and with lymphocyte characteristics, mostly large in size. The immunohistochemistry markers of the large B-cells were as follows: CD20 (+), bcl-6 (+), MUM-1 (+), p53 (+), 60% Ki-67 (+), bcl-2 (–).

The biopsy was compatible with infiltration by centroblastic DLBCL. The patient received six cycles of immunochemotherapy (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone [R-CHOP] protocol), which is the standard treatment for DLBCL.<sup>3</sup> Complete remission of the disease was achieved by the end of the treatment.

Six months later, the patient complained about difficulty digesting large food portions, epigastric pain, and vomit. Positron emission tomography-CT (PET-CT) results were not conclusive regarding the presence of disease. Upper endoscopy and endoscopic ultrasound found a mass causing almost total pyloric obstruction, not allowing for the endoscope to pass through (fig. 1). The endoscopic ultrasound showed thickening of the gastric wall, mainly of the mucosal layer. The mass was biopsied, and microscopic examination revealed gastric mucosa characteristics from the pylorus, the transitional zones and in some samples from the duodenum. The main findings were indicative of absence of DLBCL disease, presence of small-sized lymphocytes with a higher proportion of T-cells than B-cells, in clusters, hyperplasia of the mucosal layer, raising the suspicion for a gastrointestinal stromal tumor (GIST), morphological changes found in chronic atrophic gastritis and presence of *Helicobacter pylori*-like bacteria. Billroth II gastrectomy was performed, and the histopathology of the surgical resection specimen demonstrated a non-specific reactive lymphocyte response and hyperplasia of Brunner's glands, compatible with a Brunner's gland hamartoma (fig. 2). The patient had a complete recovery with no complications.

## DISCUSSION

Brunner's glands are exocrine organs that are located



**Figure 1.** Endoscopic images of the mass that was obstructing the pylorus.



**Figure 2.** Biopsy of the mass. Hyperplasia of Brunner's glands.

mainly in the submucosal layer of the duodenum and protect the proximal duodenal wall by neutralizing the acidic contents from the stomach via alkaline fluid secretion.<sup>4,5</sup> The glands are described as branched and acinotubular,<sup>6</sup> and the excretory duct of each gland reaches through the muscularis mucosae to empty its products into the crypts of Lieberkühn in the duodenum.<sup>4</sup> Brunner's glands proliferation is described differently based on the size of the lesion and its characteristics. The term "hyperplasia" is mostly used for lesions less than 0.5 cm with Brunner's gland histology observed in at least 50% of the submucosa of the biopsy under the microscope, with no characteristics indicating dysplasia,<sup>7</sup> while the terms "hamartoma" and "adenoma" are used for lesions larger than 0.5 cm and "hamartoma" specifically for those that also contain adipose tissue, smooth muscle tissue.<sup>6</sup>

Primary duodenal tumors are rare, accounting less than 1% among the total gastrointestinal tumors. BGH is a rare, benign, proliferative lesion arising from the Brunner's glands of the duodenum, accounting for 10.6% of benign tumors of the duodenum.<sup>8</sup> Since Salvioli described the first case of benign duodenal Brunner's gland adenoma in 1876,<sup>9</sup> sporadic reports have been recorded.

Patients are equally men and women of middle age and most of them are asymptomatic, and lesions are discovered incidentally.<sup>1,10,11</sup> However, these lesions manifest occasionally as a rare cause of duodenal obstruction<sup>1,2,7,12,13</sup> or upper gastrointestinal bleeding.<sup>1,8,13–22</sup> Intestinal regurgitation has also been reported.<sup>23,24</sup>

Preoperative diagnosis can be challenging. X-ray barium examinations often yield nonspecific results due to the presence of either a sessile or pedunculated polypoid-filling defect in the duodenal bulb. Endoscopy plays a

crucial role not only in diagnosing but also in treating BGH, as it allows for both histological confirmation and tumor removal. However, endoscopic pinching biopsies frequently result in negative findings because the tumors are typically covered by a thick, intact duodenal mucosa at the biopsy sites, preventing the biopsy from reaching the deeper submucosal tumor tissue.<sup>25</sup> The pathomorphological characteristics of Brunner's gland include nondysplastic, lobulated glands. Hyperplasia of these glands is categorized into three types: diffuse hyperplasia, nodular hyperplasia, and adenomatous hyperplasia, which may occur with or without erosion or ulceration.<sup>8</sup> BGH can be treated either with endoscopic<sup>11,14,16,20</sup> or surgical resection.<sup>1,2,7,10,17,18,21,24</sup> However, it is still controversial whether asymptomatic BGH requires surgical excision even though it is preferred to be removed in order to prevent future complications. BGH is a benign tumor; however, there are few reported cases with focally atypical hyperplasia.<sup>11,26</sup> It is significant to note that carcinoma can develop from Brunner's gland adenoma.<sup>27,28</sup> In a case-series of 27 patients with BCH, focal sclerosis was present in 93% of the hamartomas, potentially

resembling an adenocarcinoma. The removal of these lesions, either through surgical or endoscopic methods, was uncomplicated, and patients generally have a positive long-term prognosis.<sup>13</sup>

The pathogenesis of the disease is still incomplete. It has been hypothesized that *Helicobacter pylori* infection, hyperchlorhydria, and inflammation of the gastrointestinal tract could be contributing factors.<sup>6,29</sup> *Helicobacter pylori* has been reported at greater rates in the gastric mucosa of patients that were diagnosed with Brunner's gland hyperplasia or hamartoma.<sup>30,31</sup> There has also been a case of Brunner's gland adenoma combined with gastric neuroendocrine carcinoma.<sup>32</sup>

To our knowledge, there has been no presented link between BGH and DLBCL or chemotherapy.

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#### ΠΕΡΙΛΗΨΗ

##### Αμάρτωμα των αδένων του Brunner μετά από χημειοθεραπεία σε ασθενή με διάχυτο Β-λέμφωμα από μεγάλα κύτταρα

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Οι αδένες του Brunner είναι όργανα του εξωκρινούς συστήματος που βρίσκονται στην υποβλεννογόνια στιβάδα του δωδεκαδακτύλου. Περιγράφουμε τη σπάνια περίπτωση ασθενούς με αμάρτωμα στους αδένες του Brunner που προκάλεσε σχεδόν ολική πυλωρική απόφραξη. Ο ασθενής είχε διαγνωστεί αρχικά με διάχυτο λέμφωμα από μεγάλα Β λεμφοκύτταρα στον στόμαχο και είχε αντιμετωπιστεί επιτυχώς με έξι κύκλους ανοσο-χημειοθεραπείας: ριτουξιμάμπη σε συνδυασμό με κυκλοφωσφαμίδη, δοξορουμπικίνη, βινκριστίνη και πρεδνιζολόνη (R-CHOP). Έξι μήνες αργότερα ο ασθενής παρουσίασε συμπτώματα γαστρικής απόφραξης. Η γαστροσκόπηση ανέδειξε μια μάζα που αργότερα εξαιρέθηκε. Η ιστολογική ανάλυση ήταν συμβατή με αδένωμα των αδένων του Brunner. Ο ασθενής είχε πλήρη ανάρρωση. Η παρουσίαση του ενδιαφέροντος περιστατικού τονίζει την ανάγκη για επιτήρηση δευτερογενών παθολογιών μετά τη χημειοθεραπεία στον γαστρεντερικό σωλήνα, ακόμη και μετά από πλήρη ανταπόκριση του νεοπλασματικού νοσήματος.

**Λέξεις ευρετηρίου:** Αμάρτωμα των αδένων Brunner, Λέμφωμα, Χημειοθεραπεία

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