



Case report

The diagnostic and therapeutic management of a peculiar case of rectal submucosal adenocarcinoma

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Abstract

Introduction

We are presenting the case of a 50 years old female patient with rectal cancer, developed from the submucosal level, who raised difficulties in diagnoses process and therapeutic management.

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The patient's symptomatology began four months before the definitive diagnose. Various investigations have been performed, including multiple biopsies which were inconclusive. Surgical intervention was performed to obtain definitive malignancy HP result. The postoperative evolution was peculiar, marked by complications, which required multiple surgical interventions.

Conclusions

The development of the adenoma, predominantly at the submucosal and muscular level has caused difficulties in both establishing the diagnosis and in the therapeutic management. Sclerosing encapsulated peritonitis (SEP) is a rare clinical entity, usually discovered in postoperative intestinal obstruction cases. The etiology and frequency of SEP depend on its' type.

Keywords

: rectal cancer, sclerosing encapsulating peritonitis, chronic obstruction

Highlights

- ✓ The development of rectal submucosal adenocarcinoma leads to difficulties in respect to the diagnosis and therapeutic management.
- ✓ Sclerosing encapsulated peritonitis is a rare clinical entity, which can be primary/ idiopathic or secondary to peritoneal dialysis, abdominal tuberculosis, abdominal and pelvic surgery, etc.

To cite this article: Blajin A, Dan C, Sălcianu I, Welt L, Scăunașu RV, Berevoescu N, Blajin C, Burcoș T. The diagnostic and therapeutic management of a peculiar case of rectal submucosal adenocarcinoma. *J Clin Invest Surg.* 2018; 3(1): 47-52. DOI: 10.25083/2559.5555/31.4752

Introduction

Colorectal cancer (CRC) is the third one among the most frequently diagnosed types of cancer, and the fourth linked to cancer related death rates worldwide (1). Rectal cancer occurs in approximately 30% of the total cases of CRC and is associated with a more severe outcome (2, 3). The standard treatment of the locally advanced rectal cancer consists in preoperative radiotherapy followed by total excision of the mesorectum, with the purpose of improved preservation rates of the anal sphincter and prevention of a possible local extension (4, 5). Clinical trials have proved a significantly lower recurrence rate and toxicity among the patients who have undergone preoperative radiotherapy compared to the ones that only followed postoperative chemoradiation therapy, although there wasn't a noticeable difference in the survival rate between the two groups. Preoperative radiotherapy is the standard method of treatment for rectal cancer stage II (cT₃₋₄, N₀, M₀) and stage III (cT₁₋₄, N₊, M₀). Although, according to previously released data provided by the Mercury studies, preoperative therapies are, at this moment, frequently designated to high risk patients, with preoperative MRI imaging (6-8).

A common form of presentation, in advanced stages, is the obstructed rectal cancer (9). It is estimated that a percentage of 10-19% of patients with rectal cancer will have obstruction, at some point during the disease (10). The presence of the obstruction is also a risk factor for a poorer prognosis, with an immediate postoperative death rate of 15-30%, in comparison with the electively operated patients – 1-5% immediate death rate (11). This high percentage of mortality is explained, not only by the deterioration of the general state of the patient, but also by the late diagnosis of such cases (10).

Materials and methods

Female patient, 50 years of age, besides a cholecystectomy no other significant medical history, presented at the general practitioner complaining of flatulence, constipation and posteriorly radiated back pain, with nocturnal debut and a progressive intensity.

The blood count conducted at the time revealed moderate hypochromic microcytic anemia (Hb= 10.5 g/dl) and the test for fecal occult hemorrhages was negative.

The patient was ordered a complete colonoscopy with biopsy of a villous polyp identified at circa 4-5 cm from the dentate line (for which the histopathological result consisted in epithelial low-grade dysplasia and high-grade epithelial dysplasia of the superficially

located villi with squamous metaplasia and areas of hyperplastic mucosa and normal glandular epithelium).

Furthermore, an MRI revealed a thickening of the rectal wall suggestive for tumoral involvement, accompanied by pelvic lymphadenopathy and ascites.

For a better understanding of the imagistic results, a new colonoscopy with biopsy was performed. The histopathological result revealed a mixed polyp, both hyperplastic and adenomatous with marginal hemorrhagic erosion, of villous and tubular aspect, with low grade epithelial dysplasia at the superficial and glandular epithelium level.

One month later the patient is clinically, endoscopically reexamined. A tumor was now perceived at the physical rectal examination. Endoscopy discovered an invasive tumor at approximately 6-7 cm from the anal orifice, hemorrhaging upon contact, with retraction of the overlying mucosa, rough, 4-5 cm, from which multiple fragments for biopsy were retrieved (Figure 1).



Figure 1. Rectoscopy image which reveals a rough and hemorrhaging tumor, localized 7 cm from the anal orifice.

The histopathological result of the biopsy pleads for villous adenoma with low level epithelial dysplasia and limited areas of high grade epithelial dysplasia.

A CT scan shows the layered, round and asymmetrical aspect of the thickening of the rectal wall, located between the recto-sigmoid junction down to 5-6 cm from the anal orifice. It is also noted the invasive feature of the lesion (Figures 2, 3).

Corroborating clinical, endoscopic, imagistic and histopathological data, as well as the lack of histopathological malignancy diagnosis, the tumor board decided surgery as the first therapeutic step. Laparoscopy revealed a pelvic tumoral block between the recto-sigmoid junction and the vaginal posterior wall; white nodules in the Douglas' pouch, normal aspect of the liver and wall adhesions of the sigmoid for which is performed adhesiolysis. The surgery was then converted to the classic approach and palpation

uncovered the expansion of the pelvic tumor 15 cm down the middle part of the rectum, invasive on the posterior vaginal wall and the left levator ani muscles; the annexes and the uterus were of normal aspect considering the patients' age.



Figure 2. CT-scan image: rectal tumor, sagittal plan, level T2

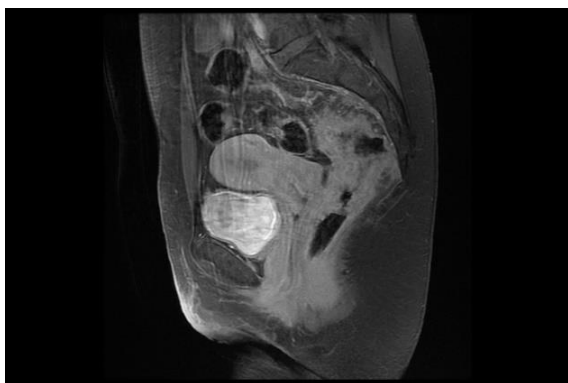


Figure 3. CT-scan image: rectal tumor, post-contrast, sagittal plan.

The operative technique consisted in low anterior resection, colo-anal anastomosis, mesorectal total excision, protective ileostomy, adhesiolysis and biopsy of the peritoneum nodule, which later revealed fibrous tissue associated with inflammatory infiltrate. After the surgery, the improvement of the patient's general state was slow, worsened by the lumbar pain which stopped after the administration of painkiller medication. The staging – stage pT3N1bMx – and the histopathological examination was based on 5 fragments (1: peritoneum nodule- fibrous tissue associated with chronic inflammatory infiltrate, and small tumoral infiltrates which consists in isolated cells and small groups of atypical malignant cells – overall aspect of a metastasis of poorly differentiated adenoma. 2: ganglion of the inferior mesenteric artery origin- metastasis of poorly differentiated adenocarcinoma, which was extended over the capsule, invaded the adipose tissue around it, and formed a tumoral thrombus. 3: tumoral formation from the middle rectum- the resection margins, distal and proximal, had no tumoral invasion. It showed poorly

differentiated adenocarcinoma with a minimal involvement of the mucosa (0.5 cm) and massive invasion of submucosal and muscularis layers and predominantly of serosa and the adipose tissue around the rectum. There was also lymphovascular and perineural invasion. The adenocarcinoma metastases were present in 3 out of 13 ganglia located in mesorectum and mesosigmoidum, which extended over ganglia's capsule and in the neighboring adipose tissue – there were present 31 perirectal deposits of adipose tissue. 4: inferior fragment (which included anus): small tumoral thrombi; 5: superior fragment with no tumoral invasion present (Figures 4, 5).

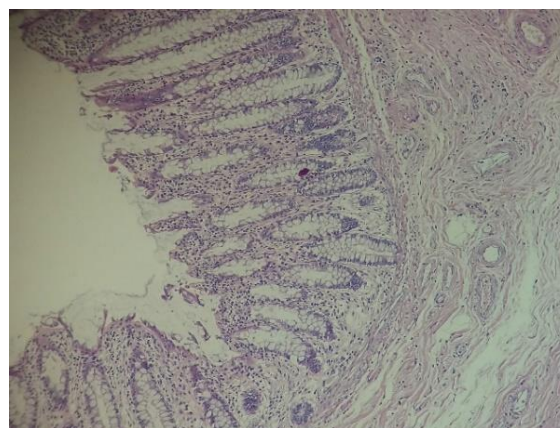


Figure 4. HEx10 Areas of mucosa and submucosa with no malignant invasion.

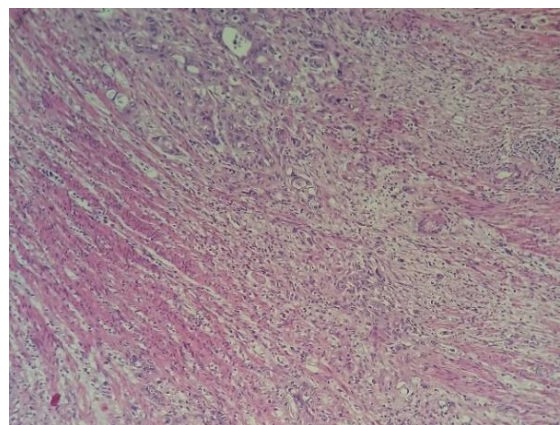


Figure 5. HEx10 Malignant invasion present in the muscularis layer.

Subsequently, the histopathological results and immunohistochemical techniques support both the poorly differentiated adenocarcinoma diagnosis and the rectal origin of the tumor. In addition, genetic testing was performed for the purpose of prognosis evaluation and establishment of oncological therapy. The test detected the presence of the K-RAS - WILD TYPE, N-RAS – MUTANT for Q61L and BRAF V600E-positive for mutations. The association of the BRAF V600E and N-RAS suggested a poor prognosis.

The MRI performed with the purpose of postoperative evaluation revealed areas of local invasion; formations present on the liver level, which were compatible to secondary determinations; nodules on the peritoneum and an ischiopubic lesion on the right side, whose aspect suggests an oncological pathology.

The multidisciplinary team consult (oncology, surgery, radiotherapy) accordant to the patients wish, decided upon delaying the chemotherapy in favor of restoring the digestive continuity. The reintegration of the ileostomy was performed; minimal enteral with a termino-terminal entero-ental anastomosis was performed. Post intervention, the general condition was slowly improved, with late reinstatement of the intestinal transit. The patient was discharged a week later.

The day after discharge the patient presented at the ER with shivers, abdominal pain, vomiting and nausea. Abdominal radiography revealed colic hydroaeric levels on the right half of the abdomen. A surgical procedure for the intestinal obstruction was performed and consisted in exploratory celiotomy, viscerolysis and segmental enterectomy with enter-ental latero-lateral anastomosis. The postoperative intestinal transit for faeces resumed soon after the intervention but the obstruction symptoms were persistent. The subsequent colonoscopy revealed a perianastomotic stenosis of the terminal ileum – at approx. 10 cm from the ileocecal valve the ileal lumen is closed by the massive congestion of the overlying mucosa and by the angulation of the trajectory; the obstacle could not be overcome (endoscopically or guide wire); the intestinal contents could not pass through the stenosis. A new exploratory celiotomy was decided which revealed SEP type III, however the viscerolysis was impracticable because of the numerous structures that were encapsulated by the fibrous membrane. The attempt caused iatrogenic lesions of the intestinal loops, which imposed enterorrhaphy, lavage and drainage.

On the fourth postoperative day a leakage of 400ml of intestinal fluids through the surgical wound occurred, managed conservatively with a drain tube. Currently, the patient is admitted in the hospital, under careful observation, the current state is grave and has a destitute prognosis.

Discussion

The particularity of the presented case consists in the development of the rectal adenocarcinoma predominantly in the submucosal and muscularis layers, and significantly less presence in the mucosa, where it

usually resides, which led to a massive delay in the diagnosis establishment. The rectal adenocarcinoma is observed in 85% of total cases of rectal cancer. It shows a well differentiated pattern in 20%, a moderate pattern in 60% and a poor one in 20% of the cases (12-14).

It is proved that preoperative radiotherapy lowers the risk of relapse. According to a meta-analysis with 8.507 patients from 22 randomized trials analyzed by Gray et al, the most notable finding was the significantly lower recurrence rate (46%) of the group which benefited preoperative radiotherapy, compared to those who only had elective surgery (15). However, the analysis showed the global survival rate was not considerable different between the two groups (62% for patients who benefited the preoperative radiotherapy vs. 63% for patients who only had surgery). In this case, the patient did not have preoperative radiotherapy due to its late diagnosis.

Although multiple biopsies were performed, histopathological results indicated villous adenoma with various grades of epithelial dysplasia, and for this reason the standard oncologic guidelines with preoperative radiotherapy could not be followed (16, 17).

The definitive diagnosis of adenocarcinoma was based on the histopathological examination of the resection piece obtained after surgery.

The multidisciplinary team, following the patient's wishes, decided upon the reintegration of ileostomy instead of chemotherapy. Ten days after the reintegration of ileostomy the patient is presenting obstruction, caused by sclerosing encapsulated peritonitis (SEP) type I. Eight days after the reoperation another obstruction occurred. The exploratory celiotomy discovered a SEP type III which made impossible any adhesiolysis attempt (18).

SEP is a rare clinical entity, usually discovered in postoperative intestinal obstruction cases. The etiology and frequency of the sclerosing encapsulated peritonitis (SEP) depend on its' type. Primary SEP is idiopathic, hence, not associated with a specific cause. It is considered, though, that cytokines and fibroblasts likely influence the development of the peritoneal fibrosis and neoangiogenesis one way or another (12-14). The reported incidence of SEP, primary and secondary, varies between 0.3-3.3% (18, 19). It was found that 75% of the total cases of SEP occur among the men, premenstrual women and children (15, 16). In contrast, secondary SEP is associated with multiple causes, thus, is more frequent. Among the main causes, worth mentioning are such as peritoneal dialysis, abdominal tuberculosis, abdominal and pelvic surgery, beta-blocker treatment, chemotherapy (e.g. methotrexate)

and autoimmune diseases such as sarcoidosis or systemic lupus erythematosus (17, 20). A high clinical presumption associated with imaging techniques, especially CT-scan, have a major role in establishing the definitive diagnosis (17). At this moment, SEP is classified as primary (or idiopathic) SEP or secondary SEP, depending on the cause and on the histopathological aspects of the encapsulating membrane (21-23). Primary SEP, also referred to as abdominal cocoon syndrome, is classified into three categories based on the extent of encasement by the membrane (24, 25). Type I and II involves the encasement of either part of or the complete intestine, respectively, by a fibro collagenous membrane. In type III, the appendix, caecum, ascending colon, stomach, liver and ovaries are also encased in addition to the small intestine (26-28).

Conclusions

The development of the adenoma, predominantly at the submucosal and muscular level has caused difficulties in both establishing the diagnosis and in the therapeutic management. SEP is a rare clinical entity, usually discovered in postoperative intestinal obstruction cases.

The etiology and frequency of the sclerosing encapsulated peritonitis (SEP) depend on its' type. In this case the therapeutic approach was reserved, the viscerolysis was avoided due to high risk of iatrogenic lesions.

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