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ORIGINAL ARTICLE

Evaluating the incidence rate of positive cytology in colorectal cancers and its relationship with local progress of the tumor

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Abstract

Introduction: Detection of malignant cells in the peritoneal cavity indicates the extension of cancer cells. The aim of this study is to evaluate the incidence rate of positive cytology in colorectal cancer and its relationship with the local progress of the tumor.

Methods: In a 2-year prospective study in Mashhad and Iran Universities of Medical Sciences, peritoneal lavage was performed on 40 patients with colorectal cancer from May 2012 to May 2013. Before any manipulation of the abdominal cavity, about 100 cc of normal saline was entered into the peritoneal cavity. Then, the samples were submitted for cytology. A sample was considered as positive if at least one cancer cell was detected.

Results: From among 40 patients, 19 were male and 21 were female. The mean age of the patients was 51 years. They consisted of 17 cases of colon cancer and 23 cases of rectal cancer. Totally, positive cytology was identified in three patients. Among them, one case had abdominal carcinomatosis and the other two cases were involved at the levels of T3 and/or T4.

Conclusions: It appears that peritoneal cytology is an appropriate method to evaluate tumor staging. Results of this method can be correlated between positive cytology and peritoneal seeding and survival, although the result of negative cytology cannot exclude advanced colorectal cancer and patients with carcinomatosis may have a negative peritoneal lavage.

Key Words: Colorectal cancer; Peritoneal cytology; Incidence

Introduction

As one of the causes of cancer death, colorectal cancer accounts for nearly 400,000 deaths per year. Approximately, 30% of patients are in advanced stages of the disease at the time of diagnosis. The cases of recurrence occur following

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the curative treatment. The most important pathological prognostic factor after surgery is the stage of the disease including blood and lymphatic spread, the number of nodes involved, and passage through the intestinal wall or perforation of the tumor. Peritoneal metastasis occurs in two stages: firstly, the cells are transferred from serosal surface of the primary tumor to the peritoneal cavity, and secondly, free cancer cells adhere favorably to the locations such as the omentum and mesenterium. Then, these cells grow and disseminate throughout the peritoneal cavity. These cells may be identified in patients with colorectal cancer in the peritoneal cavity before surgery [1, 2].

Detection of cancer cells within the peritoneal cavity is associated with high recurrence rate of tumor and poor prognosis. Identification of free cancer cells in the peritoneal cavity before surgery implicates tumor extension in the early stage of colorectal cancer. Patients who are at this stage, followed by peritoneal siding, should be monitored very accurately at the follow-up period and require supplementary treatments such as chemotherapy [3, 4].

The aim of this study is to evaluate the incidence rate of positive peritoneal cytology in colorectal cancer and its relationship with local progress of the tumor.

Methods

This 2-year prospective study, which was performed at Mashhad and Iran Universities of Medical Sciences, was approved by the ethics committee of Iran University of Medical Sciences. An informed consent was obtained from all participants.

Peritoneal lavage was performed in 40 patients with colorectal cancer from May 2012 to May 2013. Before surgery, all the patients were evaluated by computed tomography (CT) scan or magnetic resonance imaging (MRI) scan. The disease level was determined and CEA was used as a tumor marker in the follow-up of these patients. All the patients underwent curative surgery and in preoperative evaluation, no evidence of liver metastasis or peritoneal seeding was observed.

Before any manipulation of the abdominal cavity, about 100 cc of normal saline was entered into the peritoneal cavity. Then, upon gentle stirring, about 10 cc of the fluid was aspirated and submitted for cytology. Heparin (1 cc) was added to the specimen to prevent possible clotting. Thereafter, the fluid was centrifuged and evaluated for the detection of malignant cells. Cytologic features of malignant cells include increased nuclear size, variation in cell size, lack of differentiation, prominent nucleoli or irregular chromatin distribution within nuclei, and (especially irregular) mitoses.

The sample was considered as positive when at least one cancer cell was observed. In the case of rectal cancer, only upper rectal cancers were enrolled in the study and patients with cancers of middle or lower rectum were excluded.

Results

The study participants included 40 patients (19 male and 21 female) with the mean age of 51 years. The patients were comprised of 17 cases of colon cancer and 23 cases of rectal cancer. The colon cancer was identified in seven patients with right colon cancer, two cases with transverse colon cancer and eight cases with cancers of sigmoid colon and left colon. Totally, positive cytology was detected in three patients. Out of the three, one case had abdominal carcinomatosis, and the other two cases were involved in T3 and/or T4 levels. The findings are listed in Table 1.

Table 1: The cytology findings

Variable		Positive	Negative
N-40		3	37
Age (yrs)		53.3	53.8
Gender:	Male	2	17
	Female	1	20
Tumor site:	Colon	2	15
	Rectum	1	22
Histologic grade:	Well	1	19
	Mod	2	18
Depth of invasion:	pTis, T1, T2	0	5
	P3	1	22
	P4	2	10
Regional lymph nodes:	Pno	0	17
	Pn1	2	17
	Pn2	1	3
TNM stage:	0	0	3
	1	0	7
	2	2	23
	3	1	4

All the patients with rectal cancer received preoperative chemoradiotherapy for a minimum of one month and maximum period of 2 months. After preoperative chemoradiation, the surgical

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procedure was performed. The surgical technique included open laparotomy on 24 patients and laparoscopy on 16 patients.

The mean duration of follow-up was 13 months. Eight patients died during follow-up, five out of eight were in stage three of the disease, and the other three were in stage four. From the three patients with abdominal carcinomatosis, two cases died 8 and 11 months after surgery. One patient who had negative cytology at the second stage of rectal cancer referred with tumor recurrence one year after the disease. At the second laparotomy, we found abdominal carcinomatosis.

Discussion

In colorectal cancers, hematogenous spread is the most common form of metastasis to the liver and lungs. For lymph nodes, radical surgery is considered as an acceptable standard treatment to remove the involved nodes. Furthermore, hepatectomy is an acceptable treatment for liver involvement. While in these patients, peritoneal seeding is low in incidence, their treatment differs from the above methods. However, peritoneal involvement in colorectal cancer is associated with mortality and morbidity due to complications such as obstruction, resistant ascites, and more spread of the tumor [5].

Peritoneal involvement represents the end stage of the disease which is associated with poor prognosis [6]. In our patients, positive cytology was seen in cases that were at the advanced stage of the disease which was surely correlated with higher possibility of mortality and recurrence.

In addition to peritoneal fluid cytology, evaluation of the levels of tumor markers in peritoneal fluid suggested that in cases with negative cytology, the levels of tumor markers such as CEA and CA19-9 in peritoneal liquid correlate significantly with the recurrence, disease-free survival, and overall survival. Each of these two (cytology or tumor marker) methods can represent the possibility of recurrence or overall survival [7]. Negative cytology was reported among our patients with abdominal carcinomatosis. In these cases, it seems that determining tumor marker levels can also provide helpful information

Genetic evaluation, as a method with higher diagnostic accuracy, is also used to detect micro-metastasis [8]. In this study, peritoneal cytology and measurement of cytokeratin in patients with low rectal cancer were evaluated before and after surgery. It was found that in these patients, there was no relation between cytology and cytokeratin of peritoneal lavage and local recurrence and prognosis of the disease [9]. In another study, evaluation of peritoneal cytology in patients with gastric cancer suggested that cases with positive cytology were associated with poor prognosis [10]. In this study, cytology was performed under local anesthesia. In patients with gastric cancer, samples of peritoneal lavage were evaluated for cytology and RT-PCR for CEA. It was observed that in these patients, PCR method was more sensitive than cytology for diagnosis of peritoneal involvement. This sensitivity is increased in cases of advanced tumor or perineural and vascular invasion. Therefore, if this test is positive, the possibility of recurrence is increased and survival rate is decreased [11].

Conclusions

According to our findings, in patients with colorectal cancer, there is a direct correlation between the stage of the disease and positive peritoneal cytology at the same stage. Thus, it appears that peritoneal cytology is an appropriate method for evaluation of tumor staging. Results of this method can be correlated with positive cytology and peritoneal seeding and survival, although the result of negative cytology cannot exclude advanced colorectal cancer, and patients with carcinomatosis may have a negative peritoneal lavage.

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