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A Woman with a Long History of Smoking and a Debilitating Dry Cough

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Aim: to present a clinical case of colorectal cancer in a woman with a long history of smoking and a leading complaint of dry cough.
Key points. A 56-year-old patient with a long history of smoking was hospitalized in the pulmonology department of the clinic with a leading complaint of a constant debilitating dry cough during the day, not amenable to the action of drugs, as well as general weakness, sweating and weight loss by 2 kg in 3 months. The examination revealed a moderately differentiated adenocarcinoma of the hepatic bend of the colon with generalized lymphadenopathy and metastatic lung damage, iron deficiency anemia. Surgical treatment was performed at the Sechenov University surgical hospital: right-sided hemicolectomy with D2 lymph dissection (removal of epicolic, paracolic, mesocolic lymph nodes); adjuvant chemotherapy was prescribed. The patient is under the supervision of an oncologist and a coloproctologist.
Conclusion. A clinical case of colorectal cancer in a woman with a long history of tobacco smoking and extra-intestinal symptoms is presented, demonstrating the need for cancer caution in relation to patients older than 50 years with iron deficiency anemia and lymphadenopathy. The timeliness of the diagnosis of a malignant neoplasm by primary care physicians is determined by the careful identification of cancer risk factors of this localization and the targeted search for “symptoms of anxiety”, upon detection of which endoscopic, radiation and morphological examination is necessary.
Keywords: dry cough, tobacco smoking, lymphadenopathy, iron deficiency anemia, colorectal cancer
Conflict of interest: the authors declare no conflict of interest.

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Женщина с длительным анамнезом табакокурения и изнуряющим сухим кашлем

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Цель: представить клиническое наблюдение колоректального рака у женщины с длительным анамнезом табакокурения и ведущей жалобой на сухой кашель.
Основные положения. Пациентка в возрасте 56 лет с длительным анамнезом табакокурения госпитализирована в пульмонологическое отделение клиники с ведущей жалобой на постоянный изнуряющий сухой кашель в течение суток, не поддающийся действию лекарств, а также общую слабость, потливость и похудание на 2 кг за 3 месяца. В результате обследования выявлена умеренно дифференцированная аденокарцинома печеночного изгиба ободочной кишки с генерализованной лимфаденопатией и метастатическим поражением легких, железодефицитная анемия. В хирургическом стационаре Сеченовского Университета проведено оперативное лечение: правосторонняя гемиколэктомия с D2 лимфодиссекцией (удаление эпиколических, паракалических, мезоколических лимфоузлов); назначена адъювантная химиотерапия. Пациентка находится под наблюдением онколога и колопроктолога.
Заключение. Представлен клинический случай колоректального рака у женщины с длительным анамнезом табакокурения и внекишечными симптомами, демонстрирующий необходимость онконастороженности по отношению к пациентам старше 50 лет с наличием железодефицитной анемии и лимфаденопатии.

Своевременность диагностики злокачественного новообразования врачами первичного звена здравоохранения определяется тщательным выявлением факторов риска рака данной локализации и прицельным поиском «симптомов тревоги», при обнаружении которых необходимо проведение эндоскопического, лучевого и морфологического исследования.

Ключевые слова: сухой кашель, табакокурение, лимфаденопатия, железодефицитная анемия, колоректальный рак

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Colorectal cancer (CRC) holds one of the leading positions in the structure of cancer incidence and mortality from malignant neoplasms worldwide. In 2020, the Global Cancer Observatory (GLOBOCAN) database recorded over 1.9 million new cases of CRC and 935,173 deaths from it [1]. On the one hand, due to the implementation of screening programs in some Western countries, there has been a tendency of a decreasing the incidence in people over 50 years old, on the other hand, there has been an increase in the incidence of this type of cancer among younger populations [2, 3]. In Russia in 2020, 62,854 people were diagnosed with CRC, with about one-fifth (22 %) of whom died, which was primarily due to the late verification of the diagnosis [4]. The issue of timely diagnosis of malignant neoplasm in patients with risk factors and "alarm symptoms", especially in the absence of intestinal manifestations, does not lose its relevance. We present a clinical observation of a 56-year-old female patient with CRC, having a 40-year history of smoking and a primary complaint of a debilitating dry cough.

Patient M., 56 years old, was admitted to the clinic with a main complaint of a persistent debilitating dry cough throughout the day and night, not dependent on changes in body position; taking medications (acetylcysteine, salbutamol, beclomethasone) did not bring relief. She was also troubled by general weakness, sweating and a weight loss of 2 kg over 3 months, which the patient associated with an increase in her physical activity in the summer. From the medical history, it is known that in June 2021, the patient first felt weakness and decreased work capacity. She consulted a clinic at her place of residence, where hypochromic microcytic anemia was detected. The genesis of the anemia was not determined, and iron therapy was recommended, which had a positive effect. In July 2022, the patient noticed an increase in weakness, as well as the appearance of a persistent dry cough. She self-administered mucolytics without effect. Since early August 2022, the cough has become unbearable, general weakness has increased, sweating has appeared, and she also noted a weight loss of 2 kg over the summer months. In this connection, she again sought medical help at her place of residence. On August 3, 2022, a chest X-ray was performed, which revealed bronchial wall thickening. According to spirometry data: forced expiratory volume in 1 second was 92 %, with a slight decrease in flow rate at the mid-distal level. The diagnosis of bronchial asthma was established, and low-dose beclomethasone therapy was ineffective. The patient came to the clinic for examination and therapy selection. From the life history, it is known that the patient has a 40-year smoking history (smoking index — 240, pack-years index — 40, corresponding to a high risk of developing lung cancer and chronic obstructive pulmonary disease (COPD)). The family history is burdened with respiratory and oncological diseases: the 80-year-old mother and 25-year-old son suffer from bronchial asthma, the 81-year-old father suffers from COPD (long smoking history); the maternal grandmother died at 80 years old from stomach cancer.

During the physical examination: the condition is moderately severe, consciousness is clear. The body mass index is 19.6 kg/m^2. Body temperature is 36.6 °C. The skin is of physiological color, clean, and of normal moist. No edema. Peripheral lymphadenopathy was revealed: enlarged painless posterior cervical lymph nodes on the left side, soft in consistency, about 1.5 cm in size, as well as a painless conglomerate of lymph nodes in the left axillary region, soft in consistency, mobile, about 3 cm in size. The shape of the chest: conical, symmetrical; the accessory respiratory muscles are not involved in the act of breathing. Respiratory rate is 18 per minute. Oxygen saturation is 97 % while breathing air. Vocal fremitus is equal on symmetrical parts of the chest. On comparative percussion of the lungs over symmetrical areas, a clear pulmonary sound is heard. Auscultatively, the breathing is harsh, scattered dry wheezes over the entire surface of the lungs. Heart tones are clear, rhythmic, heart rate is 85 per minute, blood pressure is 120/70 mmHg. The abdomen is soft, painless. The liver and spleen are not enlarged. Stool is formed, without impurities. The "percussion" symptom on the lumbar region is negative on both sides. Diuresis is unremarkable. Based on complaints, medical history and objective examination, a preliminary diagnosis was formulated: Chronic obstructive bronchitis. Mild hypochromic microcytic anemia. Peripheral unilateral lymphadenopathy (posterior cervical and axillary lymph nodes on the left).

Figure 1. MSCT of the chest organs of Patient M., 56 years old: multiple lesions of both lungs (mts); diffusely in both lungs, multiple small foci are detected polysegmentally, some of which tend to merge

Рисунок 1. МСКТ органов грудной клетки пациентки М., 56 лет: множественные очаги обоих легких (mts); диффузно в обоих легких полисегментарно определяются множественные мелкие очаги, некоторые из которых с тенденцией к слиянию

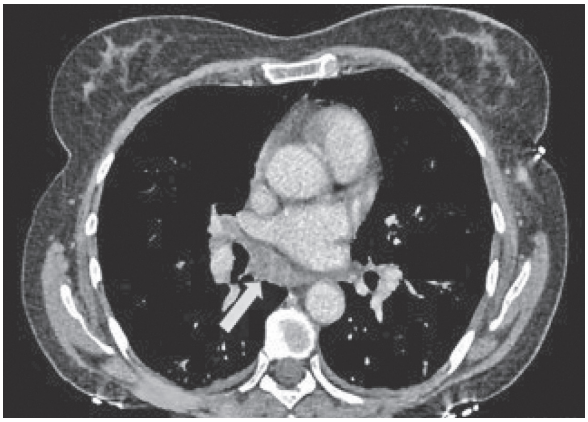


Figure 2. MSCT of the chest organs of Patient M., 56 years old: intrathoracic lymphadenopathy; at the scanning level (indicated by the arrow), enlarged para-aortic lymph nodes are detected, up to 14 mm in size; the study also revealed multiple paratracheal, bifurcation, bronchopulmonary nodes, up to 16 mm in size

Рисунок 2. МСКТ органов грудной клетки пациентки М., 56 лет: внутригрудная лимфаденопатия; на уровне сканирования (указано стрелкой) определяются увеличенные парааортальные лимфатические узлы размером до 14 мм; также при исследовании обнаружены множественные паратрахеальные, бифуркационные, бронхопульмональные узлы размером до 16 мм

In the complete blood count, mild hypochromic microcytic anemia was noted (erythrocytes — 3.0 × 10^{12}/L, hemoglobin — 106 g/L, mean erythrocyte volume — 75 fl, color index — 0.78, hematocrit — 35 %, mean corpuscular hemoglobin — 27.3 pg, mean corpuscular hemoglobin concentration — 294 g/L); normal ESR of 13 mm/h; in the biochemical blood test, a decrease in iron levels to 6.8 μmol/L and ferritin — to 2 ng/mL, and a slight increase of C-reactive protein to 5.4 mg/L were found. To exclude an occult gastrointestinal bleeding, a stool test for latent blood was performed — gastrointestinal hemoglobin: the result was positive. When assessing pulmonary function, all indicators of lung ventilation function were within normal limits. According to the data of multisliced computed tomography (MSCT) of the chest, multiple metastatic foci in both lungs (Fig. 1), intrathoracic lymphadenopathy (Fig. 2) and enlarged axillary lymph nodes (Fig. 3) were determined.

Considering the anemia, the positive fecal occult blood test, and the metastatic lung lesions, the patient underwent a CT scan of the abdominal organs. A mass in the hepatic flexure of the colon with significant enlargement of the mesenteric and retroperitoneal lymph nodes was detected (Fig. 4).

For objective confirmation of the presence of the tumor, assessment of its patency, and obtaining material for morphological verification of the process, a video colonoscopy was performed. During the procedure, a neoplasm of the hepatic flexure of the colon with significant lumen narrowing was detected, which prevented the colonoscope from passing into

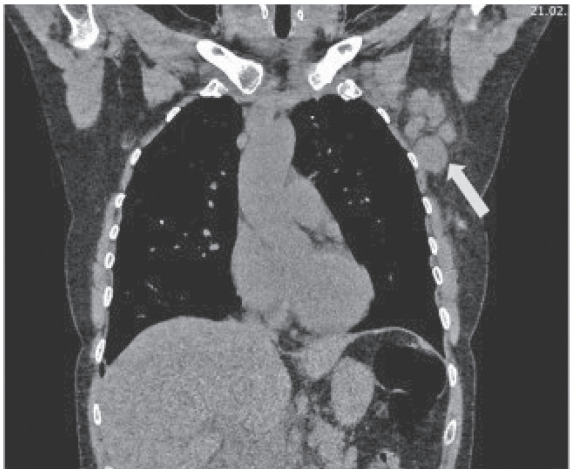
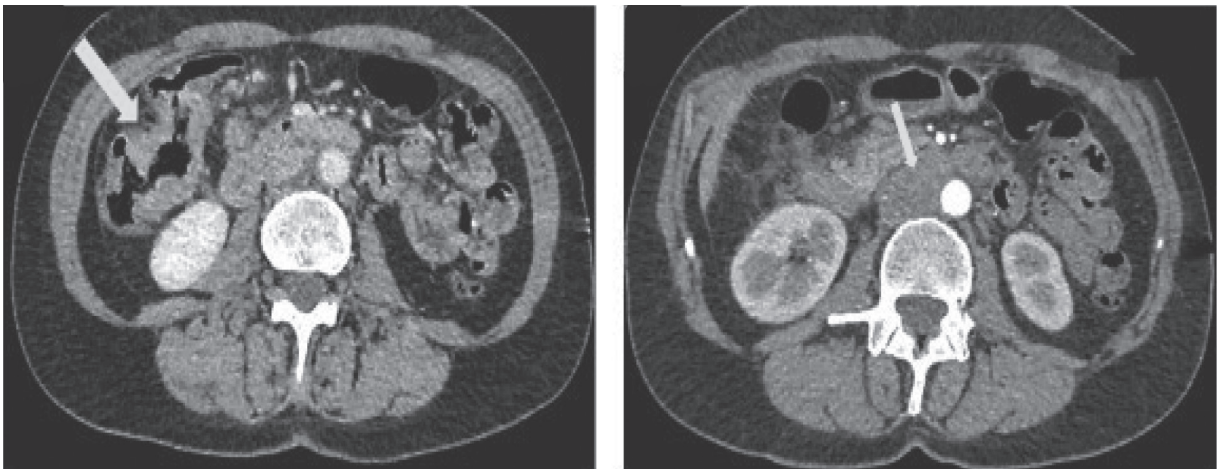


Figure 3. MSCT of the chest organs of Patient M., 56 years old: axillary lymphadenopathy; the arrow indicates multiple enlarged left axillary lymph nodes with a tendency to merge to form conglomerates, up to 44 × 20 mm in size

Рисунок 3. МСКТ органов грудной клетки пациентки М., 56 лет: аксиллярная лимфаденопатия; стрелкой указаны множественные увеличенные левые аксиллярные лимфатические узлы с тенденцией к слиянию с формированием конгломератов, размером до 44 × 20 мм



A B

Figure 4. CT scan of the abdominal cavity of Patient M., 56 years old: formation of the hepatic curvature of the colon (A), lymphadenopathy (B). A — in the area of the hepatic curvature of the colon (at the bend, indicated by the arrow), a muff-like thickening of the walls up to 12 mm with a total length of about 90 mm is noted; the intestinal lumen is moderately narrowed; the surrounding tissue is infiltrated, compacted, paracolic lymph nodes up to 9 mm in size along the short axis; medial from the formation along the mesentery, a node measuring 24 × 28 mm with pronounced contrast was noted. B — enlargement of the retroperitoneal lymph nodes: para-aortic lymph nodes on the left (indicated by the arrow) measuring 15 × 22 mm (infrarenal), 12 × 10 mm (suprarenal), interaortocaval up to 16 × 20 mm, retrocaval — conglomerates measuring up to 32 × 22 mm with moderate compression of the inferior vena cava

Рисунок 4. ПКТ органов брюшной полости пациентки М., 56 лет: образование печеночной кривизны ободочной кишки (А), лимфаденопатия (В). А — в области печеночной кривизны ободочной кишки (в месте изгиба, указано стрелкой) отмечено муфтообразное утолщение стенок до 12 мм общей протяженностью около 90 мм; просвет кишки умеренно сужен; окружающая клетчатка инфильтрирована, уплотнена, параколические лимфоузлы размером до 9 мм по короткой оси; медиальнее от образования по ходу брыжейки отмечен узел размером 24 × 28 мм с выраженным контрастированием. В — увеличение забрюшинных лимфоузлов: парааортальных слева (указано стрелкой) размерами 15 × 22 мм (инфраренальные), 12 × 10 мм (супраренальные), межаортокавальные до 16 × 20 мм, ретрокавальные — конгломераты размером до 32 × 22 мм с умеренной компрессией нижней полой вены

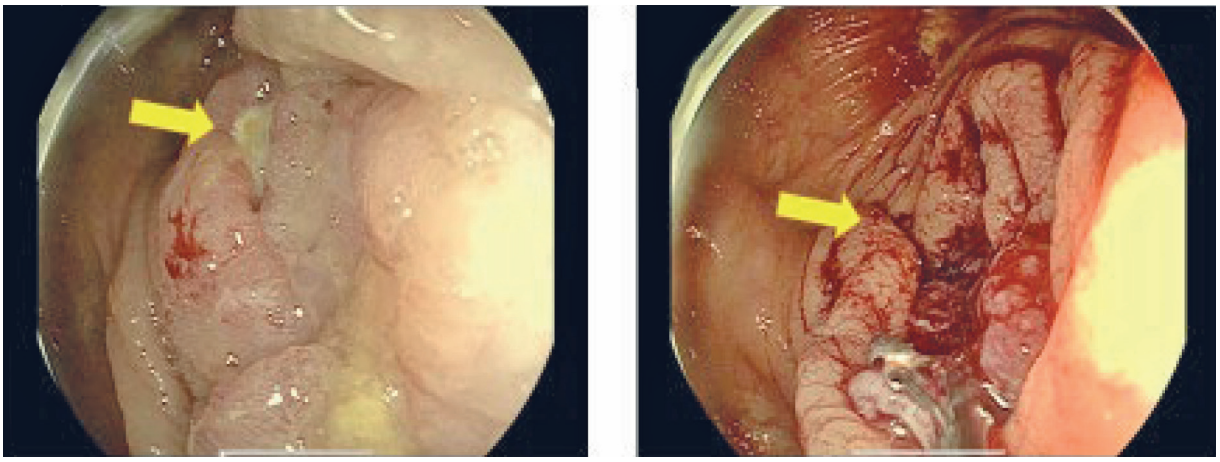
the proximal parts of the colon and endoscopically assessing the extent of the neoplasm (Fig. 5). A biopsy was taken from the distal edge of the tumor infiltration.

According to histological examination, the malignant nature of the neoplasm was confirmed: moderately differentiated adenocarcinoma. To determine the origin of the lymphadenopathy and to exclude or confirm metastatic involvement of the axillary lymph nodes, a fine-needle aspiration biopsy of the conglomerate of the left axillary lymph nodes was performed under ultrasound guidance: their secondary malignant transformation was confirmed, morphologically similar to the already verified cancer of the hepatic flexure of the colon.

Based on the data from the patient's history, objective examination, laboratory and instrumental methods of investigation, and morphological verification, the clinical diagnosis was established. Primary disease: cancer of the hepatic flexure of the colon (histologically — moderately differentiated adenocarcinoma), cT3N2aM1a (generalized lymphadenopathy — posterior cervical, axillary, intrathoracic, mesenteric, retroperitoneal lymph nodes; metastatic involvement of both lungs). Complications: iron-deficiency anemia of mild severity. After being discharged from the pulmonology department, the patient was hospitalized in the surgical department of Sechenov University, where surgical treatment was performed: right hemicolectomy with D2 lymph node dissection (removal of epicolic, paracolic, mesocolic lymph nodes); adjuvant chemotherapy was prescribed.

Discussion

The patient's long history of smoking (passive smoking since childhood, with the father as the source, and active smoking for 40 years) is an independent risk factor for the development of COPD and malignant neoplasms, among which breast cancer, lung cancer, and CRC are predominant in



A B

Figure 5. Video colonoscopy protocol for Patient M., 56 years old: the colonoscope is passed to the hepatic flexure; in the projection of the distal part of the transverse colon, the lumen is deformed, narrowed by a tuberous exophytic formation of cartilaginous density, red, with a coating of fibrin (A); the lumen for the device is impassable (less than 10 mm), narrowed in the form of a gap, the proximal edge of the tumor is not defined; biopsy shows moderate bleeding (B); in other parts of the intestine, the mucous membrane is pale, the folds are straightened with air, the vascular pattern of the submucosal layer is pronounced, peristalsis can be traced, it is active; biopsy taken

Рисунок 5. Протокол видеоколоноскопии пациентки М., 56 лет: колоноскоп проведен до печеночного изгиба; в проекции дистальной части поперечно-ободочной кишки просвет деформирован, сужен бугристым экзофитным образованием хрящевидной плотности, красного цвета, с налетом фибрина (А); просвет для аппарата непроходим (меньше 10 мм), сужен в виде щели, проксимальный край опухоли не определен; при биопсии умеренная кровоточивость (В); в других отделах кишки слизистая оболочка бледная, складки воздухом расправляются, сосудистый рисунок подслизистого слоя выражен, перистальтика прослеживается, активная; взята биопсия

women [5, 6]. According to a meta-analysis by M. Sollie et al., which included twelve cohort studies (400,944 women were diagnosed with primary invasive breast cancer), the risk of cancer death among smokers was 1.52 times higher compared to those who had never smoked [7]. According to the results of a meta-analysis by B. Pesch et al., the relative risk (RR) of lung cancer has a dose-dependent effect and is 7.8 (95 % confidence interval (CI): 6.5–9.4) for smoking women [8]. Smoking is a major risk factor for CRC, but the mechanism by which CRC develops and progresses due to smoking is not yet fully understood. A meta-analysis by E. Botteri et al. summarized data from 188 original studies: the combined RR for CRC was 1.14 (95 % CI: 1.10–1.18) for current smokers and 1.17 (95 % CI: 1.15–1.20) for former smokers. The risk of cancer increased linearly with the intensity and duration of smoking [9]. X. Bai et al. showed that this risk also increases in animal models: in mice, exposure to tobacco smoke changes the metabolomic profile (increased biosynthesis of pro-carcinogenic taurodeoxycholic acid correlates with a predominant increase in intestinal *Eggerthella lenta*). Changes in the microbiota composition lead to a dysfunction of the intestinal barrier and activation of oncogenic and pro-inflammatory signaling pathways, promoting the development of CRC [10].

Patient M., 56 years old, with a long history of smoking and a family history of malignant neoplasms (gastrointestinal cancer in the maternal grandmother), is at high risk for CRC [11]. At her first visit for medical help at the pre-hospital stage, there were already “alarm symptoms” (general weakness, iron-deficiency anemia), and therefore, CRC screening (fecal occult blood test and colonoscopy) was necessary. The persistent dry cough, which became exhausting over time, can be retrospectively explained by the compression of the airways by enlarged intrathoracic lymph nodes and lung tissue involvement of a metastatic nature.

Colonoscopy is a relatively expensive examination for the healthcare system and is rarely used in screening programs for early detection of colorectal cancer in Russia and around the world. However, currently, only colonoscopy allows the detection and removal of cancer precursors in the intestine — polyps. The presence of a positive fecal occult blood test result is not a sign of cancer, and a negative test does not guarantee its absence. In the case of a large malignant lesion, colonoscopy allows a verification

of the neoplasm and, if necessary, intervention — for example, stent placement in cases of obstructive bowel obstruction.

Timely diagnosis of CRC and adequate treatment determine a favorable prognosis for survival. Insufficient oncological vigilance of doctors, especially in the presence of risk factors and "alarm symptoms", leads to the late detection of malignant neoplasms, depriving patients of the opportunity for using organ-preserving methods of treatment [12].

Conclusion

Patients over 50 years of age with long-term smoking experience and a family history of malignant neoplasms are at high risk for CRC. The presence of such "alarm symptoms" as general weakness, weight loss, hypochromic microcytic anemia, even in the absence of intestinal manifestations, requires a fecal occult blood test and colonoscopy. Timely diagnosis of CRC at early stages by primary healthcare physicians will improve the life prognosis for such patients.

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