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RECURRENT RECTAL CANCER COMPLICATED WITH PERFORATION AND NECROTISING FASCIITIS DURING NEOADJUVANT THERAPY

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ABSTRACT:
INTRODUCTION: RECTAL CANCER LOCAL RECURRENCE IS LESS FREQUENT SINCE MULTIDISCIPLINARY APPROACH HAS BEEN IMPLEMENTED, USUALLY TME EXCISION BEING PERFORMED AFTER NEOADJUVANT THERAPY. IN CASE OF RECURRENCE, NEOADJUVANT THERAPY, INCLUDING STANDARD DOSE RADIOTHERAPY SHOULD BE CONSIDERED IF NOT PERFORMED INITIALLY. PATIENTS PREVIOUSLY IRRADIATED, CAN BENEFIT OF LOWER-DOSES RE-IRRADIATION CONCOMITANT WITH CHEMOTHERAPY, FACILITATING A CURATIVE SURGICAL RESECTION.
CASE REPORT: IT IS PRESENTED THE CASE OF A 68 YEARS OLD PATIENT, WHO PERFORMED A RECTAL ANTERIOR RESECTION WITH COLO-RECTAL ANASTOMOSIS FOR RECTAL TUMOR 4 YEARS BEFORE IN ANOTHER MEDICAL UNIT. THE PATIENT IS DIAGNOSED WITH RECURRENCE INVOLVING THE ANASTOMOSIS, FOR WHICH MULTIDISCIPLINARY TEAM RECOMMENDED RADIOCHEMOTHERAPY PRIOR TO SURGERY. DURING THE NEOADJUVANT THERAPY, BEFORE THE LAST CHEMOTHERAPY CURES THE PATIENT IS EMERGENCY SUBMITTED TO SURGERY SERVICE FOR INFLAMMATORY TUMEFACTION WITH NECROTISING FASIITIS IN THE RIGHT ISCHIORECTAL FOSSA. A FIRST SURGERY CONSISTING IN DRAINAGE AND EXTENSIVE DEBRIDEMENT ALSO OBESERVES RECTAL WALL PERFORATION. A SECOND IMMEDIATE INTERVETION CONSISTING IN A TERMINAL COLOSTOMY IS PERFORMED. AFTER ANTIBIOTHERAPY, LOCAL DRESSINGS, AND SEPTIC CONTROL OF THE WOUND AN ABDOMINO-PERINEAL SALVAGE RESECTION IS DONE, AN IMPORTANT SKIN DEFECT REMAINING.
CONCLUSION: A QUICK AND EFICCIENT MANAGEMENT OF A SEVERE CONDITION PERMITTED NOT ONLY TO CONTROL A LIFE THREATENING SITUATION , BUT ALSO PERFORMING AN ABDOMINO-PERINEAL RESECTION. A MORE OFTEN OR MAYBE ROUTINELY USE OF DIVERTING COLOSTOMY BEFORE RADIOCHEMOTHERAPY SHOULD BE CONSIDERED IN CASE OF RECURRENT RECTAL CANCER, DETAILED STUDIES BEING NECESSARY ON THIS ASPECT.

KEY WORDS: RECTUM, CANCER, RECURRENCE, PERFORATION, RADIOCHEMOTHERAPY

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INTRODUCTION

Multimodality of treatment, the use of neoadjuvant radiochemotherapy in combination with TME (total mesorectal excision) decreased rectal cancer local recurrence dramatically, to an average of about 5% according to some studies[5]. Surgery of recurrent disease has become more difficult after the introduction of TME concept and preoperative radio and chemotherapy[6]. A curative resection remains though the aim of treatment for recurrent rectal cancer, as a macroscopic residual disease cannot be compensated by radio or chemotherapy[7]. Currative resection may be facilitated by re-irradiation to lower doses concomitant with chemotherapy in previously irradiated patients[8]. Current literature data are mainly suggesting that diversion is unnecessary in endoscopically obstructed rectal cancer without clinical signs of obstruction, immediate initiation of neoadjuvant chemoradiotherapy being safe and feasible[9]. Herein we report a case of a male patient diagnosed with locally advanced recurrent rectal cancer who received neoadjuvant radio chemotherapy to facilitate radical curative surgery, but during therapy the case complicated with perforation and necrotising fasciitis.

CASE REPORT

A 68 years old male patient is emergency submitted for inflammatory tummefaction with necrotising fasciitis located in the right ischioanal fossa, associating sepsis, asthenia, fever and chills, diarrhoea.

From patients medical history we record that he was previously diagnosed with recurrent locally advanced rectal cancer, for which neoajuvant radio chemotherapy has been initiated according to the multidisciplinary board decision. The initial rectal tumour located in the medium rectum, at approximately 10 cm from the anal verge (well differentiated adeonocarcinoma) was treated with rectal resection and colorectal anastomosis (pT2pN0G2) followed by adjuvant radiotherapy (45 Gy) and chemotherapy. Follow up at 3, 6 9 months, at one year and two years observes no signs for recurrent disease at digital rectal examination colonoscopy, ecography or CT scan, tumoral markers CEA and CA19.9 being in normal range. Another colonoscopy performed at about 3 years from initial surgery suggests tumour recurrence, from 6 to 18 cm, including the anastomosis, biopsies being taken. The histopathological findings show G3 rectal adenocarcinoma. A thorax and abdominal CT scan and a pelvic MRI are performed. The results show locally advanced obstructive rectal cancer recurrence, mesorectal lymph nodes and 2 hepatic micronodules with secondary aspect.

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[5] Sebag-Montefiore, D, Stephens, RJ, Steele, R et al, M. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG CO 16): a multicentre, randomised trial. *Lancet*. 2009;373:811–820.

[6] Glynne-Jones R. et all. Rectal cancer: ESMO Clinical Practice Guineline for diagnosis, treatment and follow-up, *Annals of Oncology 28 (Supplement 4)*:iv22-iv40, 2017.

[7] Huh JW. Curative potential of surgical resection for locally recurrent rectal cancer. *Ann Surg*. 2014 Jun;259(6):e88.

[8] Guren MG, Undseth C, Rekstad BL et al. Reirradiation of locally recurrent rectal cancer: a systematic review. *Radiother Oncol* 2014; 113: 151–157.

[9] Patel JA, Fleshman JW, Hunt SR, Safar B, Birnbaum EH, Lin AY, Mutch MG. Is an elective diverting colostomy warranted in patients with an endoscopically obstructing rectal cancer before neoadjuvant chemotherapy? *Dis Colon Rectum.* 2012 Mar;55(3):249-55

The multidisciplinary team proposes neoadjuvant polichemoyherapy (PCT), re-irradiation to lower doses, followed by curative surgery. Chemotherapy with fluorouracil (5-FU) and calcium folinate associated with bevazucimab has been initiated. Under chemotherapy a febrile episode associated with chills was interpreted as paraneoplastic syndrome. Photon beam radiation therapy (VMAT tehnique) has been performed irradiating current tumor extension to a total dose of 30 Gy in 10 fractions using a 3 Gy/day fractionation schedule. Imagisitic and colonoscopy reevaluation showed slight regression of tumour and no pulmonary or hepatic metastasis on MRI and CT scan and an ulcerative rectal tumor starting at 4 cm from the anal verge with possible fistulary orifices. Afterwards PCT has been continued and before the last session the patient was emergency admitted to surgery for septic syndrome and inflammatory tummefaction with necrotising fasciitis located in the right ischioanal fossa, extended to the right scrotal area (Fig.1), associating asthenia, fever and chills, diarrhoea, but no abdominal pain or signs of peritoneal irritation. Emergency surgery has been performed consisting in incision, drainage of fecals and pus (Fig.2.A), and extensive debridement (Fig2.B). A probe for bacteriological examination and antibogram has been taken, antibiotherapy being administered conformly with the results (Pseudomonas Spp - Colistine + Metronidazole). Additional Candida Spp has been found and treated with fluconazole.

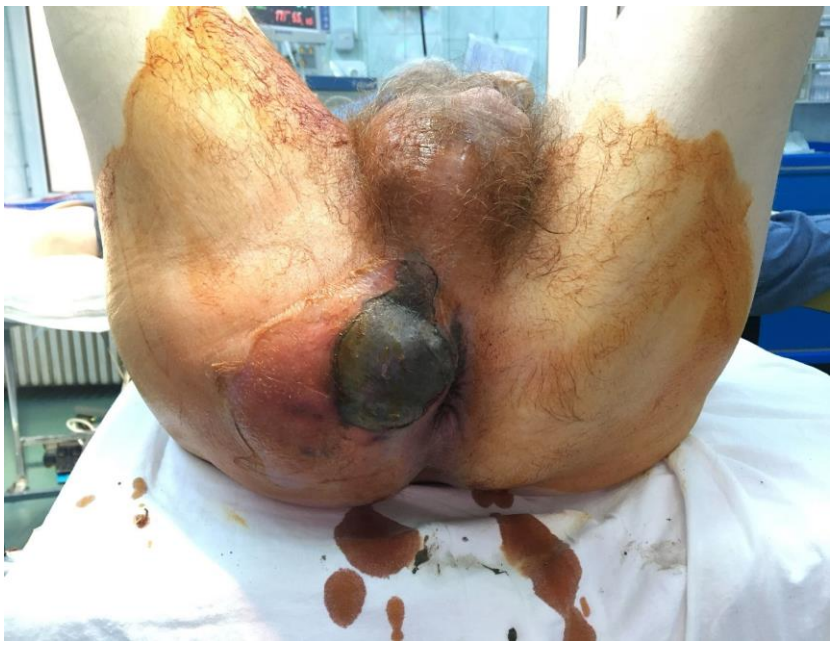

Figure 1. Inflammatory tummefaction with necrotising fasciitis

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Figure 2. (A) Incision. Drainage of pus and fecals. (B) Aspect after debridement. (C) Rectal wall perforation

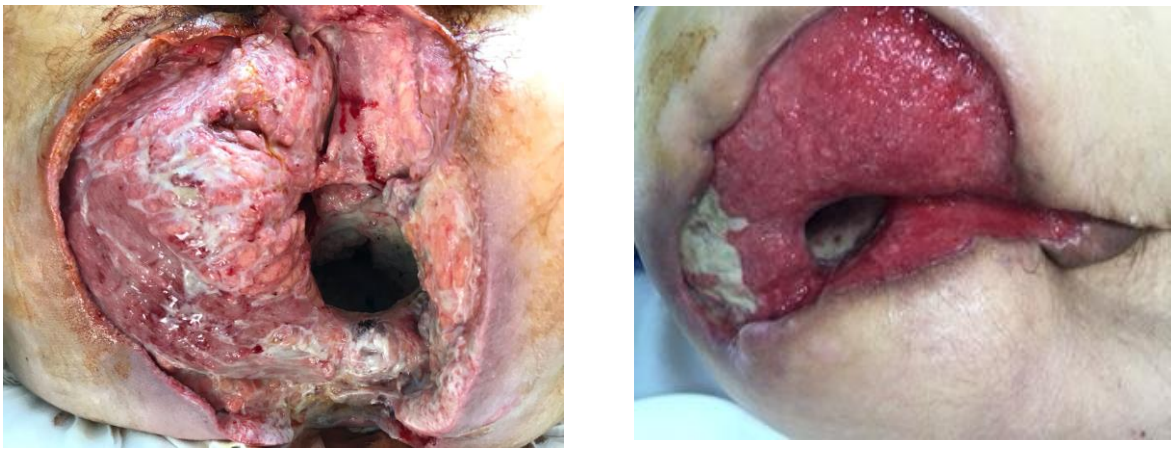

Figure 3. (A) Aspect after abdomino-perineal resection (B) Aspect at 1 month after discharge

Important rectal wall perforation has been noticed (Fig.2C) and a second intervention consisting in a terminal colostomy became mandatory. Postoperative evolution was favourable and permitted after 2 weeks an abdomino-perineal resection (Fig.3.A). The patient has been discharged with good status, granulated perineal wound, with important skin loss. The histopathological result surprisingly showed chronic inflammatory infiltrate, fibrosis and necrosis areas, but no malignant cells.

DISCUSSIONS

Regarding pretherapeutical assessment, imaging can establish the local extent of the tumour and can detect distant metastases. Current literature data suggest that approximately 50% of the patients with local recurrence have detectable distant metastases at the time of diagnoses[10]. Some studies consider the cases with distant metastases present in the initial evaluation unsuitable for curative treatment[11]. In this particular case, there were two liver micrododules with secondary aspect described on initial abdominal CT scan. After neoadjuvant chemotherapy, imagistic reassessment showed no distant pulmonary or liver metastases.

- Even though MRI is useful in assessing local recurrence, DWI-MRI (*Diffusion Weighted Imaging) is* being able to distinguish better tumour from scar tissue[12,13,14,15] PET-scan has also been useful, especially in finding unsuspected metastatic disease[16].
- Despite the fact that many surgeons prefer immediate diversion in patients with endoscopically obstructed rectal cancer before starting neoadjuvant chemotherapy, current literature data shows that immediate diversion is unnecessary in endoscopically obstructed rectal cancer without clinical signs of obstruction. Diverting colostomy delays the initiation of neoadjuvant chemoradiotherapy and proctectomy[17,18] In this particular case the use of a diverting colostomy before initiation of neoadjuvant radiochemotherapy would have not prevented the rectal wall perforation, but would have protected the patient from the consecutive necrotising

[10] Wiggers T Management of local recurrence of rectal cancer. *European Journal of Cancer*, September 2011, Volume 47, Supplement 3, Pages S290–S291

[11] van den Brink, M, Stiggelbout, AM, van den Hout, WB et al, Clinical nature and prognosis of locally recurrent rectal cancer after total mesorectal excision with or without preoperative radiotherapy. *J Clin Oncol.* 2004;22:3958–3964.

[12] Salerno G et al. Defining the rectum: surgically, radiologically and anatomically. *Colorectal Dis*. 2006;8 Suppl 3:5–9

[13] Kim DJ, Kim JH, Lim JS, et al. Restaging of rectal cancer with MRI imaging after concurrent chemotherapy and radiation therapy. *Radio Graphics* 2010;30:503–16

[14] Dzik-Jurasz A, Domenig C, George M, et al. Diffusion MRI for prediction of response of rectal cancer to chemo radiation. *Lancet* 2002;360:307–8

[15] Rania A. Marouf, Mary Y. Tadros , Tarek Y. Ahmed. Value of diffusion-weighted MR imaging in assessing response of neoadjuvant chemo and radiation therapy in locally advanced rectal cancer. *The Egyptian Journal of Radiology and Nuclear Medicine*. Volume 46, Issue 3, September 2015, Pages 553–561

[16] Franke, J, Rosenzweig, S, Reinartz, P et al, Value of positron emission tomography (18F-FDG-PET) in the diagnosis of recurrent rectal cancer. *Chirurg.* 2000;71:80–85

[17] Kaiser AM. Diversion with neoadjuvant vs surgery with adjuvant treatment for obstructing rectal cancer? *Dis Colon Rectum.* 2012 Oct;55(10):e346

[18] National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), *Rectal Cancer, Version 4.*2017 - January 18, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/rectal.pdf on February 8, 2018

fasciitis and from a life threatening situation. Even more, considering that surgery is the only curative treatment in patients with locally recurrent rectal cancer[19], the severe septic complication threatened the tumor-free resection margin (R0) and the overall survival (OS).

Although bowel perforation has been reported before as a serious side effect of bevazucimab in a limited number of cases, its association with fasciitis its rare[20]. In the presented case, bevazucimab was associated with 5-FU and calcium folinate.

Current treatment for locally advanced rectal cancer, including neoadjuvant therapy and total mesorectal excision lead to considerably fewer recurrences. In case of recurrent rectal cancer, if RT has not already been given, patients should be considered for standard-dose, preoperative CRT (45–50 Gy in 5–6 weeks)[21] or short course preoperative radiotherapy followed by a fluoropyrimidine and oxaliplatin-based chemotherapy[22] prior to an attempt of resection.

In patients previously irradiated, re-irradiation to lower doses with concomitant chemotherapy is safe and can be used in selected patients to facilitate a curative resection or per se to palliate symptoms. In the reported case, the patient was initially irradiated after the primary rectal resection, adjuvant radiotherapy being administered (45 Gy). In consequence, the multidisciplinary team considerate neoadjuvant re-irradiation to a total dose of 30 Gy in 10 fractions using a 3 Gy/day fractionation schedule.

CONCLUSIONS

A prompt and effcient surgical attitude allowed a good therapeutical control in a life threatening situation, and also permitted an abdomino-perineal resection with surprisingly satisfying histopathological result. A more often or maybe routinely use of diverting colostomy before neoadjuvant therapy should be considered in case of recurrent rectal cancer, especially when re-irradiation and polichemotherapy associated with bevazucimab are taken into consideration.

[19]Selvaggi F1, Fucini C, Pellino G, Sciaudone G, Maretto I, Mondi I, Bartolini N, Caminati F, Pucciarelli S. Outcome and prognostic factors of local recurrent rectal cancer: a pooled analysis of 150 patients. T*ech Coloproctol.* 2015 Mar;19(3):135-44. doi: 10.1007/s10151-014-1241-x. Epub 2014 Nov 11.

[20]Shimada A1, Nakamura T, Ishii M, Chiba N, Ishikawa S, Arisawa Y, Hashimoto M. A case of necrotizing fasciitis developed in a patient with recurrent rectal cancer treated with chemotherapy [Article in Japanese] *Gan To Kagaku Ryoho.* 2013 May;40(5):663-5.

[21]Braendengen M, Tveit KM, Berglund A et al. Randomized phase III study comparing preoperative radiotherapy with chemoradiotherapy in nonresectable rectal cancer. *J Clin Oncol* 2008; 26: 3687–3694.

[22]Bujko K, Wyrwicz L, Rutkowski A et al. Long-course oxaliplatin-based preoperative chemoradiation versus 5 x5Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study. *Ann Oncol* 2016; 27: 834–842.

REFERENCES

1. **Braendengen M,** Tveit KM, Berglund A et al. Randomized phase III study comparing preoperative radiotherapy with chemoradiotherapy in nonresectable rectal cancer. *J Clin Oncol* 2008; 26: 3687–3694.
2. **Bujko K,** Wyrwicz L, Rutkowski A et al. Long-course oxaliplatin-based preoperative chemoradiation versus 5 x5Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study. *Ann Oncol* 2016; 27: 834–842.
3. **Dzik-Jurasz A**, Domenig C, George M, et al. Diffusion MRI for prediction of response of rectal cancer to chemo radiation. Lancet 2002;360:307–8
4. **Franke, J**, Rosenzweig, S, Reinartz, P et al, Value of positron emission tomography (18F-FDG-PET) in the diagnosis of recurrent rectal cancer. *Chirurg.* 2000;71:80–85 **Glynne-Jones R**. et all. Rectal cancer: ESMO Clinical Practice Guineline for diagnosis, treatment and follow-up, *Annals of Oncology 28 (Supplement 4)*:iv22-iv40, 2017
5. **Guren MG**, Undseth C, Rekstad BL et al. Reirradiation of locally recurrent rectal cancer: a systematic review. *Radiother Oncol* 2014; 113: 151–157.
6. **Huh JW.** Curative potential of surgical resection for locally recurrent rectal cancer. *Ann Surg*. 2014 Jun;259(6):e88.
7. **Kaiser AM.** Diversion with neoadjuvant vs surgery with adjuvant treatment for obstructing rectal cancer? *Dis Colon Rectum.* 2012 Oct;55(10):e346
8. **Kim DJ**, Kim JH, Lim JS, et al. Restaging of rectal cancer with MRI imaging after concurrent chemotherapy and radiation therapy. Radio Graphics 2010;30:503–16
9. **National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Rectal Cancer, Version 4.2017 -- January 18, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/rectal.pdf on February 8, 2018**
10. **Patel JA**, Fleshman JW, Hunt SR, Safar B, Birnbaum EH, Lin AY, Mutch MG. Is an elective diverting colostomy warranted in patients with an endoscopically obstructing rectal cancer before neoadjuvant chemotherapy? *Dis Colon Rectum.* 2012 Mar;55(3):249-55
11. **Rania A**. Marouf, Mary Y. Tadros , Tarek Y. Ahmed. Value of diffusion-weighted MR imaging in assessing response of neoadjuvant chemo and radiation therapy in locally advanced rectal cancer. The Egyptian Journal of Radiology and Nuclear Medicine. Volume 46, Issue 3, September 2015, Pages 553–561
12. National Comprehensive Cancer Network, Clinical Practice Guidelines in Oncology (NCCN Guidelines®), Rectal Cancer, Version 4.2017 -- January 18, 2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/rectal.pdf on February 8, 2018
13. **Salerno G**, Sinnatamby C, Branagan G, et al. Defining the rectum: surgically, radiologically and anatomically. Colorectal Dis. 2006;8 Suppl 3:5–9
14. **Sebag-Montefiore**, D, Stephens, RJ, Steele, R et al, M. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG CO 16): a multicentre, randomised trial. *Lancet*. 2009;373:811–820.
15. **Selvaggi F,** Fucini C, Pellino G, Sciaudone G, Maretto I, Mondi I, Bartolini N, Caminati F, Pucciarelli S. Outcome and prognostic factors of local recurrent rectal cancer: a pooled analysis of 150 patients. T*ech Coloproctol.* 2015 Mar;19(3):135-44. doi: 10.1007/s10151-014-1241-x. Epub 2014 Nov 11.
16. **Shimada A**, Nakamura T, Ishii M, Chiba N, Ishikawa S, Arisawa Y, Hashimoto M. A case of necrotizing fasciitis developed in a patient with recurrent rectal cancer treated with chemotherapy [Article in Japanese] *Gan To Kagaku Ryoho.* 2013 May;40(5):663-5.
17. **van den Brink M**, Stiggelbout AM, van den Hout WB et al, Clinical nature and prognosis of locally recurrent rectal cancer after total mesorectal excision with or without preoperative radiotherapy. *J Clin Oncol.* 2004;22:3958–3964.
18. **Wiggers T.** Management of local recurrence of rectal cancer. *European Journal of Cancer*, September 2011, Volume 47, Supplement 3, Pages S290–S291