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SIMULTANEOUS MULTICENTRIC COLORECTAL CARCINOMAS, DIAGNOSIS, THERAPEUTIC OPTIONS, PROGNOSIS CASE REPORT

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ABSTRACT. Simultaneous multicentric colorectal carcinomas (SMCRC) are rare, but the incidence is increasing significantly lately due to the progress of diagnostic procedures, which are more and more performing. The etiopathogenic and prognostic factors of these tumors are only partially known. Therapist does not have a well-defined protocol, which is why the treatment is strictly personalized depending on the staging of tumors, clinic's performances and patient options. The role of preoperative imaging is essential in the discovery of multiple and simultaneous cancerous localizations. The golden rule of intraoperative detailed and complete exploration remains valid today. The mirage of discovering a colonic tumor must not distract the attention of the surgical team, which must not forget to control the whole colon and the rectum and , also, the other abdominal organs. A rare case of simultaneous multicentric colorectal carcinomas is presented in the current context of diagnostic and therapeutic possibilities.
KEY WORDS: colorectal, multicentric , simultaneous, etiopathogenesis, personalized treatment.

INTRODUCTION

The spectacular development of current diagnostic procedures leads to the early detection of colorectal cancers and therefore, lately , cases of SMCRC are reported more and more frequently (1).

From the beginning we must distinguish the SMCRC from synchronous cancers which, after Warren , complies with two mandatory criterias taken from Rokitansky (1889), respectivly that the cancers must be of different types and located in different organs. This classification remained valid until today, although a lot of confusions are made (2).

On the other hand, the term simultaneous multicentric cancers defines the presence of malignant tumors of the same type with multiple localizations in the same organ and discovered at the same time. So , we are talking about cancers occurring simultaneously, having the same histopathological structure, aspects suggested by other authors too (3,4).

The very clear distinction between multiple synchronous and multicentric cancers is sometimes difficult to be done because of the associated tumors found sometimes on both the resection piece and especially on the colonoscopic biopsy fragments.

The association of initially benign tumors (polyps) with their malignant forms adds additional difficulty in classifying concomitant cancers.

It is necessary, from the beginning, to establish the moments of concomitant tumors. Some authors suggest that the time interval , between diagnosis of the first tumor and the discovery of the second or of the others , must be maximum 6 months in order to be able to fit into the group of simultaneous multicentric cancers (2, 3). This period of six months is not only relative but also debatable in the clinical context of each patient.

The diagnosis, the correct inclusion in the right pathology and terminology is sometimes confusing.

The name of simultaneous multicentric colorectal adenocarcinomas includes those cases in which the neoplastic process is discovered concurrently, which have an identical histopathological structure and are located in the colon and rectum.

We present a suggestive case in this regard.

Case presentation

We report the case of a 72-year-old man , a patient who was consulted at the surgery cabinet on October 10, 2014, showing weight loss, defecation disorders and intermittent rectal bleedings.

The clinical examination revealed a discreet pallor and the palpation of the abdomen discovered a tumor in the right iliac fossa imprecisely delimited, of 5/6 cm. Rectal digital examination revealed another vegetative tumor approximately 5 cm from the anus. Anamnestic data related to family history are irrelevant.

The colonoscopic examination reveals at 130 cm from the anus a 5/5 cm vegetant tumor near the ileocecal valve and 9 polyps of various sizes located in different segments of the colon.

On the rectum, at 5 cm from the external anal orifice, there is a 2/2cm mobile polyp.

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Biopsies are done. The histopathological examination of the cecal tumor revealed a differentiated tubulo-papillary carcinoma with invasion in the lamina propria, and the other 9 examined polyps (at 133,108,102,101,100,85,84,80 cm and 70 cm respectively) had a tubular adenomatous appearance, respectively the rectal polyp was tubular dysplastic.

The patient is hospitalized in the surgery department on November 5, 2014, where he is also investigated, discovering new associated pathologies like a type 2 diabetes mellitus, hypertension and chronic ischemic heart disease. Laboratory analyzes revealed a moderate anemia with hemoglobin of 11.5 mg/dl and the abdominal ultrasound exam also discovered gall bladder stones. Other analyzes were normal.

It is decided in the first phase to perform a transanal rectal tumor resection (6.11.2014), including the excision of two tumors of 2.1 cm and 2.15 cm in size , both located at 5 cm from the anal orifice.

After a preoperative preparation, on 13.11.2014, a median laparatomy was performed (PO1160) and two tumors were discovered during the abdominal exploration, one of 6/6 cm located in the cecum and the other of 4/4 cm, stenosing the median 1/3 of the transverse colon (the last one was not seen endoscopicaly). The rest of the abdominal organs, including the liver, were of a normal appearance, excepting the gall bladder with thickened wall and full of stones.

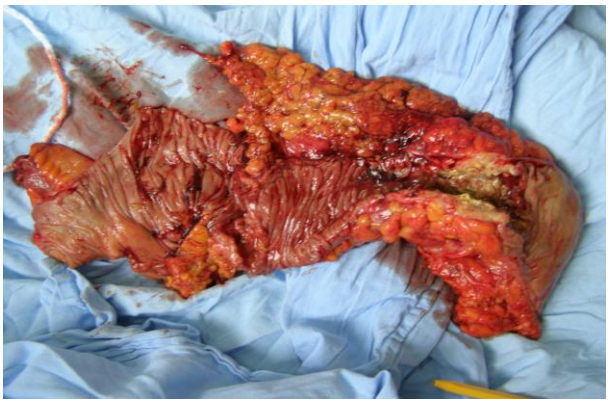

FOTO 1 multiple colon cancer

A bipolar approach cholecystectomy was performed, followed by right extended hemicolectomy with end to end ileo-colic anastomosis.

The patient's post-operative evolution was favorable both rectally and abdominaly, leaving the hospital on 24.11.2014 in good clinical condition.

The postoperative histopathological examination of the resected colon tumors revealed the presence of a mucinous adenocarcinoma with muscular and serous invasion, and the 18 examined lymph nodes had aspects of acute non-specific lymphadenitis.

Two weeks postoperatively came the result of genetic examination of colonoscopic endoscopic biopsy specimens. This investigation at a Bremen clinic reveals a decrease level of Glutathione S transferase (GSTT) to 48%, indicating a global decrease in the antioxidant capacity of the body.The gene responsible for producing GSTT had also been studied and had shown sufficient activity. So there was a mismatch between the normal genetic function and the marked decrease in GSTT.

Postoperative the patient followed a cytostatic cure and made radiotherapy in the rectal area.

The patient was monitored and on March 10, 2015, after a rectoscopic examination , a 2/2 cm rectal tumor was discovered and resected transanally (at the patient's express desire). The histopathological result of the resection piece was also a tubular adenocarcinoma with extensive mucinous areas (G2).

There followed two more resection sessions of relapsed rectal tumors on 05/10/2015 and 28/03/2016 respectively with the same histopathological result.

The CT exam on August 21, 2016 showed a thickening of rectal wall over a distance of 10 cm without any other notable modifications.

The patient was hospitalized on March 28, 2017, accepting a Miles abdominoperineal resection procedure for a mucinous infiltrative rectal adenocarcinoma invading the muscle layer and rectal serosa.

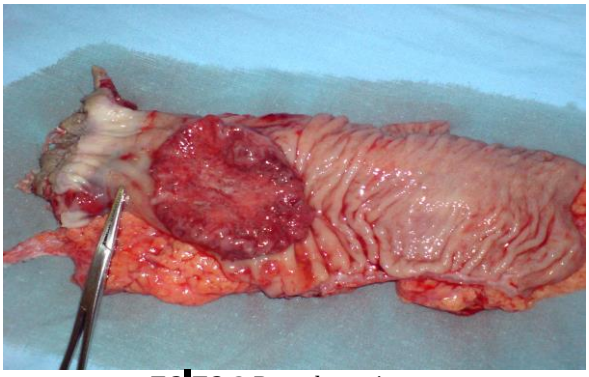

FOTO 2 Rectal carcinoma

The last hospitalization was performed on 21.09.2017 for a possible bowel obstruction determined by numerous intraabdominal tumor masses, hepatic and splenic metastases confirmed by the computed tomography, the patient being discharged after five days of medical treatment with normal bowel habit , digestive tolerance and improved condition.

DISCUSSIONS

The discovery of multiple colorectal neoplasms is rarely communicated, although it is known that colorectal polyps are frequently suffering cancerous transformation (5). Causes of concomitant malignisation of colorectal polyps are still unknown , because the genetic mechanisms that trigger the adenocarcinogenetic process have not been elucidated completly. In our case we did not find genetic risk factors. (6)

A complementary study based on the analysis of 71 articles studied by some authors found an incidence of synchronous adenocarcinoma with adenomatous polyps between 2.5 to 12.4% (1) (7).

Data from the literature reveals an increased frequency of multiple adenocarcinomas in elderly males, but this claim is denied by other studies showing a prevalence of multiple adenocarcinomas in young male subjects. In our case, the patient was male and elderly, which confirms the statements of the first authors (9).

Some authors report the presence of 2 or even 7 colonic adenocarcinomas simultaneously. (1)

There is a mismatch in assessing the timeframe for finding tumors to be considered as simultaneous and multicentric. While some authors consider that the period is up to 6 months, others believe that this period should be extended to 1 year (10).

Ambiguities also occur with SMCRC localizations in the different segments of the colon. While some authors (11) show a high incidence of localization in the right colon, others describe it as being more frequent in the left colon (12).

In the case of the two concomitant colonic cancers with identical histopathological exams , these were localized both in the right colon and transverse colon, which resulted in an extension of the hemicolectomy on the transversal region.

Oya (12) compared the lesion index of colorectal synchronous adenocarcinomas versus single colorectal adenocarcinomas and found significant differences between tumor size, tumor differentiation, localization, lymphatic staging and metastasis between the two types of lesions. He also found more frequent metastases in the case of synchronous adenocarcinomas. These findings indicate an increased aggressiveness in multiple cancers, probably due to the marked decrease in immunity and in antioxidant capacity of the body, which we found by GSTT analysis.

In our case, the lymphatic and distal metastasis was not significantly elevated, because , after the right hemicolectomy, the histopathological result did not show any metastasis in the 18 lymph nodes studied. We consider that carcinogenic dissemination is conditioned not only by tumor volume, but also by TNM stage and their grading. In our patient, a grading 2 was found, which explains the absence of metastasis for that moment.

The simultaneous development of multiple adenocarcinomas is known in colon polyposis. In our case, the presence of three simultaneous neoplastic formations on the right colon, on the transverse colon and the rectum , reveals the existence of very strong carcinogenetic factors that could simultaneously trigger the development of these tumors.

The analysis of known risk factors was relevant to our patient as he consumed smoked foods, he was a smoker, and he consumed alcohol but we did not found any relevant family history, which is why genetic analysis was needed.

The GSTT1 study showed a 48% decrease in global antioxidant activity , which certainly participated in the aggressive development of colorectal cancers.

The study of the gene responsible for GSTT synthesis showed a sufficient activity. This inconsistency between the normal activity of production gene and the GSTT antioxidant enzyme deficiency can be explained either by enzymatic blocking or by increased consumption. The perturbation of these antioxidant mechanisms was very likely at the base of the simultaneous triggering of the multicentric carcinogenetic process.

The role of preoperative imaging is essential in the discovery of multiple and simultaneous cancerous localizations, idea sustained by other authors too (13,14), combining CT PET scan and MRI with colonoscopy .

Considering that, doubts occur in diagnosis of multicentric colorectal cancer despite of development of imagistic invastigations, so the golden rule of intraoperative detailed and complete exploration remains valid today. The mirage (5) of the discovery of a colonic tumor may distract the attention of the surgical team, which will forget to control the other abdominal cavity organs, especially in emergency situations. The ommission of finding other neoplastic lesion or other lesions will result in the patient's very serious evolution. In our case, a tumor located in the distal 1/3 of the transverse colon completely unknown was discovered. Operational strategy and technique were adapted following this intraoperative discovery which has led to the extension of right hemicolectomy in the first operation.

The intraoperative lesion brief should not exclude a more complete preoperative imaging and laboratory investigations. On the contrary, it is currently provided in all preoperative diagnostic guidelines so that additional intraoperative results could be better. We believe that carcinogens in our case acted simultaneously with maximum intensity on concomitant precancerous lesions, which led to the emergence of SMCRC.

Of course, a total proctocolectomy with permanent ileostomy would have solved the disease more radically, but the patient's options were restricting the surgical procedures and determined the necessity of the serial operations.

Although the patient underwent a complex surgical-oncologic treatment, the prognosis of SMCRC was finally unsatisfactory as it resulted in multiple metastases, data found by other authors too (1,7).

CONCLUSIONS

The incidence of concomitant multicentric colorectal adenocarcinomas is rare but steadily increasing over the last period of time. The disease is most common in 3rd aged men.

New imaging investigations, as well as the discovery of new immunohistochemical markers, contribute significantly to the discovery of multiple colorectal cancers in early stages.

Exposure to carcinogenic risk factors and diminishing body immunity, including its antioxidant capacity by lowering GSTT, compete with pathogenesis.

Surgical treatment of these cancers with multiple locations must include a careful intraoperative exploration, with a complete brief of lesions , the golden rule of any open surgeries. Exploration should not be stopped when a tumor is discovered because we must not ignore the possibility of simultaneous multicentric or synchronous cancers. The operation must include wide resections associated with an extensive lymphadenectomy to prevent recurrences.

Mortality and morbidity in SMCRC is higher than in single cancers, and the prognosis of these patients is often unfavorable.

With the clarification of the molecular mechanisms of carcinogenesis, more advanced therapeutic guidelines can be developed, which will increase the survival time for these patients.

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