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Prevalence of Duodenum Brunner Gland Crush Artifact: A Retrospective Study

Duodenum Brunner Bezi Ezilme Artefaktının Görülme Sıklığı: Retrospektif Bir Çalışma

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ÖZ

Amaç: Bu çalışmanın amacı, az bilinen bir antite olan Brunner bezi ezilme artefaktının şiddeti ile yaş, cinsiyet ve patolojik tanı gibi hasta özellikleri arasındaki ilişkiyi araştırmaktır.

Araçlar ve Yöntem: Ocak 2019 - Ocak 2020 tarihleri arasında Selçuk Üniversitesi Tıp Fakültesi patoloji laboratuvarına gelen 128 hastaya ait duodenum endoskopik biyopsileri retrospektif olarak incelendi. Biyopsi materyallerinden Hematoksilen-eozin ve histokimyasal PAS boyalarına sahip hasta lamları veri kaynağı olarak kullanıldı. Hastalar ezilme artefaktının şiddeti ve lokalizasyonuna göre birkaç sınıfa ayrıldı. Kategorik değişkenlerin karşılaştırılmasında ki-kare testi kullanıldı.

Bulgular: Toplam 91 (%71) olguda ezilme artefaktı izlenmiştir. Ezilme artefaktının miktarına gore sınıflandırma sonuçları, 91 olgudan 64 (%50) olgunun hafif, 20 (%16) olgunun orta ve 7 (%5) olgunun şiddetli olduğunu göstermektedir. Ayrıca 28 (%21) olgu mukozada, 14 (%11) olgu submukozada ve 15 (%12) olgu dış alanda lokalizedir. Ezilme artefaktı ile yaş, cinsiyet ve patolojik tanı arasında istatistiksel olarak anlamlı ilişki bulunamamıştır.

Sonuç: Brunner bezi ezilme artefaktı, patolojik bir bulgu olmamasına rağmen neoplazmlar ve enfeksiyöz hastalıklar gibi çeşitli hastalıklar ile morfolojik olarak karışıklığa neden olabilmektedir. Çalışma, gereksiz prosedürleri ve daha da önemlisi yanlış tanıyı ve gereksiz tedaviyi önlemek için Brunner bezi ezilme artefaktına ilişkin değerli bilgiler sağlamaktadır.

Anahtar Kelimeler: artefaktlar; brunner bezleri; duodenum; endoskopi

ABSTRACT

Purpose: The overall purpose of this study is to raise the awareness of the Bruner gland crush artifact, which is a less known entity. Specifically, this study investigates the relationship between the severity of crush artifact and patient characteristics such as age, gender, and pathological diagnosis.

Materials and Methods: Duodenum endoscopic biopsies of patients who presented to the pathology laboratory of the Selcuk University Medical Faculty between January 2019 and January 2020 were retrospectively examined. The data source is patients' slides possessing Hematoxylin-eosin and histochemical PAS stains from biopsy materials. The patients are grouped into several classes according to the crush artifact's severity and location. Chi-square was used in the comparison of categorical variables.

Results: Crushing artifacts were found in 91 (71%) patients. Classification results show that out of 91 (71%) cases, 64 cases (50%) are mild, 20 cases (16%) are moderate, and 7 cases (5%) are severe according to the amount of crush artifact. Also, 28 cases (21%) are located in the mucosa, 14 cases (11%) in the submucosa, and 15 cases (12%) are in the outer area. There was no statistically significant relationship between the amount of crush artifact and age, gender, and pathological diagnosis

Conclusion: Although it is not a pathological finding, Brunner gland crush artifact can be morphologically confused with various diseases such as neoplasms and infectious diseases. The study provides valuable insight regarding the Brunner gland crush artifact to prevent unnecessary procedures and, more importantly, misdiagnosis and unnecessary treatment.

Key Words: artifacts; brunner glands; duodenum; endoscopy

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INTRODUCTION

Histomorphology is a procedure based on the examination and interpretation of tissues under a microscope, and it is the gold standard for definitive diagnosis.[1,2] It is very important to maintain the morphological details of tissue components to make the correct diagnosis.[3]

Artifacts can disrupt or alter the normal structure of tissue components. This can lead to misdiagnosis or difficulty in interpretation. In the gastrointestinal system pathologies, discohesive cells which are shed from the denuded superficial epithelium can be confused with signet ring cell carcinoma.[1,4] Thus, it is very important to identify the commonly occurring artifacts during the histopathological diagnosis of tissue sections.[2]

Crush artifact after an endoscopic biopsy is common in duodenal Brunner glands. Generally, the artifact area may not be noticed in cases with the small size of this area and in cases examined without histochemical Periodic acid Schiff (PAS) staining. If it is noticed, it may cause difficulty in diagnosis or misdiagnosis, especially in pathologists who have no previous experience or have not seen it before. Crush artifact was variable present in the mucosa within or among crypts, in the submucosa, and between villi or completely outside. There is only one publication about this subject[5] and it has been mentioned in several books.[6,7,8]

MATERIALS and METHODS

Duodenum endoscopic biopsies of patients who presented to the pathology laboratory of the Selcuk University Medical Faculty between January 1st of 2019 and January 1st of 2020 were retrospectively examined. The data source is patients' slides possessing Hematoxylin-eosin and histochemical Periodic acid Schiff (PAS) stains from duodenum endoscopic biopsy materials. Patient age, gender, and histopathological diagnosis were obtained from pathology reports of the patients. Cases without histochemical PAS staining were excluded from the study. No ancillary staining was performed. The areas where the regular tubuloalveolar glandular structure disappeared and flattened and the spindle of cells were defined as Brunner gland crush artifact. The materials were divided into two groups as with crush artifact and without crush artifact. Also, the group of crush artifacts was divided into three subgroups as "mild" (visible at high magnification or histochemical PAS staining), "moderate" (visible at low magnification), and "severe" (creates mass effect). The materials were divided into three groups according to localization of artifact as located in the "mucosa" (Figure 1, 2), located in the "submucosa" (Figure 3), and located in the "outer area" (Figure 4). The patients were additionally divided into four age groups as 0-20, 21-40, 41-60, and >60 years old. Recorded data comprised patient age and gender and the histopathologic diagnosis. Statistical analyses were carried out using SPSS 18.0 software (IBM Inc, Chicago). Chi-Square was used in the comparison of categorical variables. $P<0.05$ values were considered statistically significant.

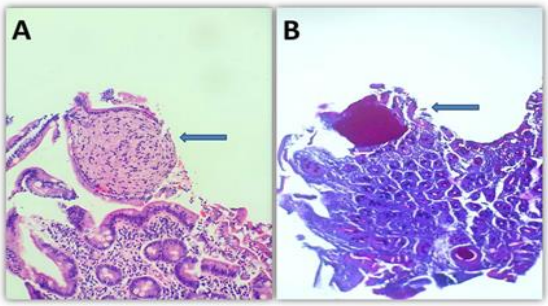

Figure 1. A- Crush artifact in the mucosal area within the villi (arrows) (H&E, ×100). B- Histochemical PAS staining (HC, ×40).

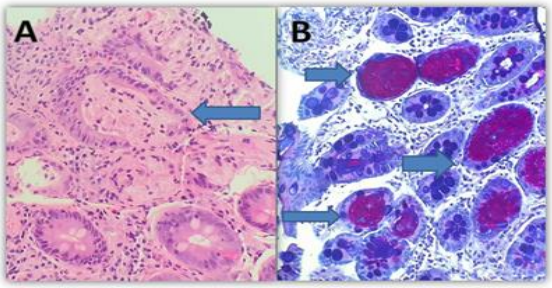

Figure 2. A- Crush artifact in the duodenal crypts (arrows) (H&E, ×200). B- Histochemical PAS staining (HC, ×200).

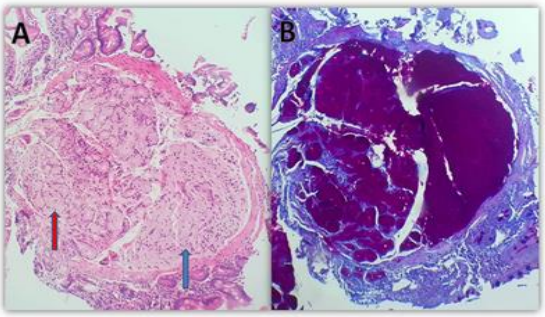

Figure 3. A- Crushed Brunner glands (blue arrow) adjacent to non-crushed glands (red arrow) in the submucosa (arrow) (H&E, ×40). B- Histochemical PAS staining (HC, ×40).

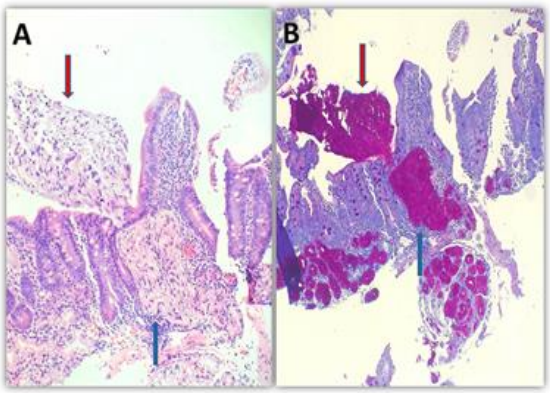

Figure 4. A- Crush artifact within the mucosa (blue arrow) and located in the outer area (red arrow) (H&E, ×40). B- Histochemical PAS staining (HC, ×40).

This retrospective study was approved by the Institutional Ethics Committee on December 30th, 2020 by the decision number 2020/568.

RESULTS

The sum of 128 cases was included in the study. The mean age of the patients was 29 years. 82 (64%) of all the patients were female and 46 (36%) were male. Histopathologically, 22 (17%) of the cases were diagnosed as celiac, 18 (14%) were diagnosed as peptic duodenitis, 3 (1%) were diagnosed as non-specific chronic duodenitis. No pathological diagnosis was detected in 85 (66%) cases.

Crushing artifacts were found in 91 (71%) patients. The distribution of the cases according to the amount of crush artifact is provided in Table 1.

Table 1. Percentage distribution by size of cases showing crush artifact.

Cases with crush artifact	% (n)
Mild (+)	50% (64)
Moderate (++)	16% (20)
Severe (+++)	5% (7)
Non-crushing artifact	29% (37)

The distribution of Brunner gland crush artifact according to its localization is provided in Table 2.

Table 2. Distribution percentage of Brunner glands showing crush artifact according to localization.

Localization	% (n)
Mucosa	21% (28)
Submucosa	11% (14)
Outer area	12% (15)
Mucosa and submucosa	6 % (8)
Mucosa and outer area	12% (15)
Submucosa and outer area	8 % (10)
Mucosa, submucosa and outer area	1 % (1)
Non-crushing artifact	29% (37)

The distribution of the cases with Brunner gland crush artifact showing mass effect according to their localization is provided in Table 3.

Table 3. Distribution of cases showing the mass effect of Brunner gland crush artifact according to their localization.

Localization	Severe (+++) crushing artifact (n)
Mucosa	2
Submucosa	0
Outer area	1
Mucosa and submucosa	2
Mucosa and outer area	0
Submucosa and outer area	1
Mucosa, submucosa and outer area	1

The regular appearance of the Brunner gland was observed in 103 (80%) cases. The distribution of Brunner glands showing crush artifact with regular Brunner glands is provided in Table 4.

Table 4. Percentage distribution of regular Brunner glands with Brunner glands showing crush artifact.

Parameters	% (n)
RBN- CA+	5%(6)
RBN+ CA-	15%(19)
RBN- CA-	14%(18)
RBN+ CA+	66%(85)

RBN: Regular Brunner glands, CA: Crush artifact.

There was no statistically significant relationship between the amount of crush artifact and age, gender, and pathological diagnosis. Also, there was no statistically significant relationship between the localization of crush artifact and age, gender, and pathological diagnosis (p>0.05) (Table 5).

Table 5. Relationship between amount and localization of Brunner gland crush artifact and age, gender, and pathological diagnosis.

Relations	Pearson Chi-square	p
ACA - Age	21.628	0.421
ACA - Gender	2.685	0.913
ACA - PD	20.841	0.469
LCA - Age	11.403	0.249
LCA - Gender	0.474	0.902
LCA - PD	19.653	0.386

P<0.05 (ACA: Amount of the crush artifact, LCA: Localization of the crush artifact, PD: pathological diagnosis)

DISCUSSION

Tissue artifacts can arise from any of the numerous steps between removal of the tissue by endoscopic biopsy and examination under the microscope by the pathologist.[2]

Brunner glands are lobular structures of tubuloalveolar glands, lined by cuboidal to columnar cells with pale, uniform cytoplasm and oval, basally located nuclei. They are usually limited to the submucosa of the duodenum; however, up to one-third of them can stay within the deep mucosa in the absence of pathology. In this study, 40 percent of the Brunner glands showing crush artifacts were localized in the mucosa and 26 percent of the Brunner glands in the submucosa. In the Brunner glands showing crushing artifact, the normal tubuloalveolar structure disappeared, and it was generally observed as solid structures. The crushing artifact contains spindled, compressed epithelial cells, and these cells show positive staining with histochemical PAS as in normal structure.[6]

Crushing artifacts may comprise while pushing the biopsy forceps, removing tissue with forceps, or cutting tissue, particularly when a blunt blade is used. Crushing can compress the chromatin out of nuclei resulting in loss of cytological details. The force also causes mucosal hemorrhage and tissue distortion.[7]

Duodenal inflammation may develop due to various reasons and different pathological mechanisms may cause the same histological appearance. Duodenal inflammation may be divided into two main groups in terms of etiology: duodenitis secondary to H pylori infection and duodenitis due to other reasons such as Celiac disease, inflammatory bowel diseases, drugs, Whipple's disease, or parasitic infections.[8,9] In the study named "A Brief Examination of Brunner Gland Paste" by Gonzalez R.S[5], which is the only study related to this subject in the literature, no significant relationship was found between Brunner gland crush artifact and pathological diagnosis, patient age, and sex. Similarly, in this study, no significant relationship was found between crush artifact and pathological diagnosis, age, and gender.

Brunner gland proliferative lesions include Brunner gland hyperplasia, Brunner gland adenoma, and Brunner gland hamartoma. A limited number of Brunner gland adenocarcinomas have been reported in the literature. The crushing artifact observed in such pathological conditions can easily lead to misdiagnosis.[6,10] Among our cases, there was no proliferative lesion.

Although Brunner gland crush artifact can often be seen in duodenal endoscopic biopsy materials, it does not cause diagnostic confusion as it is usually mild. If the crush artifact has a mass effect and is detected outside of its normal localization, it may cause diagnostic difficulties.[5] In this study, there were severe crushing artifacts in the Brunner glands in seven cases that could cause a mass effect. Additionally, these cases with crush artifacts were outside of their normal localizations.

Brunner glands are stained positively with histochemical PAS stain. Among infectious diseases, Whipple disease and Mycobacterium avium complex (MAC) disease can occur in the duodenum lamina propia with the accumulation of a large number of foamy histiocytes. Foamy macrophages react positively with PAS staining. Brunner gland crush artifact can mimic these lesions both histomorphological and histochemically with PAS-positive staining. The demonstration of histiocytes with CD68, which is the specific marker of histiocytes, can be evaluated in fa-

vor of Whipple disease and MAC disease. Also, the clinical symptoms of Whipple disease and MAC disease can be helpful in differential diagnosis.[11,12]

Granular cell tumors are another lesion that may confuse diagnosis with the Brunner gland crush artifact. They are extremely rare in the duodenum, and most of them have a submucosal location. Tumor cells are stained positively by histochemical PAS stain, such as Brunner glands. Immunohistochemically, positive staining of tumor cells with S100 and CD68 may help evaluate in favor of granular cell tumor. Furthermore, endoscopic and radiological detection of a mass in the duodenum is the finding in favor of granular cell tumor.[13,14]

Crushed artifacts of Brunner gland lesions may give spindle cells appearance mimicking spindle cell lesions. Spindle cell neoplasms may cause histological confusion in the small endoscopic biopsy, especially when the crush artifact is located in the submucosa. Among these, the myxoid type peripheral nerve sheath tumor may exhibit similar morphological features to the crush artifact particularly.[10,15] Crushed Brunner glands are stained with histochemical PAS staining while tumor cells are not stained with PAS staining. Also, positive staining is observed in tumor cells with immunohistochemical S100 staining.[16,17] Morphological features similar to the Brunner gland crush artifact can also be observed in other spindle cell neoplasms. Diagnostic confusion can be avoided by evaluating clinical, radiological, and endoscopic findings together. The use of immunohistochemical markers as an auxiliary technique may be beneficial in the differential diagnosis.

Crush artifact is a common and easily recognizable entity. With the crush artifact, the normal structure of the Brunner glands can be completely disrupted, and it can be seen outside of the normal localization of it as in our study. In such cases, clinical findings, radiological findings, and ancillary staining techniques may help in the differential diagnosis. The study provides valuable insight regarding the Brunner gland crush artifact to prevent unnecessary procedures and, more importantly, misdiagnosis and unnecessary treatment.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Authors' Contributions

Concept/Design: MÇ. Data Collection and/or Processing: MÇ. Data analysis and interpretation: MÇ. Literature Search: MÇ. Drafting manuscript: MÇ. Critical revision of manuscript: MÇ. Supervision: MÇ.

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