MULTI-COURSE PHOTODYNAMIC THERAPY IN A PATIENT WITH MALIGNANT TUMOR OF THE MAJOR DUODENAL PAPILLA. CLINICAL CASE

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Abstract

The article presents a clinical case of successful elimination of mechanical jaundice by means of a course of photodynamic therapy in a patient with a malignant neoplasm of the major duodenal papilla and multimorbid concomitant pathology. The patient, admitted with a clinical picture of mechanical jaundice, after additional examination was given a final diagnosis - moderately differentiated adenocarcinoma of the major duodenal papilla, stage IIa (T2N0M0), complicated by moderate mechanical jaundice. After primary stenting, a series of three consecutive courses of combined systemic and local photodynamic therapy were performed with a three-month interval between them. During the last course, stent migration into the duodenum was detected. Nevertheless, the complex therapy allowed to effectively eliminate the manifestations of mechanical jaundice, stabilize the patient's condition, prevent further growth of the primary tumor, restore the patency of the ducts of the major duodenal papilla and avoid relapses of mechanical jaundice, despite the migration of the stent. This experience demonstrates the promise of the photodynamic approach for solving complex clinical situations associated with tumor damage to the biliary system and allows to consider this method as an alternative in situations of high risk of complications of traditional surgery.

Key words: malignant tumor of the major duodenal papilla; course photodynamic therapy; survival.

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МНОГОКУРСОВАЯ ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ У ПАЦИЕНТА СО ЗЛОКАЧЕСТВЕННЫМ НОВООБРАЗОВАНИЕМ БОЛЬШОГО ДУОДЕНАЛЬНОГО СОСОЧКА. КЛИНИЧЕСКИЙ СЛУЧАЙ

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Резюме

В статье представлен клинический случай успешного устранения механической желтухи посредством проведения курсовой фотодинамической терапии у пациента со злокачественным новообразованием большого дуоденального сосочка и мультиморбидной сопутствующей патологией. Пациенту, поступившему с клинической картиной механической желтухи, после дообследования был поставлен окончательный диагноз – умеренно дифференцированная аденокарцинома большого дуоденального сосочка, стадии IIa (T2N0M0), осложненная механической желтухой средней степени тяжести. После первичного стентирования выполнена серия из трёх последовательных курсов комбинированной системной и локальной фотодинамической терапии с трёхмесячным интервалом между ними. Во время последнего курса была выявлена миграция стента в двенадцатиперстную кишку. Тем не менее, комплексная терапия позволила эффективно устранить проявления механической желтухи, стабилизировать состояние пациента, предотвратить дальнейший рост первичной опухоли, восстановить проходимость протоков большого дуоденального сосочка и избежать рецидивов механической желтухи, несмотря на миграцию стента. Данный опыт демонстрирует перспективность фотодинамического под-

хода для решения сложных клинических ситуаций, связанных с опухолевым поражением билиарной системы и позволяет рассматривать этот метод как альтернативное средство в ситуациях высокого риска осложнений традиционной хирургии.

Ключевые слова: злокачественное новообразование большого дуоденального сосочка; курсовая фотодинамическая терапия; выживаемость.

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Introduction

Cancer of the major duodenal papilla (MDP) is a rare malignant pathology, which in oncological statistics is considered in combination with other malignant neoplasms of the bile ducts [1, 2, 3, 4]. The structure of morbidity and mortality in biliary cancer is assessed together with hepatocellular cancer [1, 2, 3, 4]. In the overall structure of malignant neoplasms of the digestive tract, the share of MDP cancer is only 0.2%. Being one of the rarest oncological pathologies, estimated together with hepatocellular carcinoma with a prevalence of 6.7 per 100,000 population, malignant neoplasms of the bile ducts have one of the highest overall mortality rates (35.2%) and mortality rates in the first year from the date of diagnosis (66.8%), while MDP cancer in the structure of biliary cancer is only 16.4%, which corresponds to a prevalence of 6 per 1,000,000 population [1, 2, 3, 4].

Despite the development of radiation and chemotherapy methods, the main method of treating MDP cancer remains surgical with a predominance of two types of operations: various modifications of pancreatoduodenal resection and local resection or papillectomy. However, radical surgical treatment is usually difficult due to late diagnosis of the disease: 80.3% of patients have an advanced or locally advanced process [1, 2, 3, 4]. Among the palliative treatment options, the main one remains the chemotherapeutic method, which is difficult to perform in patients with the most common complications of MDP cancer - mechanical jaundice, cholangitis, multiple organ failure, which are the leading clinical manifestations of MDP cancer [5].

One of the methods of palliative treatment, complementing surgical treatment is photodynamic therapy (PDT). PDT is a method of treating malignant neoplasms, in which the tumor is irradiated with light of a certain wavelength, which brings the molecules of a special substance selectively accumulated in the tumor tissue - a photosensitizer, into an excited state in the presence of oxygen. The released singlet oxygen has a direct cytotoxic effect, causing tumor cells to die by apoptosis, necrosis and autophagy. Based on the conducted studies of the effectiveness of PDT of malignant neoplasms of the pancreatobiliary zone, the authors developed a PDT technique that seems promising for the treatment of patients who are not indicated for radical surgical treatment [6].

Materials and Methods

Developed PDT technique

Algorithm of the developed PDT technique is the following: fluorescence diagnostics on the laser electron-spectral unit "Biospec" (LLC "Novyere Surgical Technologies", Russia) and local and systemic PDT on the software specialized laser dual-wave apparatus "LAMI-Gelios" (LLC "New Surgical Technologies", Russia) according to Technical Specifications 9444-001-53807582-2010. For PDT, a photosensitizer based on chlorin e6 (radachlorin, OOO "RADA-PHARMA", Russia) is used. Systemic PDT is performed through a peripheral intravenous access using an apparatus for intravenous blood irradiation (monochromatic light with a wavelength of 662-665 nm, irradiation time of 30 min, light exposure dose of 1200-1400 J/cm^2, output power of the light fiber of 0.7 W, radiation power density of 0.22 W/cm^2) with intravenous administration of a photosensitizer at a dose of 1-1.2 mg/kg of body weight according to the instructions for the drug. Local contact PDT is performed after 3 hours (5 hours for solid tumors) from the start of systemic PDT through antegrade percutaneous transhepatic and/or retrograde endoscopic access, depending on the localization of the malignant neoplasm (irradiation with monochromatic light with a wavelength of 662 nm, with an exposure dose of light of 220 J/cm^2). To perform local PDT, a specialized dual-wave laser software device with a fiber output power of 0.7 W and a radiation power density of 0.22 W/cm^2 with a radial diffuser is used.

In the case of pancreatic head cancer, endoscopic ultrasound is used for navigation, and in the case of malignant neoplasms of the intrahepatic and extrahepatic bile ducts, transluminal PDT is used during choledochoscopy on a guiding catheter for direct peroral cholangioscopy with its fixation (Fig. 1). In the case of pancreatic head cancer, if it is possible to install a stent without percutaneous transhepatic drainage, only retrograde endoscopic access is used.

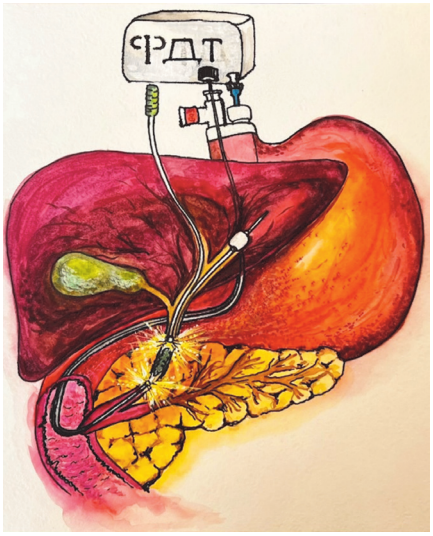

Рис. 1. Схема проведения локальной ФДТ у пациентов со злокачественными новообразования желчевыводяших протоков.
Fig. 1. Scheme of local PDT in patients with malignant tumors of the bile ducts.

The purpose of local PDT is to normalize the outflow through the extrahepatic bile ducts by reducing the volume of tumor tissue. Monitoring is carried out both visually and fluoroscopically and in the laboratory. At the same time, due to one of the advantages of PDT - low toxicity of treatment, the method can be carried out as part of a course of therapy to prevent recurrence of mechanical jaundice and increase patient survival, which is especially important for tumors of the pancreatobiliary zone, which have the worst prognosis among tumors of the digestive system [1, 2, 3].

In order to illustrate the method of course PDT, we considered it possible to present a clinical example of a patient with MDP cancer after stenting, in whom, with the help of course PDT, it was possible to prevent recurrence of mechanical jaundice despite the migration of the stent into the duodenum.

Clinical observation

The patient, 87 years old, was hospitalized in the surgical department of the State Healthcare Institution of the Novosibirsk Region "Novosibirsk Regional Clinical Hospital" in July 2024 with complaints of yellowness of the skin for 3 weeks. No other symptoms were noted. The patient underwent an ultrasound examination of the abdominal organs and magnetic resonance imaging of the abdominal organs, where biliary hypertension was detected. The final clinical diagnosis was made after video esophagogastroduodenoscopy with a biopsy from the major duodenal papilla and morphological verification of the diagnosis - moderately differentiated adenocarcinoma of the major duodenal papilla, stage IIa (T2N0M0), complicated by moderate mechanical jaundice. Among the concomitant pathologies, the patient had chronic urinary retention due to prostatic hyperplasia, chronic kidney disease stage IV (stage C4 A1) against the background of acute kidney injury (history of acute tubular necrosis). The patient also had significant concomitant cardiological and endocrine pathologies: hypertension with high cardiovascular risk stage III, degree 3, risk 4; chronic heart failure, functional class IIA; ischemic heart disease with episodes of stable angina pectoris functional, class II; diffuse multinodular goiter with signs of subclinical hyperthyroidism; diverticulosis of the colon; compensated type 2 diabetes mellitus; diabetic nonproliferative retinopathy of both eyes, and polyneuropathy.

Due to multiple concomitant pathologies and high perioperative risk, it was decided to refrain from radical surgery. The patient underwent endoscopic retrocholangiopancreatography, papillosphincterotomy and stenting of the common bile duct with biopsy from the major duodenal papilla. Two months later, before replacing the stent, the patient underwent the first course of local and systemic PDT according to the method described above in the surgery department of the Regional State BBudgetary Institution of Health Care "City Hospital No. 5, Barnaul". A month later, the stent was replaced at the State Healthcare Institution of the Novosibirsk Region “State Novosibirsk Regional Clinical Hospital”, followed by two courses of local and systemic PDT with an interval of 3 months between each course. During planned hospitalizations, the patient did not have clinical and laboratory signs of mechanical jaundice. During video esophagogastroduodenoscopy after ultrasound examination of abdominal organs, where no stent was detected, during planned hospitalization for the third course of PDT 6 months after stent placement, stent migration into the duodenum was detected (Fig. 2). At the same time, traces of bile were present in the duodenum, and the lumen of the major duodenal papilla was visualized. When comparing the dynamics according to the data of previous endoscopic studies, it was possible to

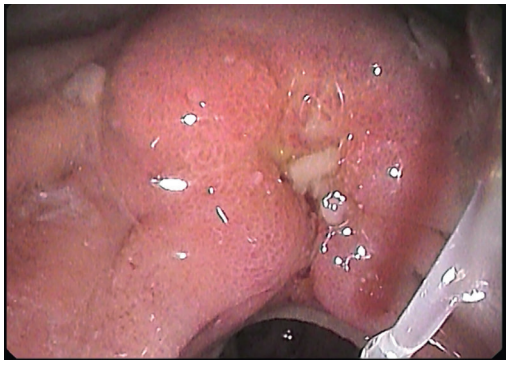

Рис. 2. Злокачественное новообразование БСДПК с наличием свободного просвета и следов желчи в двенадцатиперстной кишке.
Fig. 2. Malignant tumor of the major duodenal papilla with visualisation of free lumen and signs of bile in the duodenum.

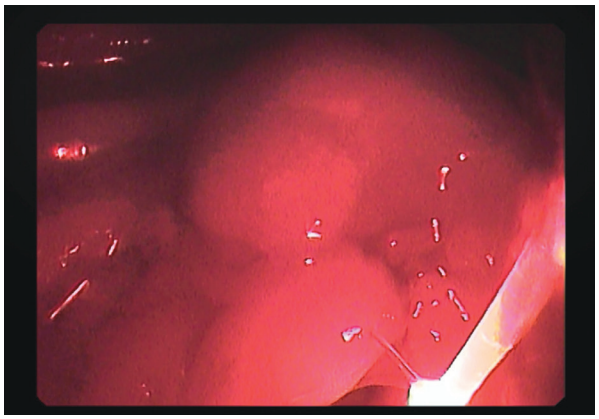

Рис. 3. Злокачественное новообразование БСДПК с наличием свободного просвета и следов желчи в двенадцатиперстной кишке.
Fig. 3. Malignant tumor of the major duodenal papilla with visualisation of free lumen and signs of bile in the duodenum.

identify the absence of clinically significant growth of the neoplasm into the lumen of the major duodenal papilla.

The patient underwent local PDT using a single technique similar to previous courses (Fig. 3) with recommendations for planned stenting.

From the moment of morphological verification of the diagnosis to the moment of discharge after the third course of PDT, 10 months have passed, outpatient monitoring of the patient continues. Of particular importance is the absence of side effects from the use of the photosensitizer on the urinary system and the absence of negative dynamics of clinical and laboratory markers of chronic renal failure against the background of multiple courses of PDT before and after surgery.

Conclusion

At the present stage, a number of studies of the effectiveness of PDT of malignant neoplasms of the bile ducts have been conducted, summarized in two meta-analyses: a meta-analysis of Moole H. *et al.* [7], which presents the main outcomes of heterogeneous studies, some of which used only PDT, while most patients underwent combined treatment (PDT and chemotherapy); and a meta-analysis of Tseimakh A.E. *et al.,* which analyses homogeneous studies that assessed only the effectiveness of PDT without the influence of other methods of specific treatment. Despite significant difficulties in the combined assessment of PDT studies due to significant variability between photosensitizers, different regimens and treatment plans for patients, both meta-analyses equally show an increase in survival when using PDT in patients with malignant neoplasms of the bile ducts by more than 8 months (240 [7] and 256 [8] days, respectively) with the elimination of the clinical picture of mechanical jaundice and the prevention of its relapses. Thus, course PDT is a promising method for treating mechanical jaundice and subsequent prevention of its recurrence in patients with malignant neoplasms of the major duodenal papilla, which allows, in the absence of significant side effects, to improve survival, which is especially important for older patients with multimorbid pathology.

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