



Photodynamic Therapy as Alternative Method of Treatment of Metastatic Ovarian Cancer with Many Recurrence: Case Report

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Abstract

Photodynamic therapy (PDT) is a minimally invasive therapeutic modality used for the treatment of a variety of cancers and benign diseases. The destruction of unwanted cells and tissues in PDT is achieved by the use of visible or near-infrared radiation to activate a light-absorbing compound (a photosensitizer), which, in the presence of molecular oxygen, leads to the production of singlet oxygen and other reactive oxygen species. Thus, the purpose of the report is to describe the clinical case of the effective use of intraoperative PDT as a method of treatment of a patient with metastatic cancer. Patient A, 59 years old, had ovarian cancer T3N1M0 stage III with peritoneal carcinomatosis. After intraoperative PDT (1.5 year) treatment, the progression of the process was not revealed by PET/CT. The results show that photodynamic therapy is one of the high efficiency methods of palliative treatment and it can be used for metastatic cancer. This technology should be included as a technique to the guidelines for the treatment of malignant tumors.

Keywords Photodynamic therapy · Ovarian cancer · Metastatic cancer

Malignant tumors today remain one of the unsolved problems of modern world medicine. The problems of diagnosis, treatment, and rehabilitation of cancer patients are actually a major breakthrough in this area [1].

According to the “American cancer society” in the year 2018, 1,735,350 new cases of cancer and 609,640 deaths from this pathology were registered [2].

In 2018, the total number of patients with malignant tumors in the Russian Federation amounted to about 7 million, an increase compared with 2017, 4%; while the mortality rate from cancer, 14% [3].

Ovarian cancer is the seventh most commonly diagnosed form of malignant neoplasms among women [4]. About a quarter of a million new cases of ovarian cancer are reported worldwide every year [4]. Unfortunately, there are no clearly recognized signs, and there are no preventative measures. Symptoms of the disease appear with an advanced stage of the disease. In this regard, malignant tumors of the ovaries in

70% of cases are detected in stage III–IV. Ovarian cancer is more common in the 51–60 age group [5].

The standard treatment for many ovarian cancers is maximal cytoreductive surgery and chemotherapy [6]. A total of ~70% of advanced ovarian cancer recurs, so advanced ovarian cancer ultimately has a 5-year survival rate of between 30 and 40% [7]. In the case of progression of the tumor in the first line of chemotherapy, we can use platinum and non-platinum drugs [8]. Unfortunately, in majority cases, chemotherapy does not have the opportunity to help patients, that is why we can use symptomatic therapy or clinical trials, may be some alternative methods.

Photodynamic therapy (PDT) has garnered attention as a novel therapy to reduce the tumor burden on a patient. PDT has been used to treat superficial esophageal cancer, early lung cancer, and early gastric cancer [9–11].

The method of photodynamic therapy is based on the introduction of photosensitizers into the patient’s body, selectively accumulated in the tumor tissue, which, with laser exposure (depending on the wavelength and mode of irradiation) can lead either to the emission of a quantum of light, so that it is possible to register their fluorescence or to produce the formation of cytotoxic substances, primarily singlet oxygen O₂ and other active radicals; the accumulation of which leads to the destruction of vital structures of tumor cells and their death [12]. PDT can induce cell death by triggering four

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Fig. 1 Results of PET/CT 18 April 2018

different death pathways—apoptosis, necrosis, autophagy, and paraptosis [13].

Fluorescence 5-aminolevulinic acid (ALA) visualization techniques (photodiagnosis) are helpful in the staging as well as in monitoring the effects of laparoscopic treatment [14]. The method can also detect disseminated microfoci during surgery. The effectiveness of PDT with Photofrin and ALA in treating ovarian cancer has been evaluated in two studies [15, 16]. These were focused, however, more of the nature of feasibility rather than for evaluation of efficacy.

Thus, the purpose of the report is to describe the clinical case of the effective use of intraoperative PDT as the method of treatment of metastatic ovarian cancer.

1 Material and Methods

Patient A, 59 years old, was treated in the “Hospital of the Medical Center of the Office of the President of the Republic of Kazakhstan” from April 2016, with complaints of weakness and sharp weight loss.

The tentative diagnosis was “ovarian tumor.” Supravaginal amputation of the uterus with appendages and omentectomy was performed. The histological type of cancer was low-grade adenocarcinoma. The final diagnosis is ovarian cancer T3N1M0 stage III.

In February 2017, after 6 courses of chemotherapy (paclitaxel 175 mg/m², carboplatin AUC = 6 mg/ml/min), the second surgery was performed—the extirpation of the cervical stump (second look).

In September 2017, the relapse occurred. During instrumental examination, the patient was found to have a progression of the tumor process (peritoneal carcinomatosis).

In October 2017, the next surgery was performed, i.e., Hartmann-type resection of the sigmoid and descending colon.

The following 6 cycles (2 line) were carried out by bevacizumab 15 mg/kg + carboplatin AUC = 4 + gemcitabine 1000 mg/m².

In April 2018, the relapse occurred by PET/CT (Fig. 1). Taking into account that the patient had a limited number of lesions and had the intolerable toxicity of chemotherapy, she was recommended for surgical treatment with intraoperative PDT.

In this case, photodynamic therapy was carried out by the LAHTA-MILON-970/20–662/4 (wavelength was 662 nm), with using of light guide with a diameter of 400 μm, the output beam power of 1.4 kW, and exposition of 3–5 min (energy of 150 j), after the introduction of the Photolon® solution at the rate of 2 mg/kg body weight before 2.5 h of the surgery.

2 Results and Discussion

In November 2019, PET/CT was done. Information for the progression of the process was not revealed—stabilization of the process (Fig. 2). Results of the SUVmax are presented in Table 1. The tumor marker CA-125 was taken before and after operation, but it was in normal value in both cases. The results can show us that the method of PDT can be used in serious cases, like alternative type of treatment.

Multimodal treatment of ovarian cancer involves surgery, radiotherapy, and chemotherapy. However, disease recurrence is common, and most patients cannot be salvaged with additional anticancer treatment. For these cases, photodynamic therapy can be an appealing alternative, since there is no

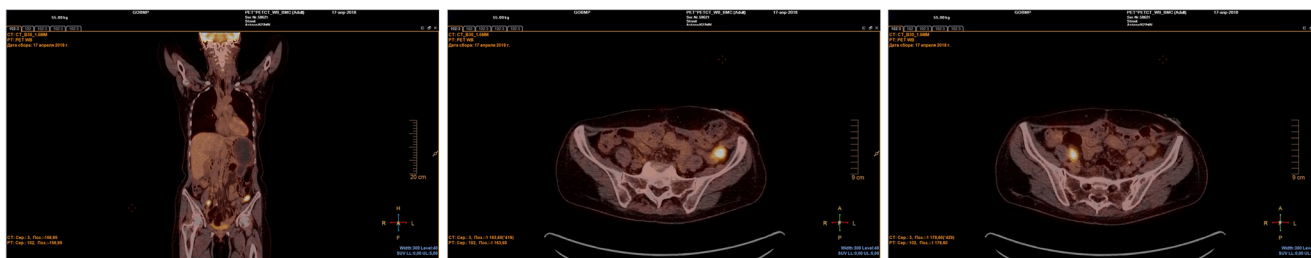


Fig. 2 Results of PET/CT 21 October 2019

Table 1 Results of PET/CT

	The common iliac lymph nodes (size/SUVmax)	The paracolic lymph nodes (size/SUVmax)
18 April 2018	0.5–0.7 cm/2.1	1.8 cm/6.4
21 October 2019	Not defined	Not defined

tissue resistance or exposure limitation to its use, and modern surgical techniques allow direct irradiation. Photodynamic therapy has its own side effects, however, diffuse PDT in the anatomically complex peritoneal cavity often results in significant toxicity to the surrounding healthy tissue [17].

The current stage of drug therapy development is the use of immune drugs that allow stimulating the immune system to treat the tumor, T cell activating cytokines, immune checkpoint inhibitors, depletion of regulatory T cells (Tregs), and cell-based therapies to selectively control tumor growth [18].

The next stage in the development of photodynamic therapy technology is to combine it with immunotherapy. Photoimmunotherapy (PIT) is based on the injection of a conjugate of an antibody, which binds a cell surface marker on the cancer and a photoactivating chemical (APC). A major feature of PIT compared with other approaches is its specificity for cancer. The specificity derives from targeting by the monoclonal antibody (mAb). Cell killing is initiated by excitation of the antibody-bound photoactivating chemical, IRDye700DX (IR700), with near-infrared light at 690 nm. Since the APC binds predominantly to cancer cells that overexpress the targeted cancer-associated antigens, light activation results in selective cancer cell killing while not harming adjacent normal cells including tumor-infiltrating immune cells [18].

3 Conclusion

Photodynamic therapy is one of the high efficiency methods of palliative treatment of local malignant tumors and it can be usable for metastatic process. It shows good survival rates with high quality of life. This technology should be included as a technique of choice to the guidelines for the treatment of malignant tumors.

Further research in this area will help to select more targeted sensitizers, to create new sources of radiation, which will also contribute to popularization of this procedure for the treatment of cancer, and used it with immunotherapy methods.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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