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The main histopathological gastric lesions in obese patients who underwent sleeve gastrectomy

Tüp gastrektomi yapılan obez hastalardaki ana histopatolojik lezyonlar

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ABSTRACT

Objectives: The prevalence of obesity has been increasing in recent decades in developed countries. Slight and moderate obesity is associated with various co-morbidities. The most severe forms of obesity are consistently associated with the development of various health problems. The aim of this study was to investigate and analyze the most important histopathological lesions obtained by sleeve gastrectomy postoperatively.

Materials and methods: We investigated 87 surgical interventions, performed between October of 2007 and June of 2008 for bariatric therapy procedures, using sleeve gastrectomy. All the specimens (gastric, liver and adipose tissue) were processed in the Pathology Department. The specimens were fixed in buffered formalin, and then stained with hematoxilin eosin.

Results: The female to male ratio was 2/1. Young patients aged between 31-40 years were most frequently (39.1%) affected. The frequent histopathological lesions were parietal cells hyperplasia (63.2%), ulcerations (34.5%), lymph nodes hyperplasia in lamina propria (33.3%), active gastritis (23.0%) and other lesions (10.3%). The parietal cells hyperplasia found in fornix and corpus mucosa was the most frequent lesion encountered in obese patients. All three cases showed an important steatosis of the hepatocytes by liver biopsy.

Conclusions: Our results suggest that the histopathology analysis of the gastric mucosa of the fornix and other tissues (as the liver) is relevant for the comorbidities of the obese patients. The evaluation of the histopathological gastric and liver aspects could improve the understanding of the local mechanism and the outcome of the patients.

Key words: Morbid obesity, sleeve gastrectomy, histopathology, lesions

ÖZET

Amaç: Obezite prevalansı son on yıllarda gelişmiş ülkelerde artmaktadır. Hafif ve orta obezite çeşitli morbidite ile birliktedir. Obezitenin ağır formları çeşitli sağlık problemleri ile birliktedir. Bu çalışmanın amacı tüp gastrektomi ile elde edilen dokudaki histopatolojik lezyonları araştırmak ve analiz etmektir.

Yöntemler: Ekim 2007 ile haziran 2008 arasında tüp gastrektomi uygulanan 87 cerrahi girişimden elde edilen dokular incelendi. Tüm doku örnekleri (mide, karaciğer, yağ dokusu) Patoloji bölümünde incelendi. Doku örnekleri formalinde fiske edilerek hematoksieln eozinle boyandı.

Bulgular: Kadın/erkek oranı 2/1 idi. Yaşları 31-40 arasında olan geç hastalar en sık etkilenmişti (%39.1). Sık rastlanan histopatolojik lezyonlar pariyetal hücre hiperplazisi (%63.2), ülserasyonlar (%34.5), lamina propriada lenf nodu hiperplazisi (%33.3), aktif gastrit (%23.0) ve diğer lezyonlar (%10.3) oranlarında saptandı. Mide forniks ve korpus mukozasındaki pariyetal hücre hiperplazisi obez hastalarda en sık rastlanan lezyon idi. Karaciğer biyopsi yapılan üç hastada hepatositlerde steatozis saptandı.

Sonuç: Bizim sonuçlarımız obez hastalarda mide forniks mukoza ve karaciğer gibi diğer dokuların histopatolojik analizi ko-morbiditelerle birlikte bulundu. Obez hastalardaki gastrik ve karaciğer lezyonların histopatolojik incelenmesi lokal mekanizmaları ve hastaların sonuçlarını daha iyi anlamaya yardımcı olabilir.

Anahtar kelimeler: Ağır obezite, tüp gastrektomi, histopatoloji, lezyonlar

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INTRODUCTION

According to the World Health Organization, there are an estimated 1 billion adults who are overweight (body mass index, BMI>25 kg/m^2), and 300 million of these are considered clinically obese (BMI>30 kg/m^2)[1]. Such staggering statistics clearly suggest that, despite the overt recognition of the taxing effects of obesity on both medical and social programs, Westernized societies are still succumbing to this global epidemic[1]. While technological progress made over the last 20 years has yielded the tools necessary to comprehensively explore the perturbed biochemistry underlying the obesity, it has also demonstrated that interactions between genetic background and environment are critical for the regulation of adipose mass function[2]. However, prior to our society realizing either of these ambitious concepts, the genetic components underlying common diseases such as obesity must be elucidated with confidence[3].

There are several types of obesity[4]. Monogenic obesity, which is associated with a single gene mutation, has been described in 200 cases. These cases, which abide by the Mendelian laws, are characterized in children by extremely severe phenotypes, and are associated frequently with behavioral, development and endocrine disturbances[5].

Syndromic obesity: There are 20-30 illnesses with Mendelian inheritance in which the patients are obese, are mentally retarded, have dysmorphic features and development anomalies specific to each organ. The analysis of the genetic component of these diseases suggests that multiple genes can produce identical phenotypes. The most known diseases are the Prader-Willi Syndrome (PWS), the Bardet-Biedl Syndrome and the Alström syndrome, but a few more have been reported[6].

Polygenic obesity, or common, regular obesity, appears when the genetic mark of an individual is influenced by the environment, conditioning a low consumption of energy and a great weight gain. In order to understand the genetics - environment interactions, several studies have been initiated based on the analysis of the polymorphism of nucleotides (SNP), or of the repetitions of the bases (poliCA / adenine cytosine or microsatellites) at the level of the candidate genes[7]. Unlike with monogenic obesity, in the case of common obesity, many genes and chromosomal regions contribute to the obese phenotype[8].

Bariatric surgery is an option in severely obese patients, where lifestyle/medication has not been effective[9]. Surgery can be combined with other treatments. Referrals are usually made via a specialist to obesity management service[10].

There are clear guidelines from NICE about who should be considered for bariatric surgery[10,11]. Research suggests that it may be worthwhile for those with a BMI over 30-35. The risk/benefit ratio is less certain for the young, the elderly and those with a BMI >70.

Our study emphasizes the most frequent histopathological lesions detected post surgery, on gastric wall specimens, and liver tissue. The histopathology report is more detailed than the report provided by endoscopy and offers a wide spectrum of lesions according to the pathological status and the outcome of the patients.

MATERIALS AND METHODS

Between October of 2007 and June of 2008, 87 surgical interventions were registered for bariatric therapy procedures, using only sleeve gastrectomy, for morbid obesity diagnosis.

All these cases were processed using only sleeve gastrectomy (LSG). LSG involves a longitudinal resection of the stomach on the greater curvature from the antrum starting opposite of the nerve of Latarjet up to the angle of His[12,13]. The gastric fornix contains 10 to 20 times more ghrelin per 1×g of tissue than the duodenum with diminishing concentrations being found in the jejunum and ileum[14]. The devascularisation of the greater curve is performed using a high complex device named LigaSure Atlas. The part of the stomach along its greater curve is resected. The stomach is "tubulized" with a residual volume of about 150 ml. This volume reduction provides the restricted food intake[15]. This type of gastric resection is anatomically and functionally irreversible[16,17,18]. The rational for starting closer to the pylorus and using a small calibre bougie to fashion the gastric tube is to increase the restrictive character of the procedure. The use of the staplers allows a mechanical three layers suture and then, for a perfect haemostasis a manual continuous suture is used. During the surgery, other interventions were registered, for other conditions; colecystectomies (4/87), hiatal hernia (5/87), abdominoplasty (2/87), abdominal hernias (3/87) and

a liver biopsy (3/87). Written informed consent was obtained from the patients before processing and analyzing the specimens, using consent forms and protocols approved by the Hospital Committee of Ethics in Medical Research.

All the specimens (gastric and liver tissue) were brought into the Pathology Department, fixed and examined using hematoxylin eosin stain. We performed the histopathology on 6 slices of gastric fornix wall and liver tissues. It was performed the standard hematoxilin eosin stain. Mayer's hematoxylin is used because it eliminates the necessity for differentiation and bluing of the section. It can be considered a progressive stain, which produces a stained section with a clearly defined nucleus while the background is completely colorless. The biggest objection to Mayer's hematoxylin as used in the past was that stained slides often became fade after 1 to 3 years. This problem can be eliminated, however, when the slides are washed, after the hematoxylin, in running water for a minimum of 20 minutes.

This method gives consistent results even when more than one person stains sections from the same block. Also, slides may be left in the hematoxylin for hour without over staining.

The cutting of paraffin blocks has been done on the microtom, thickness of 4-5 μ. As an adhesives used to attach sections onto the slides we had egg albumin. Then we have analysed the slides on the Nikon microscope Elipse 200.

RESULTS

The investigated and treated patients were 58 females and 29 men. The range of the age showed the following distribution (Figure 1)

On macroscopic examination we noticed a diverse amount of blood within the cavity of the stomach (Table 1). The blood content of the stomach is the consequence of the revascularization after the removal of the LigaSure Atlas.

Table 1. The repartition of the cases according to the blood amount within the gastric cavity

Blood content of the stomach	No of cases (21)
Massive hemorrhage (100 ml)	14
Moderate hemorrhage (50 ml)	4
Low hemorrhage (15 ml)	3

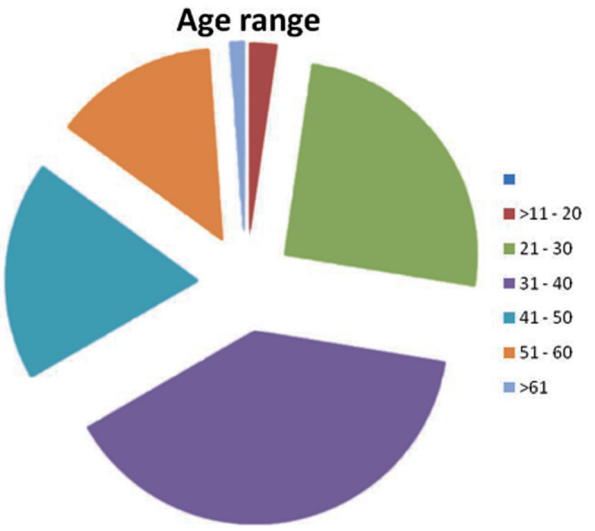

Figure 1. The distribution of patients' ages

Other lesions registered during the macroscopic examination were atrophy gastritis (2 cases) and gastric ulcerations (5 cases). The microscopic examination, on hematoxilin eosin stain, revealed a range of lesions of the gastric wall, especially on the mucosal and submucosal layer (Figure 2).

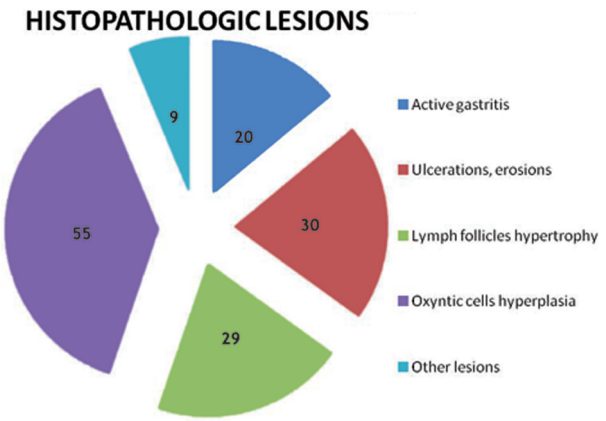

Figure 2. The main gastric mucosal lesions post gastrectomy

We noticed that the most frequent lesion was the hyperplasia of the parietal cells, especially at the gastric fundus (Figure 3, Figure 4). In all the three cases with hepatic steatosis we noticed important cellular lesions on the histologic level (Figure 5, Figure 6).

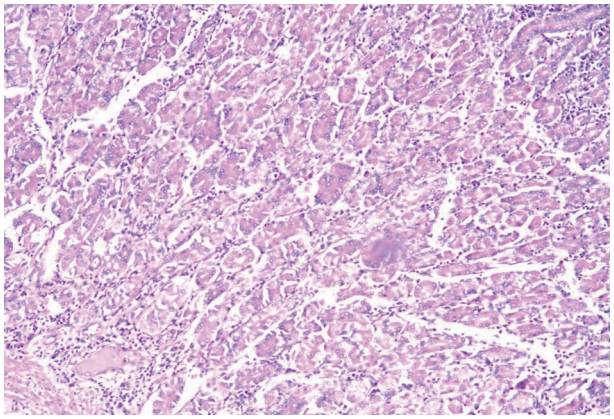

Figure 3. Histological aspect of fornix mucosa in a patient with morbid obesity. Hematoxilin eosin stain, 200x.

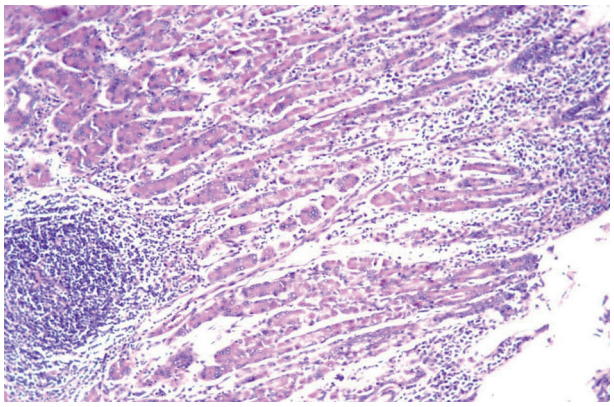

Figure 4. Aspect of the active gastritis in obese patient. Hematoxilin eosin stain, 200x.

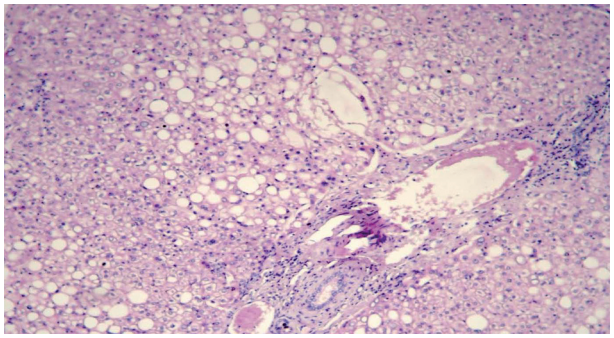

Figure 5. Histopathology aspect of liver steatosis in a patient who underwent bariatric surgery. Hematoxilin eosin stain, 200x.

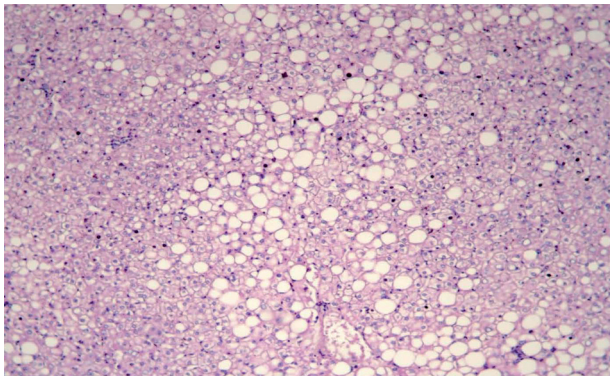

Figure 6. Histopathological pattern in liver steatosis in obese patient. Hematoxilin eosin stain, 200x.

DISCUSSION

Obesity is defined as the body mass index over 30 kg/m^2. [1,4] Obesity has become widespread in developed countries along with a corresponding increase in the prevalence of type 2 diabetes. Although the precise underlying mechanisms in the development of diabetes are as yet unknown, the initial pathophysiological event is usually insulin resistance, which involves a genetic component that is exacerbated by obesity and a sedentary lifestyle[2,3]. There is a significant risk factors and correlation between obesity and insulin resistance in nondiabetic subjects, and obesity exacerbates insulin resistance in diabetic subjects[7,8].

Because of these risks and the evidence for risk reduction associated with weight loss, the National Institutes of Health has recommended weight loss surgery as an appropriate alternative in carefully selected individuals with severe obesity (BMI >40 kg/m2 or those with a BMI >35 kg/m2 and with serious comorbid conditions) when dietary, behavioral, and pharmacotherapy interventions failed[19,20]. Bariatric surgery results in sustained and significant weight loss. The rising prevalence of obesity and the success of surgical interventions led to a marked increase in the number of weight-loss surgeries performed in the United States, from 13.365 in 1998 to 102.794 in 2003[21].

Society of American Gastrointestinal Endoscopic Surgeons has recently published clinical guidelines related to the application of laparoscopic bariatric operations, where the best available evidence of grading and recommendations for practice[19]. The surgical literature awaits the publication

of randomized trials comparing the different surgical therapies. In the absence of such data, present study contributed to determine the most appropriate surgical procedure by investigating the factors related to patients and surgery and the relevance of the histopathology and the provided data, also. Laparoscopic adjustable gastric banding (AGB) is shown to have the lowest perioperative risk and the lowest rate of metabolic complications, but the lowest mean potential weight loss. Biliopancreatic diversion with duodenal switch (BPD-DS) provides the highest and most durable long-term loss of excess body weight, but is the most complex and has the highest complication and mortality rate. All procedures improve comorbidities, though BPD-DS and Roux-en-Y gastric bypass (RGB) provide the most rapid comorbidity improvement. AGB is most reversible, and RGB is the least likely to require reoperation. Experience is accumulating for the sleeve gastrectomy (SG) which is safe and results in early weight loss and ppears to be comparable with other procedures[16].

The gastric sleeve laparoscopic procedure is becoming a well standardized intervention which, after going through the learning process, supposes an operating time of 60 minutes[16,22,23]. Sleeve gastrectomy was first applied in humans as a component of biliopancreatic diversion with duodenal switch (BPD-DS) in 1988[14,24,25]. An important advantage of this procedure is also the removal of the fundic portion of the stomach, which produces ghrelin, a hormone involved in the hunger and fullness mechanisms. Consequently, the hunger sensation is significantly reduced. Besides the waiting period from the first few weeks after the surgery, the patients have little restrictions in what concerns the type of food they eat, but the quantity is drastically reduced[26,27]. In comparison with other procedures, the sleeve gastrectomy lacks the complications induced by the intestinal by-pass: anemia, deficiencies of vitamins and protein and osteoporosis[28,29]. The range of patients to which the procedure is indicated is very wide, including those with an extreme body mass index, both over 60 or between 30 and 35. The sleeve gastrectomy is an irreversible procedure, this being its main disadvantage[17].

The most common complications described by the literature were dumping syndrome, which includes vomiting, reflux, and diarrhea (nearly 20 percent); anastomosis complications (complications resulting from the surgical joining of the intestine and stomach), such as leaks or strictures (12 percent); abdominal hernias (7 percent); infections (6 percent); and pneumonia (4 percent). The overall death rate for the entire 180-day postoperative period studied was low — 0.2 percent (9,10). Readmissions of post-obesity surgery patients for these conditions increased from 6.5 percent to 10.6 percent between 30 and 180 days[9,10].

In the present study, we investigated a group of 87 patients who underwent sleeve gastrectomy as the surgical procedure for obesity between October of 2007 and June of 2008. The study intends to outline the most important histopathological lesions found during the postoperative procedure, more relevant when they are provided by a detailed histological analysis of tissue.

The selection for treatment with this surgical procedure (longitudinal sleeve gastrectomy) was performed only after rigorous laboratory tests were carried out in specialized clinics.

In our study, the females are especially affected (66%), compared with the males (34%); we consider that women's addressability and the wish to look fine are more relevant than in the case of the men.

The analysis of the age range (Figure 1) shows that the most affected are the young patients, between 31-40 years old (39.1%). It is very important to note that this age range at which social accomplishment is achieved.

In the present study, the most frequent histopathological lesions encountered on microscopy were parietal cells hyperplasia (63.2%) (Figure 3), ulcerations (34.4%), lymph nodes hyperplasia in lamina propria (33.3%), active gastritis (23.0%) (Figure 4) and other lesions (10.3%). The oxintic cells hyperplasia was noted in the gastric fornix and corpus and was the most constant lesion encountered in obese patients (Figure 2).

Three cases that underwent liver biopsy showed notable hepatic steatosis (Figure 5, Figure 6). Non-alcoholic fatty liver disease is an increasingly recognized condition varying in degrees of severity from mild steatosis to end-stage liver disease[30,31,32]. The term non-alcoholic steatohepatitis (NASH) has been used to describe the clinical condition[31]. NASH affects 10 to 24% of the general population in various countries[30]. The prevalence is closely related to

concurrent obesity and disturbances in glucose tolerance and insulin resistance[33]. Insulin resistance is linked to the hepatic metabolism of fatty acids and concurrent observed dyslipidemia. The susceptibility to the more advanced forms of NASH is poorly understood. Due to the high prevalence of NASH in subjects with features of the metabolic syndrome and suggested common pathophysiological mechanisms, NASH has been suggested as a new component of the metabolic syndrome[33].

Our study has focused on two important items: firstly, the advantages of the surgical procedure used, longitudinal sleeve gastrectomy and second, the impact of the informations provided by the pathology report according to the most frequent histopathological gastric lesions.

We consider that the histopathological gastric lesions detected after the surgery have an important role, taking into account the prognostic pathology of the patients. It is well known that the complications of these surgical procedures are rare, but may be serious. Therefore, our study proposes to outline that the gastric histopathologic aspects are at least as relevant as the preoperative endoscopy is. Despite the large number of gastric bypasses performed for morbid obesity, very little is known about the histological aspects of the gastric mucosa of obese patients and the relevance of the lesions for the near future outcome post surgery.

For the moment, we have not a histopathological database concerning the follow-up of the obese patients post surgery in order to compare the gastric lesions pre and postoperative but future researches can focus on this issue.

• **Competing interests.** The authors declare that they have no competing interests.

• **Authors' contributions.** The main contribution is part of Dr Vrabie, who processed the specimens in the hospital. Dr Copaescu C helped with their counseling on surgical management. Mrs. Waller and Prof Cojocaru carried out the literature research and helped in drafting the manuscript preparation. Ruxandra Sindelaru helped the translation and improvement of the text.

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