INTRODUCTION: Colorectal cancer (CRC) advanced stage (stage IVA) is characterized by distant metastasis in one organ or in one site. The aim of this study is to present a relatively rare localization of CRC dissemination, i.e. pleural metastases clinically presenting with malignant pleural effusion.

PATIENTS AND METHODS: A total of 12 patients, 10 males and two females at a mean age of 61.4±13.3 years (range, 39-78 years) with malignant pleural effusion because of CRC were included in this four-year study (2012-2016). Physical examination and Karnofsky performance status score were evaluated. Radiographic studies were used to establish pleural effusion. Pleural effusion drainage and pleural fluid cytological examinations were performed. Patients' survival rate was established.

RESULTS: Pleural metastasis developed approximately 1.8±0.7 years after radical operation in all the patients. Patient's Karnofsky performance status score was ≤50. Pleural effusion evacuation was accomplished by tube thoracostomy in all the patients. The cytological examination established adenocarcinoma cells in the pleural effusion. The mean patient's survival rate was 3.1±1.9 months.

CONCLUSION: This study described a rare localization of CRC metastasis in the pleural cavity characterized by an extremely low patient's survival rate. Scr Sci Med 2017; 49(3): 35-39

Keywords: advanced colorectal cancer stage, malignant pleural effusion, tube thoracostomy, survival
ment of other sites in the absence of liver and lung metastases is unusual (4-6).

The aim of this study is to present a relatively rare localization of CRC dissemination, the pleural space clinically presenting with malignant pleural effusion.

PATIENTS AND METHODS

A total of 12 patients, 10 males and two females at a mean age of 61.4±13.3 years (range, 39-78 years) with malignant pleural effusion because of CRC in the Department of Special Surgery, Medical University of Plovdiv, were included in this four-year study (2012-2016). All the patients were previously operated for CRC and operation type was established based on their previous medical history. The disease-free period up to diagnosis of the malignant pleural dissemination was analyzed. Physical examination and Karnofsky performance status score were evaluated. Radiographic studies were used to establish the side and size of pleural effusion, i.e. conventional thoracic x-ray (performed in all the patients) and thoracic computed tomography (CT) additionally done in five patients. Pleural effusion drainage and pleural fluid cytological examinations were performed. The stay of drain in pleural cavity was calculated. Patients’ survival rate was established. IBM - SPSS Statistics software, v. 20 was used for statistical analysis and data is presented as mean values and standard deviation. P-value <0.05 was considered statistically significant.

RESULTS

Patients’ demographic and clinical characteristics are presented on Table 1.

Medical history provided information about radical operations for CRC in all the patients. The number of patients operated for left-sided colon cancer was significantly higher (p<0.01) (Table 1). Abdominoperineal resections and anterior resections were performed in three patients each while left hemicolectomy in four ones. Right hemicolectomy was carried out for right-sided colon cancer in two patients only (Table 1).

It was established that malignant pleural effusion had developed 1.8±0.7 years after radical operation. For each patient, Karnofsky performance status score was not greater than 50, with expression of dyspnea being significant in eight (66.67%) and moderate in four patients.

Table 1. Patients’ demographic and clinical characteristics

| Parameters                          | n   | %    |
|-------------------------------------|-----|------|
| Gender                             |     |      |
| male                                | 10  | 83.33|
| female                             | 2   | 16.67|
| Age (years)                         |     |      |
| range                              | 39-78 |     |
| mean                               | 61.4±13.3 |   |
| Colon cancer localization          |     |      |
| rectum                             | 3   | 25.00|
| recto-sigmoid segment              | 3   | 25.00|
| sigmoid colon                      | 4   | 33.33|
| right colon                        | 2   | 16.67|
| Pleural effusion localization      |     |      |
| right-sided                        | 7   | 58.3 |
| left-sided                         | 5   | 41.7 |
| Management of pleural effusion     |     |      |
| tube thoracostomy                  | 12  | 100  |
| mean patient’s survival (months)   | 3.1±1.9 |     |

Right-sided localization of the pleural effusion was established in seven patients (in 58.3% of the cases). There were no cases of bilateral pleural effusion. Radiographic studies showed large pleural effusions as opacity covered almost the entire hemithorax and typically produced contralateral shift of the mediastinal structures (Fig. 1, Fig. 2).

Figure 1. Chest x-ray shows massive left-sided malignant pleural effusion with contralateral mediastinum shift
Pleural effusion evacuation by tube thoracostomy and short-term chest tube drainage was performed in all the patients. Cytological examination revealed adenocarcinoma cells in the pleural effusion (Fig. 3A, Fig. 3B). The chest tube drain was removed after 5.6±1.9 days (range, 3-9 days). After malignant pleural effusion drainage, the patient’s following-up established mean survival rate of 3.1±1.9 months.

DISCUSSION

According to the AJCC/UICC stage IV CRC denotes distant metastasis (M1) and it is defined in IVA with distant metastasis confined to one organ or site, and in IVB with metastasis in more than one organ/site or the peritoneum. As a Department of Thoracic and Abdominal Surgery, one of our objects of practical and scientific interest is the topic of ‘malignant pleural effusion’. After reviewing the medical literature available, we didn’t find any published article dealing with the role of CRC as a cause of malignant pleural effusion. This is the main reason why, by using our own database, we decided to describe the pleural space as a rare isolated site of CRC dissemination (IVA stage) clinically presenting with malignant pleural effusion.

The peak CRC incidence rate is in the seventh decade of life, in general, around the age of 65 years (1,2). This strongly correlates with patients’ age in this study. The fact that rectal cancer and left-sided colon cancer are more common in men, whereas women have a higher incidence rate of more proximal cancers explains the gender distribution in our database (2-5).

In many regions of the world, both rectum and left colon remain the predominant site for CRC. This epidemiological fact of colon cancer localization is confirmed by our data (1).

Because the colon is drained solely by the portal system, one would not expect metastases to organs and sites without evidence of tumour in the liver. In
contrast, rectal cancers may spread through the portal or systemic venous systems and can, theoretically, give rise to isolated pulmonary metastases (1-5). From the lung, parenchymal tumour cells may spread and involve pleural surfaces via pulmonary circulation. If or not this theory may explain the way of CRC metastasis is not so important in our study. For us, the presentation of one extremely rare isolated site of CRC dissemination is of major importance. In this point of view, this study is an evidence of unpredictable behaviour of malignant solid tumour spreading, with CRC being one of them. There weren’t significant differences in the site of malignant pleural effusion localization, just as we expected.

The major indication for palliation in patients with a malignant pleural effusion is relief of dyspnea (6-8). Several methods may be used to remove the pleural effusion with the objective to relieve dyspnea: therapeutic thoracocentesis, short-term chest tube drainage, chronic indwelling catheter, and chemical pleurodesis. Therapeutic thoracocentesis should be the sole therapeutic option in patients with far-advanced disease, poor performance status, tumours associated with a poor survival, and significant dyspnea, like the cases included in our study (9-11). However, on the base of our long-term clinical practice, we preferred short-term chest tube drainage in cases of such kind.

Pleural fluid cytology is the least invasive method for diagnosis of a malignant pleural effusion (12,13). With improvement in cytological techniques and appropriate specimen handling, exfoliative cytology warrants the diagnosis in 60% to 90% of patients with the sensitivity depending on the extent of pleural involvement and the primary malignancy. In the patients with significant dyspnea and low performance status score, pleural fluid cytology is the only diagnostic option that was presented in this study.

Malignant pleural effusions are the end stage of solid tumour disease, with median patient’s survival rate of four-six months only. Our own results confirm the poor prognosis of the patients with malignant pleural effusion, especially in CRC.

**CONCLUSION**

This study was dedicated to one of the relatively rare localizations of CRC dissemination, i.e pleural space, clinically presenting with malignant pleural effusion. The role of short-term chest tube drainage as a method of palliation and the diagnostic value of pleural fluid cytology in malignant pleural effusion caused by CRC dissemination were demonstrated. The study confirmed the poor prognosis of malignant pleural effusions with extremely short patient’s survival.

**REFERENCES**

1. National Cancer Institute. Colon cancer treatment. Available at: http://www.cancer.gov.
2. Dominitz JA, Samsa GP, Landsman P, Provenzale D. Race, treatment, and survival among colorectal carcinoma patients in an equal-access medical system. Cancer. 1998;82(12):2312-20.
3. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al.; Gastrointestinal Consortium Panel. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology. 2003;124(2):544-60. doi:10.1053/gast.2003.50044
4. Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. N Engl J Med. 1992;326(10):653-7. doi:10.1056/NEJM199203053261001
5. O’Connell JB, Maggard MA, Ko CY. Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. J Natl Cancer Inst. 2004;96(19):1420-5. DOI: 10.1093/jnci/djh275
6. August DA, Ottow RT, Sugarbaker PH. Clinical perspective of human colorectal cancer metastasis. Cancer Metastasis Rev. 1984;3(4):303-24.
7. American Thoracic Society. Management of malignant pleural effusions. Am J Respir Crit Care Med. 2000;162(5):1987-201. DOI: 10.1164/ajrccm.162.5.ats8-00
8. Sahn SA. Talc should be used for pleurodesis. Am J Respir Crit Care Med. 2000;162(6):2023-4; discussion 2026. doi: 10.1164/ajrccm.162.6.pc09-00a.
9. Saffran L, Ost DE, Fein AM, Schiff MJ. Outpatient pleurodesis of malignant pleural effusions using a small-bore pigtail catheter. Chest. 2000;118(2):417-21. doi:org:10.1378/chest.118.2.417.
10. Putnam JB Jr, Walsh GL, Swisher SG, Roth JA, Sulant DM, Vaporiyan AA, et al. Outpatient management of malignant pleural effusion by a chronic indwelling pleural catheter. Ann Tho-
Martínez-Moragón E, Aparicio J, Sanchis J, Menéndez R, Cruz Rogado M, Sanchis F. Malignant pleural effusion: prognostic factors for survival and response to chemical pleurodesis in a series of 120 cases. Respiration. 1998;65(2):108-13.

Burrows CM, Mathews WC, Colt HG. Predicting survival in patients with recurrent symptomatic malignant pleural effusions: an assessment of the prognostic values of physiologic, morphologic, and quality of life measures of extent of disease. Chest. 2000;117(1):73-8. doi: 10.1378/chest.117.1.73.

Tremblay A, Michaud G. Single-center experience with 250 tunnelled pleural catheter insertions for malignant pleural effusion. Chest. 2006;129(2):362-8. doi: 10.1378/chest.129.2.362.