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OBESITY - RISK FACTOR FOR THE OCCURRENCE AND RECURRENCE OF COLORECTAL CANCER

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Colorectal cancer has a significant impact on morbidity and mortality of the population and is a major public health issue. In this context, we propose to discuss three cases of colon or rectum cancers in patients with obesity, nonsmokers, without family or personal history of malignancy and without colonic polyposis. Patients, with ages between 51 and 64 years old, are diagnosed with cancer of the colon or rectum in our clinic and they do not represent surgical emergencies. Surgical interventions were performed without perioperative complications, and patients followed the cancer treatment as recommended. Postoperatively, patients were followed for a period of 5 years, the first 2 years every 3 months, then every 6 months. We present detailed evolution, and we discuss various aspects of these cases.

Key words: colorectal, cancer, obesity, young.

INTRODUCTION

The association of obesity with various cancers is a topic of current interest in the medical literature, as the prevalence of obesity is increasing and oncological treatment costs justify the need for prevention[1]. International Agency for Research on Cancer has proven that there is a clear association between obesity and these cancers: endometrial cancer, esophageal adenocarcinoma, colorectal cancer, postmenopausal breast cancer and renal cell carcinoma[1]. Colorectal cancer has a significant impact on morbidity and mortality of the population, being a major public health issue. According to WHO (World Health Organisation), colorectal cancer is responsible for 694,000 deaths annually, ranking 7th in terms of causes of death in developed countries[2].
The purpose of presenting the next cases, is to contribute to a better understanding of the necessary medical treatment for this pathology and to the implementation of preventive measures.

CASE REPORT

We present the **first case** of a 51 years old female patient (C.G.) known obese for about 20-25 years, with type II diabetes for 10 years, being treated with oral antidiabetics, without any other known disease. She seeks medical attention for abdominal pain in hypogastrium, slowed intestinal transit and thin stool, with insidious onset of symptoms approximately 1 year ago, accompanied by weight loss (about 10kg in the last 6 months) and fatigue. The patient denied a family history of oncological pathology and also denies smoking or alcohol consumption. On physical examination is found grade III obesity with BMI (body mass index) = 43kg / m^2, waist circumference of 130 cm and slightly dehydrated skin[3]. At local examination, we found increased volume abdomen by adipose tissue, slightly sensitive at touch in hypogastrium, without signs of peritoneal irritation and rectal examination with supple rectal ampoule and faeces of normal aspect.
In the groin, bilateral, we can feel lymph nodes under a centimeter diameter, mobile, painless. No other changes were detected in clinical examination.
The patient is hospitalized for performing investigations in the department of surgery. On admission were performed blood tests, electrocardiogram (ECG), chest X-ray and abdominal radiography.
Blood tests revealed neutrophilic leukocytosis (13 340 WBC /mm^3 with 76% neutrophils), normal hemoglobin and platelets, blood glucose of 135mg /dl, normal CEA (carcinoembryonic antigen) and CA19.9 (cancer antigen 19-9), without any other changes. The electrocardiogram did not show any signs of arrhythmias or ischemia. Chest radiography and abdominal radiography did not show any pathological changes.
We decided to perform a colonoscopy in addition to other investigations. It highlighted, at about 35 cm from the anus, a stenosing tumor, brittle to the touch and that can not be surpassed with the flexible tube.
For staging the disease an abdominal pelvic CT scan (X-ray computed tomography) was performed. It detected grade III hepatic steatosis without liver secondary tumors, in physiological involution uterus and annexes,

and sigmoid colon wall thickening on a 5 cm length with luminal narrowing and edema of the adjacent tissues; mesenteric lymphadenopathy milimetric in thickness; no other injuries detected in CT scanning. Based on clinical and laboratory data, we diagnosed the stenosing sigmoid tumor with malignant potential[4] and surgery was decided. Preoperative preparation was done with osmotic laxative (macrogols), rifaximin taken orally and 3rd generation cephalosporin intravenously, all administered 24 hours before surgery. Under general anesthesia with intubation was practiced exploratory laparotomy and was discovered a sigmoid stenosing tumor, without macroscopic secondary determinations. We decided to practice sigmoid colectomy (figure 1) with splenic angle mobilization and colorectal end-to-end anastomosis.

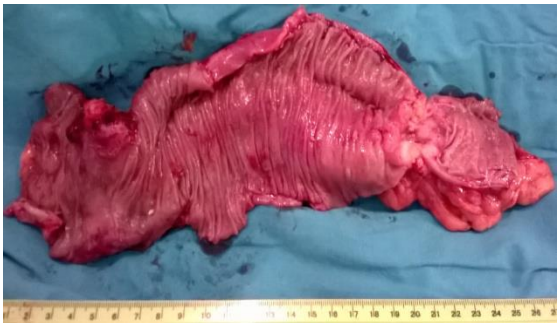

Figure 1. Sigmoid colectomy

Postoperatively, under treatment (antibiotic therapy, anti-inflammatory, oral antidiabetic agents, painkillers, low molecular weight heparin, gastric secretion inhibitors, prokinetic and intravenous fluid and electrolyte support), the patient has favorable evolution and is discharged in good condition following to be taken into oncological evidence. Histopathological examination diagnosed adenocarcinoma of colon T3N0 G2 and corroboration with clinical data helps us to find out the disease stage - T3N0M0=IIA. In the scientific literature, this stage has 84.7% survival at 5 years, and the risk of relapse up to 8%[2]. Postoperatively the patient received chemotherapy - 6 cycles - as the oncologist indicated and returned to regular checks every 3 months for 2 years and then every 6 months for another year. For periodic evaluations were performed blood tests, abdominal ultrasound, colonoscopy and CT scans that showed no progression of the disease.

From diagnosis to two years after surgery, under nutritionist medical supervision the patient has improved obesity reaching a body mass index of 36kg/m^2 and then stalled[3]. Three years after surgery the patient was assessed at periodic check claiming 5kg weight loss in two months, fatigue, nausea and loss of appetite, evolving symptoms for 2-3 months. On physical examination we found skin jaundice, dehydration, abdominal diffuse pain with maximum intensity in the right upper quadrant, without any other changes.

We performed blood tests, colonoscopy and computerized tomography. Blood tests revealed leukocytosis (WBC-white blood cells) with neutrophilia (15,400 WBC/mm^3 with 76% neutrophils), hypochromic, microcytic anemia (Hb=10g/dl), elevated transaminases (approximately 3 times higher than normal) and jaundice with predominant indirect bilirubin (total bilirubin of 3.5 mg/dl, with direct bilirubin of 1.1 mg/dl and indirect bilirubin of 2.4mg/dl).

Colonoscopy was performed only up to the splenic flexure because the patient can not tolerate the continuation of the investigation and, up to this level, no pathological elements can be detected and colorectal anastomosis is supple. Computerized tomography detected multiple intrahepatic tumors disseminated in both lobes with diameters between 0.5 cm and 3 cm, some with central necrosis, without any other pathological changes.

That lifts suspicion of multiple liver metastases outside the surgical resources and we advised patient to the oncological sector, where she received special treatment.[5] Despite treatment, the patient died 10 months after the diagnosis of liver metastases. The peculiarity of the case lies in the favorable initial evolution, interrupted by an unexpected fulminant recurrence of the disease.

The second case that we want to discuss is a 64 years old female patient who went to the doctor for weight loss, lower abdominal pain and slow intestinal transit. The patient denied a family history of cancer. In the anamnesis, the patient denied smoking and alcohol consumption. Among previous medical history, we mention cardiovascular diseases evolving for more than 10 years (hypertension, ischemic heart disease) and left lower limb lymphoedema with unspecified etiology evolving for 2 years. The patient presented about a year ago, obesity grade II which turned after weight loss in grade I listed above.

On physical examination the patient is found in good condition, with slightly dehydrated, normal colored skin, left lower limb lymphoedema and grade I obesity with BMI = 32kg/m^2 and waist circumference of 110 cm.[3] Abdomen, enlarged by fat tissue is painful on palpation in hypogastrium, left flank and left iliac fossa, without signs of peritoneal irritation. On digital rectal examination we found, at 8-9 cm of the anal orifice a circumferential stenosing, brittle tumor.

Blood tests revealed thrombocytosis (540.000/mm^3 platelets) without anemia or leukocytosis , with an increased erythrocyte sedimentation rate (110mm / h).

We also metered tumoral markers and revealed increased CEA (45.89 ng /ml), without changes of CA19-9, CA 72 or CA 125. We also performed electrocardiogram, chest X-ray and abdominal radiography. These did not provide any additional data.

We decided to do a colonoscopy in completion of investigations. It highlighted at 9 cm of the anus, stenosing, brittle, bleeding to touch tumor that cannot be surpassed with colonoscope. We took six bioptical

fragments. Histopathological examination diagnosed intestinal adenocarcinoma.
Abdomino-pelvic MRI (magnetic resonance imaging) was performed for staging the disease[2] and that highlights voluminous pelvic tumoral mass with local infiltration and grade III (figure 2) secondary right hydronephrosis, important lymphoedema of pelvic area and thighs (figure 3). It is also observed the importance of colonic and ileal loops air distension upstream (figure 2).

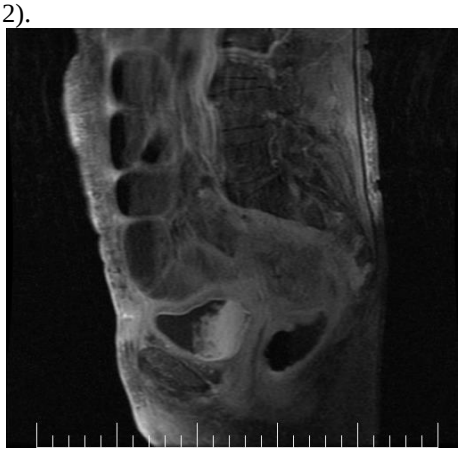

Figure 2. Abdomino-pelvic MRI longitudinal section

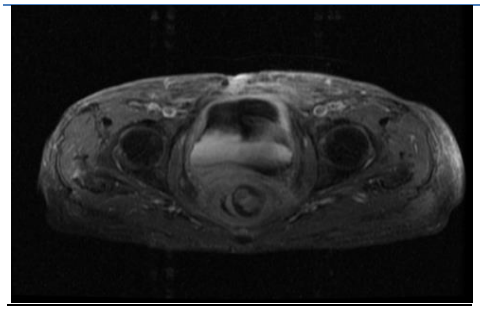

Figure 3. Abdomino-pelvic MRI transversal section

Based on clinical and laboratory data, stenosing middle rectal tumor with secondary subocclusion was diagnosed and we decided surgery.[2]
Preoperative preparation is done with enemas and third generation cephalosporin administered 24 and 12 hours before surgery. We avoided osmotic laxatives due to the risk of intestinal obstruction.
Under general anesthesia with intubation we practiced exploratory laparotomy and found stenosing rectal tumor, invading the bladder and sacrum. That was considered without radical surgical resources at the moment. The peritoneal cavity exploration finds no other detectable macroscopic lesions. We practiced a loop colostomy. After surgery, under treatment (antibiotic, low molecular weight heparin, painkillers, gastric secretion inhibitors, prokinetic, fluid and electrolyte support), the patient has favorable evolution and was discharged in good condition. Four months after surgery, radiotherapy and chemotherapy, the patient returns for an evaluation.
Taking blood test shows no pathological changes and tumoral markers were at the same values as before the surgery.
We performed abdominal-pelvic CT (Figure 4) which found lack of response to cancer treatment and describe so-called "frozen pelvis."

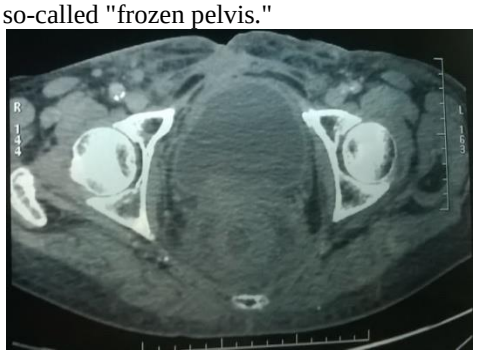

Figure 4. Abdominal-pelvic CT – transversal section

The patient is currently in oncological treatment but is still followed up in our department too.
The peculiarity of the case lies in the diagnosis of advanced disease, inoperable and lack of response to oncological therapy.
The **third case** we present it is a 53 years old female patient known with grade I obesity in development for 15 years, without any previous history of associated pathology, which goes to the doctor for pain on defecation, haematochezia and slow intestinal transit. The patient denied family history of oncological pathology and also denies alcohol consumption and smoking.
On physical examination was found grade I obesity with BMI = 33kg/m^2 with waist circumference of 110 cm^3; normal colored and hydrated skin, without palpable lymphadenopathy and without pulmonary or cardiac changes. At local examination, we found increased volume abdomen by adipose tissue, painless at palpation, without signs of peritoneal irritation and without any detectable tumors. Digital rectal examination revealed a tumor, at 4 cm from the anal orifice, which occupies half of the circumference of the lumen, vegetative, brittle, which bleeds at palpation. The patient was hospitalized in the surgery department in order to continue the investigations and for specialized treatment. On admission were performed blood tests, electrocardiogram and chest X-ray.
Blood tests revealed hypoproteinaemia (proteins - 6g/dl) and increased erythrocyte sedimentation rate (89mm/h), without changes in blood counts and coagulation assays. ECG showed any arrhythmias or terminal phase disorders, and chest radiography we found any evolutionary pleural or lung lesions.
We decided to perform a colonoscopy in completion of investigations. It highlighted at 4 cm from anal orifice, vegetative tumor which occupies half of the lumen and

extends 3-4cm. The tumor was surpassed with the colonoscope and no other lesions were found up to the hepatic flexure. Bioptical fragments were collected. Histopathological examination diagnosed intestinal adenocarcinoma.. For disease staging was performed abdominal-pelvic CT. It revealed rectal tumor localized at 4-5 cm from anal orifice that covers 3 cm in length, with overlying rectal wall edema and satellite milimetric lymph nodes (Figure 5). It also founds grade II hepatic steatosis but excludes liver metastases. It also excludes any other oncological injuries in the examined segments.

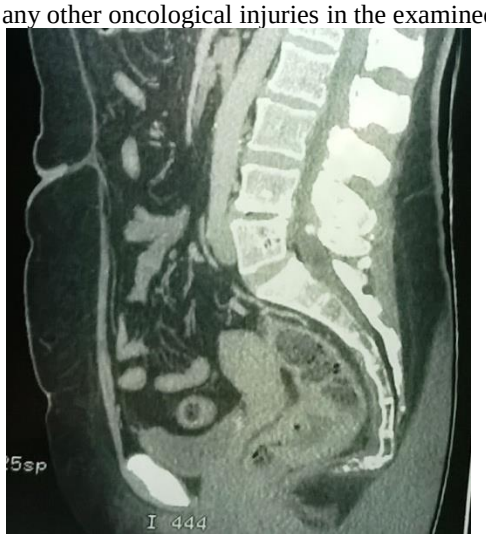

Figure 5. Abdominal-pelvic CT longitudinal section

Based on clinical and laboratory assays, stenosing lower rectal tumor was diagnosed and we decided surgery.
Preoperative preparation was done with osmotic laxative (macrogols), rifaximin taken orally and 3rd generation cephalosporin intravenously.
Under general anesthesia with intubation was practiced exploratory laparotomy and was discovered a lower rectal tumor without any other intraperitoneal organs injuries. We decided and perform an abdomino-perineal rectal excision.[2] (figure 6).
Postoperative therapy (antibiotics, low molecular weight heparin, pain reliever, gastric secretion inhibitors, prokinetic, fluid and electrolyte support), the patient had favorable evolution and was discharged in good condition following to be taken into oncological evidence.
Histopathological examination results: G2 conventional adenocarcinoma with infiltrating pattern to the subserous level, with complete surgical resection, without locally nodal metastases (20 lymph nodes with reactive characteristics) pT3N0M0G2 (Stage IIA).[2]
Postoperatively the patient received chemotherapy and radiotherapy as the oncologist indicated. She returned to regular checks every 3 months for the first 2 years and then after 6 months, without any signs of local reccurence or metastases.

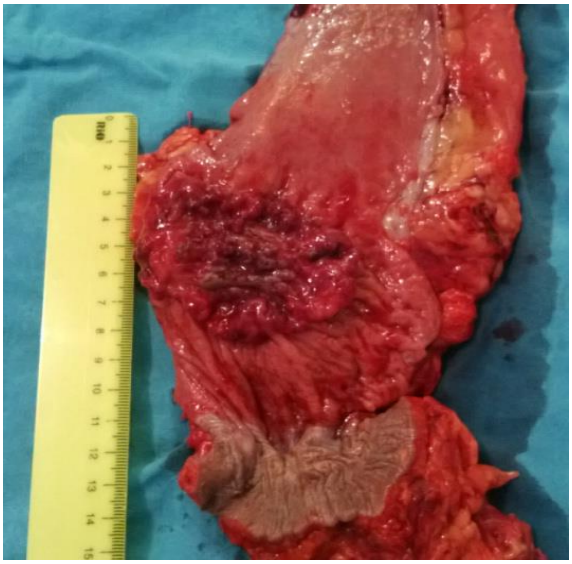

Figure 6. Amputated rectum

DISCUSSIONS

Obesity is a well known risk factor for oncological pathology diseases and is underlined in those cases as an important risk factor for colorectal cancer occurrence, reccurence and complications[2].
We have shown in these cases that obesity is also a factor of poor prognosis in both immediate and late postoperative evolution because it prone to infectious, respiratory and cardiologic complications.
Surgical treatment of colorectal cancer is often mutilating and its psychosocial impact is significantly higher than that of other types of malignancy. The economic impact of this disease also justify the need for a real prevention.
Among the risk factors that are preventable we can count obesity, which leads not only to oncological pathology but affects every organ in part.

CONCLUSIONS

The three cases have in common the same type of cancer (colorectal adenocarcinoma) and obesity. Also none of the 3 patients had oncological type comorbidities.
Obesity increases the likelihood of various diseases, particularly heart disease, type 2 diabetes, obstructive sleep apnea, certain types of cancer, and osteoarthritis.[6,7]
More than 75–95% of colon cancer occurs in people with little or no genetic risk[8]. Other risk factors include high intake of fat, alcohol or red meat, obesity, and a lack of physical exercise[9] Approximately 10% of cases are linked to insufficient activity[10]
We will try improving methods of surgical and oncological treatment of these tumors and continue studying these cases.

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