UNIVERSITY OF MEDICINE AND PHARMACY

OF CRAIOVA

RECTAL CANCER: CLINICAL, HISTOPATHOLOGICAL, MOLECULAR, PROGNOSIS ASPECTS

IN SURGICAL RESECTIONS WITH CURATIVE VISA

ABSTRACT

Ph.D. Coordinator **PhD Student**

Professor Ion GEORGESCU **Vlad Pârvănescu**

2016

TABLE OF CONTENTS

KEY WORDS: rectal cancer, MMP-9, radical treatment

INTRODUCTION

Colorectal cancer is the third most frequent cancer in women and men in USA. Regarding the mortality, it occupies the third place after pulmonary cancer which remains on the first place. The fact that this malignant pathology is diagnosed extremely late in most cases represents one of the biggest problems in the management of this disease.

STAGE OF KNOWLEDGE

CHAPTER I- RECTUM AND MESORECTUM ANATOMY

The rectum represents the last portion of the digestive tract. It has a double origin from the ectodermis and the endodermis.

From the topographic point of view, there are two segments: the pelvic rectum and the perineal rectum.

There are 4 layers that form the rectal wall. At the exterior there is the serous layer which is the peritoneum. Under it there is the muscular layer formed by longitudinal and circular fibers. The next layer is the subumucosal layer which contains vascular and lymphatic plexuses. The last layer is the lining of the rectum on the inside which is the mucosa.

The arterial vascularisation has three sources: superior, middle and inferior rectal arteries. The venous drainage is represented by veins that accompany the above mentioned arteries. The lymphatic drainage is done with the help of one plexus above the pectineal line and another one under the pectineal line.

The rectum has double innervation, both sympathetic and parasympathetic, the muscular layer being the main layer that benefits from this.

CHAPTER II-RECTAL CANCER-GENERAL DATA

The colorectal cancer is the fourth most frequent cancer in men and the third in women worldwide. At European level, rectal cancer represents approximately 35% of all colorectal cancers with a mortality rate of 4-10/100000 people/year.

Smoking is associated with rectal cancer in men, generally after the age of 35 years. Hiperproteic nutritional regimes, especially red meat, raise the risk, while white meat diminishes the risk. Fibers have a protective role because they decrease the pH of the stool as the fibers are decomposed by the intestinal flora.

Metastasis process is produced on the lymphatic route or on the hematogenous route. The lymphatic extension starts with the invasion of the lymphatic vessels in the submucosal layer and perirectal layer. The hematogenous metastasis is done with the help of neoformation vessels or when the tumor invades the wall of a larger vessel.

CHAPTER III-DIAGNOSIS PRINCIPLES IN RECTAL CANCER

Rectal cancer evolves asymptomatically a long period of time. Initial symptoms are modifications of the rhythm of defecation with the alternation of constipation with diarrhea or the presence of blood in the stool. The clinical picture is different according to the topography of the tumor. So cancers at the level of rectosigmoid junction have a clinical picture resembling the one in the left colon cancer with the alternation between constipation and diarrhea, rectal bleeding or a clinical picture of intestinal subocllusion.

Rectal exam can locate tumors situated in the lower half of the rectum.

CT is rarely used to detect the primary tumor, but especially to evaluate local extension, to detect invaded pelvic or abdominal lymph nodes or systemic metastasis. MRI is used both preoperatively and postoperatively for stage T3 and T4 tumors. Rigid rectosigmoidscopy allows detecting tumors up to 25 cm proximal to the anal orifice. Intrarectal ultrasonography is very useful in evaluating local extension, degree of invasion in the rectal wall, extension of the tumor in the near organs or structures or sometimes even evaluating local lymph node invasion.

Regarding the gross aspect, tumors can be fungating, ulcerated, infiltrating or combinations. From the anatomopathological point of view we can have the following types of rectal cancer: adenoarcinoma, squamous carcinoma, mucinous carcinoma, signet ring cell carcinoma, medullary carcinoma, undifferentiated carcinoma. Rectal cancer can also be classified as well differentiated tumors (G1), moderately differentiated tumors (G2) and low differentiated tumors (G3).

CHAPTER IV- TREATMENT PRINCIPLES IN RECTAL CANCER

The surgical treatment is the only treatment that has a curative visa. Its objective is to eliminate the rectum,mesorectum and regional lymph nodes when a curative surgery is performed. It is indicated in Dukes A and B rectal cancers. The following curative surgeries may be performed: abdominoperineal resection, high anterior resection, low anterior resection and others.

Radiotherapy is a very useful method in the treatment. It is used as a radical, adjuvant or palliative radiotherapy. Chemotherapy is utilized with less success because rectal cancers have a low response to it. 5-fluoro-uracil is used in medical practice.

PERSONAL CONTRIBUTION

CHAPTER V- MATERIAL AND METHOD

This part of the thesis utilizes 196 patients interned in the first Surgical Department of the Emergency County Hospital from Craiova between 2006-2014. The immunohistochemistry study contained 31 stage III colorectal adenocarcinomas operated in the year 2014 in the first Surgical Department of the Emergency County Hospital from Craiova. A retrospective and prospective study was realized.

CHAPTER VI-CLINICAL STUDY

Almost two thirds of the patients were men and one third women. The male/female ratio was 1.64. Collected data showed an increased tendency of cases from fifth decade of life to the eighth decade. The urban/rural ratio was 0.92. Three quarters of cases were interned through the chronic system while a quarter presented themselves in the emergency department. The ratio chronic/emergency was 2.84.

The most frequent symptom was the pain, followed by rectal bleeding, defecation disorders and neoplastic impregnation syndrome. Radical interventions were abdominal rectosigmoidectomy with sigmodo-rectal anastomosis (Dixon operation) and the abdominoperineal resection with terminal colostomy in the left iliac fossa (Miles operation). Palleative surgeries included anterior rectosigmoidectomy with closing the remaining rectal distal stump and terminal colostomy in the left iliac fossa (Hartmann operation) or lateral colostomy in the left iliac fossa to evacuate the stool.

Pus discharge at the level of the abdominal wall was the most encountered complication (7% of cases). The dehiscence of the anastomosis complicated 4% of the operated rectal cancers.

Collected data showed an increased tendency of the period of hospitalization from 1-7 days to 15-21 days. The mortality in our group was 7%.

CHAPTER VII- MORPHOLOGICAL STUDY

The rectosigmoid junction topography is the most frequent localization with almost a third of cases.. The fungating and ulcerated form dominated the gross aspects with over a half of the cases.

The partially laterally extended/circumfentially extended ratio was 1.22. The common form adenocarcinoma was detected in over three quarters of cases, the mucinous carcinoma was detected in approximately a tenth of cases and the squamous carcinoma was present in the rest. Moderately differentiated forms counted over a half. The ratio between tubular form and papillary form is 1.5.

Inflammation was generally present in the samples from the surgical pieces, being absent in a third of cases.

The most frequent category of pT was pT3 with over a half of cases. The most frequent categories of pN were pN0 and pN1, both with a third of cases. Metastasis occurred in 15% of cases. The patients referred to a doctor most frequently in stage III (over a half of cases).

The most intense reaction to MMP-9 was discovered in the malignant cells so we can conclude they are the main source of MMP-9. There were observed stromal cells of fibroblastic type and peritumoral macrophages which presented a positive reaction to MMP-9. Cancers with high MMP-9 expression had a larger number of blood vessels.

CONCLUSIONS

The clinical profile of the patients with rectal cancer was represented by a man in the seventh or eighth decade of life, interned through the chronic system, presenting pain, rectal bleeding, defecation disorders who benefitted mostly from the Dixon operation.

The anatomopathological profile of the patients was represented by the fungating or ulcerated and fungating adenocarcinoma, evenly distributed at the different segments of the rectum, partially laterally extended, well or moderately differentiated, tubular form with the presence of a chronic inflammation with high or moderate intensity, with necrosis and in an advanced stage of the disease.

In rectal cancer, MMP-9 had generally a high but inconstant expression in the malignant cells. The most powerful expression was found in moderately and low differentiated cancers and a lower expression was found in well differentiated cancers. Ocasionally, MMP-9 expression was identified in peritumoral macrophages and stromal cells. An intense reaction was observed in the macrophages and lymphocytes from the areas with tumoral necrosis. The angiogenesis process was correlated with the intensity of the reaction to MMP-9.