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CLINICAL CASE REPORT

SUCCESSFUL EXTIRPATION OF A PERFORATED ESOPHAGUS AFTER CHEMORADIOTHERAPY IN INFILTRATIVE ULCERATIVE SQUAMOUS CELL CARCINOMA

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ABSTRACT

Esophageal cancer is one of the most aggressive malignant neoplasms of the gastrointestinal tract, occupying the eighth place in the structure of morbidity worldwide. Despite comprehensive approaches to treatment, mortality continues to grow in both gender groups, which moves this pathology to the sixth position in the structure of mortality from malignant tumors. A lot of patients undergo radiation therapy in the preoperative period or in an independent version due to the peculiarities of the localization of the tumor or the spread of the process. One of the serious complications of the disease on the background of ongoing conservative therapy is perforation of the esophagus, which, according to the literature, can develop from 5.6 to 33 % of cases, and the risk factors for the development of this complication are infiltrative-ulcerative form of cancer, disease stage T3–4 and the presence of esophageal stenosis, as well as the use of chemotherapy drugs such as fluorouracil and cisplatin. The article describes a clinical case of esophageal perforation in a patient with infiltrative-ulcerative form of squamous cell carcinoma of the esophagus on the background of preoperative chemoradiotherapy. The total focal dose (TFD) at the time of complication development was 24 Gy. As a result of a comprehensive additional examination, which revealed a developed complication in the form of perforation of the esophagus, an interdisciplinary council decided on an immediate surgical intervention, during which extirpation of the esophagus with gastro- and esophagostomy was performed. The patient was discharged on the 15th day in a satisfactory condition with a recommendation to conduct an IHC study for the presence of PD-L1 expression to determine further management tactics. This clinical case demonstrates the role of the infiltrative-ulcerative form of tumor growth, the stage of the disease, as well as the use of chemotherapy drugs during radiation treatment as risk factors for the development of esophageal perforation; an important task at the prehospital stage in the selection of such patients is a thorough examination in specialized oncological centers to exclude possible complications in the process of the above conservative treatment.

Keywords: chemoradiation therapy, esophageal cancer, esophageal perforation

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КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

УСПЕШНАЯ ЭКСТИРПАЦИЯ ПЕРФОРИРОВАННОГО ПИЩЕВОДА ПОСЛЕ ХИМИОЛУЧЕВОЙ ТЕРАПИИ ПРИ ИНФИЛЬТРАТИВНО-ЯЗВЕННОМ ПЛОСКОКЛЕТОЧНОМ РАКЕ

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РЕЗЮМЕ

Рак пищевода – одно из самых агрессивных злокачественных новообразований (ЗНО) желудочно-кишечного тракта, занимающее восьмое место в структуре заболеваемости во всем мире. Несмотря на комплексные подходы к лечению, смертность продолжает расти в обеих гендерных группах, что перемещает данную патологию на шестую позицию в структуре смертности от ЗНО. Множество пациентов проходят лучевую терапию в предоперационном периоде или в самостоятельном варианте в силу особенностей локализации опухоли или распространенности процесса. Одним из серьезных осложнений заболевания на фоне проводимой консервативной терапии является перфорация пищевода, которая, по литературным данным, может развиваться от 5,6 до 33 % случаев, а факторами риска развития данного осложнения являются инфильтративно-язвенная форма рака, стадия заболевания T_{3-4} и наличие стеноза пищевода, а также применение таких химиопрепаратов, как фторурацил и цисплатин. В статье описан клинический случай развития перфорации пищевода у пациента с инфильтративно-язвенной формой плоскоклеточного рака пищевода на фоне проводимого предоперационного химиолучевого лечения. Суммарная очаговая доза (СОД) на момент развития осложнения составила 24 Гр. Вследствие комплексного дообследования, выявившего развившееся осложнение в виде перфорации пищевода междисциплинарным консилиумом было принято решение о немедленном хирургическом вмешательстве, в ходе которого была выполнена экстирпация пищевода с гастро- и эзофагостомией. Пациент был выписан на 15-е сутки в удовлетворительном состоянии с рекомендацией проведения ИГХ-исследования на наличие экспрессии PD-L1 для определения дальнейшей тактики лечения. Данный клинический случай демонстрирует роль инфильтративно-язвенной формы роста опухоли, стадии заболевания, а также применение химиопрепаратов во время лучевого лечения как факторы риска развития перфорации пищевода; важной задачей на догоспитальном этапе при отборе таких пациентов служит тщательное обследование в специализированных онкологических центрах для исключения возможных осложнений в процессе вышеописанного консервативного лечения.

Ключевые слова: химиолучевая терапия, рак пищевода, перфорация пищевода

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Соблюдение этических стандартов: в работе соблюдались этические принципы, предъявляемые Хельсинкской декларацией Всемирной медицинской ассоциации (World Medical Association Declaration of Helsinki, 1964, ред. 2013). Информированное согласие получено от всех участников исследования.

Финансирование: финансирование данной работы не проводилось.

Конфликт интересов: все авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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RELEVANCE

Esophageal cancer is one of the most aggressive malignant neoplasms of the gastrointestinal tract, occupying the eighth place in the structure of morbidity worldwide [1]. Despite comprehensive approaches to treatment, mortality continues to grow in both gender groups [2], which places this pathology to the sixth position in the structure of mortality from MNs [1].

Surgical intervention may be delayed or even impossible due to the features of the localization of the tumor or the prevalence of the process [3; 4], therefore, many patients undergo complex treatment, including radiation therapy, in the preoperative period or in an independent version.

One of the serious, high mortality rate complications of the disease on the background of conservative therapy is perforation of the esophagus. The causes of esophageal perforations are multiple, the main factors are iatrogenic effects and mechanical damage (barogenic ruptures, damage by foreign bodies, blunt chest injuries). According to a number of authors [5–7], the formation of an esophageal fistula as a complication of radiation therapy can develop in 5.6 to 33 % of cases, therefore, patients with a widespread tumor process require a thorough examination before starting treatment.

Purpose of the study: to present the results of clinical observation of a patient who developed a complication in the form of esophageal perforation at the stage of the preoperative course of chemoradiotherapy.

CLINICAL CASE INTRODUCTION

Patient B., 55 years old, was admitted to the radiotherapy Department No. 2 at the National Medical Research Centre for Oncology, Rostov-on-Don. The diagnosis was: (C15) Cancer of the middle and lower third of the esophagus T3N2M0, III stage, cl. gr. 2, with chronic bronchitis as concomitant pathology. From anamnesis: ill for 1 month, worried about weakness and increasing dysphagia. During fibrogastroduodenoscopy (FGDS) at the place of residence, an infiltrative ulcerative tumor of the esophagus was detected, a biopsy of the formation was performed. A histological examination of the biopsy material was carried out, conclusion No. 13420-21 of 07/27/2022: low-grade cancer. Independently applied to the National Medical Research Centre for Oncology, for further examination and determination of treatment tactics. When reviewing histological preparations at the National Medical Research Centre for Oncology No. 2011/22 dated 08/10/2022, fragments of the esophageal mucosa with complexes of low-grade carcinoma were determined. For the purpose of differential diagnosis between squamous cell carcinoma without keratinization and adenocarcinoma, an IHC study was recommended. 08/10/2022 a CT scan of the chest, abdominal cavity and pelvis was performed, conclusion: tumor of the middle and lower third of the esophagus for 6.7 cm with thickening of the walls to 1.6 cm with infiltration of the surrounding fiber, metastatic lesion of the intra-thoracic, retroperitoneal, subclavian lymph nodes (Fig. 1). Conclusion of immunohistochemical study No. 2524/22 dated 08/22/2022: The morphological picture and immunophenotype of tumor cells in the volume of esophageal biopsy (SC5/6+) are most characteristic of low-grade squamous cell carcinoma. Based on the data obtained, a consultation of physicians at the National Medical Research Centre for Oncology recommended a course of chemoradiotherapy as the first stage of treatment. Objectively upon admission: the general condition is close to satisfactory. Complaints of general weakness. The skin is of ordinary color, clean. There is vesicular respiration above the pulmonary fields, with no wheezing identified. Heart tones are muted, rhythmic, blood pressure of 121/78 mmHg, 76 beats/min heart rate. Body temperature 36.5 °C. The abdomen is soft, painless on palpation, the liver is at the edge of the costal arch, the spleen is not palpable. Healthy bladder and bowel habits. Weight of 80 kg, height of 180 cm, body area about 2 m^2.

Since 08/23/2022, a course of remote chemoradiotherapy on a linear accelerator Truebeam (Varian, USA) has been started using the technology of volume-modulated arc therapy (VMAT) for the esophageal tumor area and regional lymphatic collector with a single focal dose (SFD) of 2 Gy to a total focal dose (TFD) of 50 Gy for 25 fractions. No abnormalities were detected during the control of hematological parameters. On 08/25/2022, chemotherapy drugs were administered against the background of infusion therapy according to the scheme: paclitaxel 50 mg/m^2 (100 mg) and car-

boplatin AUC2 (360 mg). On 09/01/2022 the 2nd administration of drugs in the previous dose was carried out. 09/07/2022 after the 12th session with TFD 24 Gy, the patient complained of pain in the chest area on the right, in connection with which he was immediately examined to exclude cardiac pathology. On the ECG from 09/07/2022, a sinus rhythm with a heart rate of 70 beats/min, frequent supraventricular extrasystole episodes by the type of bigeminia, violation of intraventricular conduction, signs of left ventricular myocardial hypertrophy are recorded. An hour after the appearance of chest pain, complaints of shortness of breath joined. During the spiral computed tomography (CT) scan of the chest organs, signs of perforation of the esophagus with the formation of a right-sided hydropneumothorax were revealed (Fig. 2). The patient was urgently taken to the operating room for life-threatening indications. Intraoperatively: the patient is laid on his left side in the position for anterolateral thoracotomy on the right in the V intercostal space. Under endotracheal anesthesia with artificial ventilation, a thoracotomy was performed in the V intercostal space on the right. During revision up to 200 ml of serous-purulent effusion with digestive contents in the pleural cavity. In the mid-thoracic part of the esophagus, a tumor with necrotic changes was palpated, the latter up to 5 cm in size with a transition to the visceral pleura of the middle lobe of the lung. In the center of necrosis there is a perforating hole up to 1.5 cm in diameter. Tumor-necrotic-inflammatory infiltrate involved v.azygos and tributaries. With technical difficulties due to localization and prevalence of the process, v.azygos and tributaries were mobilized, bandaged twice, crossed. Mobilization of the esophagus with mediastinal lymphadenectomy was performed, necrectomy of the visceral pleura of the middle lobe of the lung was performed, areas suspected of leakiness (with an aqueous sample) were sutured with monolithic sutures, the pleural cavity was drained with 2 PVC tubes installed along the posterior axillary line in the 7th and 8th intercostals on the right. The patient was turned over to a position on his back. The cervical esophagus was decorated on the neck in the form of an esophagostomy. Upper median laparotomy was performed. The abdominal part of the esophagus is extracted into the abdominal cavity. The diaphragm legs are sutured. An additional row of stitches was applied to the stump of the esophagus. A gastrostomy was applied for nutrition – it was removed through a separate puncture, and the laparotomy wound was sutured in layers, tightly.

After surgery, the patient stayed in the anesthesiology and intensive care unit for 8 days. Further, in the specialized department he received treatment, including: infusion therapy (glucose-electrolyte and colloidal solutions), antibacterial therapy, antispasmodics, analgesics, prevention of postoperative pancreatitis, thromboembolic complications, metabolic and restorative therapy, inhalations, regular dressings. Drains from the abdominal and pleural cavities have been removed. Postoperative wound – healing by primary tension in suture conditions. The gastrostomy is functioning.

The patient was discharged on the 15th day in a satisfactory condition with a recommendation to conduct an IHC study for the presence of PD-L1 expression to determine further treatment tactics.

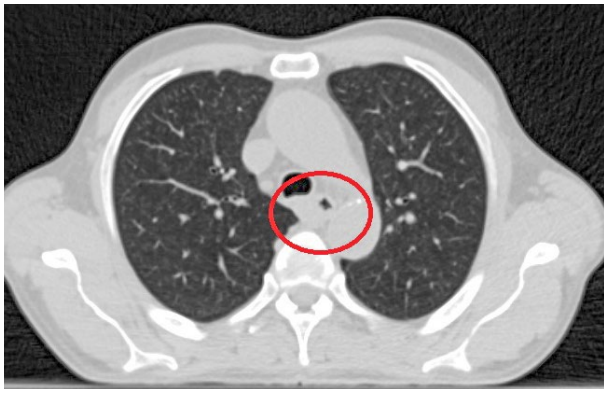

Fig. 1. Spiral chest CT before treatment.

Fig. 2. Perforation of the esophagus with the formation of a hydropneumothorax on the background of radiation therapy course.

DISCUSSION

Zhu C et al. [5] analyzed 78 studies conducted in between 1990 and 2018. They included 1,866 patients with an established diagnosis of esophageal cancer receiving radiation treatment (chemoradiotherapy, brachytherapy or radiation therapy in an independent version). Esophageal perforation was detected in 200 cases and amounted to 10.7 %. The authors found out that patients younger than 60–65 years were at risk; no statistically significant results were obtained regarding gender. In patients with ulcerative form of the tumor, stage T3–4 and squamous histological structure of cancer, perforation also developed more often. Esophageal stenosis has also been described as a risk factor. When analyzing studies describing the results of chemoradiotherapy in various modes, it was found that the complication developed more often against the background of the use of fluorouracil and cisplatin, in contrast to treatment with a combination of taxanes and cisplatin.

A retrospective analysis of risk factors for esophageal perforation against cancer, conducted by Hai-yan Chen et al. [8], included 322 patients who underwent radiation therapy due to the unresectability of the tumor, or relapse of the disease. The complication occurred in 10 patients during radiation therapy, and 8–40 weeks after completion in 8 more patients, which totaled 5.8 %. All the patients were male. 14 of the 18 patients (77.7 %) were under 60 years of age. 12 patients (66.6 %) were treated with stage T4. Chemoradiotherapy was received by 9 people (50 %). The average radiation dose at which perforation occurred was 54 Gy. Based on the above data, the authors concluded that the risk of esophageal perforation is male, age under 60 years and stage T4. The dependence of the complication development relative to the histological type has not been described.

Bing Hu et al. [9] analyzed 414 cases of chemoradiotherapy of squamous cell carcinoma of the esophagus in various regimens from 2012 to 2018 and found that esophageal perforation occurred in 46 patients (11.1 %), among whom 40 patients were men (86.96 %); 20 of them (43.48 %) were under the age of 60. 27 patients (58.7 %) were treated with stage T4. All patients with the developed complication were diagnosed with esophageal stenosis of varying degrees.

Based on the above research results, as well as our own experience, we can identify such risk factors for the development of esophageal perforation as an infiltrative-ulcerative form of the tumor, stages of the disease T3-4, esophageal stenosis and the use of fluorouracil and cisplatin drugs.

CONCLUSION

Taking into account the improvement of technical equipment, the possibilities of selecting patients for the provision of neoadjuvant radiation therapy of malignant neoplasm (MN) have expanded. It is necessary to remember and take into account the role of the infiltrative-ulcerative form of tumor growth as a risk factor for the development of esophageal perforation in esophageal cancer with squamous cell histotype. An important goal in the selection of such patients is a thorough examination in specialized cancer centers to exclude possible complications during the conservative treatment process.

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Vlasov S. G., Karnaukhova E. A., Rodionova O. G., Soldatkina N. V., Malinin S. A. – data collection, analysis and interpretation, technical editing, article preparation;

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Komandirov M. A. – data collection, analysis and interpretation, scientific editing;

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