



The Clinical Case of Successful Application of Photodynamic Therapy in the Skin Metastases Treatment of Breast Cancer

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Abstract

The article describes the experience of using photodynamic therapy in the treatment of skin metastases of a patient with breast cancer. The authors note the high effectiveness of this method of treatment in combination with safety. The obtained data allow us to conclude that photodynamic therapy is a very promising method of treating this cohort of patients. Patient K., 69 years old, was diagnosed with cancer of the left breast in October 2015. T2N3M0. Stage IIIC. Complex treatment was carried out: 2 courses of neoadjuvant chemotherapy + radical mastectomy + remote radiation therapy summation of the focal dose 30gr + 4 courses of adjuvant chemotherapy. In the period up to February 2020, the patient repeatedly received supportive treatment in the palliative care department. Taking into account the volume of metastatic skin lesions, palliative multi-course PDT was recommended. As a result of the treatment, a partial regression of the tumor was obtained. On examination, the scar in the area of PDT is pale pink; the continued growth of the tumor is determined in the form of separate areas of infiltration along the anterior edge of the scar.

Keywords Breast cancer · Skin metastases · Photodynamic therapy

One of the most pressing problems of modern oncology is breast cancer, which annually affects about 1200 thousand women in the world, including more than 4 thousand in the Republic of Kazakhstan. Its significance is determined by the increasing incidence: the report of the International Agency for Research on Cancer predicts an increase in the

incidence of breast cancer by almost 2 times in the next 20 years [1].

The problem of breast cancer is also very relevant for the Republic of Kazakhstan; in 2018, 4648 patients with this diagnosis were registered, that is amounted to 25.3 per 100 000 of the population and breast cancer took the first rank in the structure of cancer incidence [2].

Accordingly, one of the major problems in the treatment of breast cancer is the treatment of metastases. Meanwhile, cancer of this localization is characterized by quite frequent metastasis, mainly in the skin [3].

In the treatment of metastatic breast cancer, as a rule, systemic therapy (chemo-, hormone-) is used in combination with radiation therapy and, if possible, surgical treatment [4].

Given the above, it seems natural that in recent years, the specialists have shown interest in the method of photodynamic therapy (PDT). This method is based on the ability of tumor tissues to selectively accumulate some photosensitizers to a much greater extent than the surrounding healthy tissues [5, 6]. The advantages of PDT are the high selectivity of

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tumor cell damage, the absence of serious side effects, and the possibility to combine treatment and diagnosis [7, 8].

Some experience has already been accumulated in the use of PDT in the treatment of skin metastases. Thus, E.V. Goranskaya and M.A. Kaplan demonstrated that PDT with the use of the Photolon photosensitizer was effective in 85% of cases [9]. The authors of another study in the treatment of intradermal metastases of breast cancer by PDT noted an even higher clinical effectiveness — the therapeutic effect was achieved in 89% of cases [10, 11].

One of the studies was conducted in which 7 patients with skin metastases of breast cancer were included. A total of 89 metastatic skin nodes were treated in 11 PDT sessions. The complete clinical effect was noted. The authors noted a good cosmetic result, demonstrating minimal scar formation [12].

The work of T. S. Mapds et al. demonstrated the effectiveness of PDT in this category of patients. Eighty-six metastatic skin lesions (average diameter 2.4 cm) were treated in 8 patients. Each was given a single PDT session. The following results were obtained: the complete response was recorded in 92%, a partial response in 8% of cases [13].

R. R. Allison conducted studies to evaluate the effectiveness of PDT in patients with breast cancer with skin metastases. The study included 9 patients with 102 skin metastatic foci. The size of the lesion varied from 0.57 to 9 cm. The authors recorded the results obtained from the treatment for 6 months. The result of the study showed a complete response in 89%, a decrease in the size of foci was noted in 8%, and without the effect of treatment in 3% of cases [14]. The purpose of this publication is to present a clinical case demonstrating the potential of PDT in the treatment of skin metastases.

1 Material and Methods

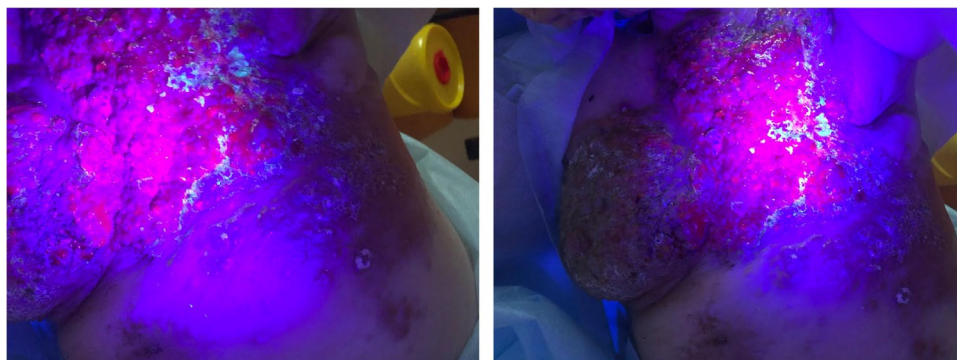
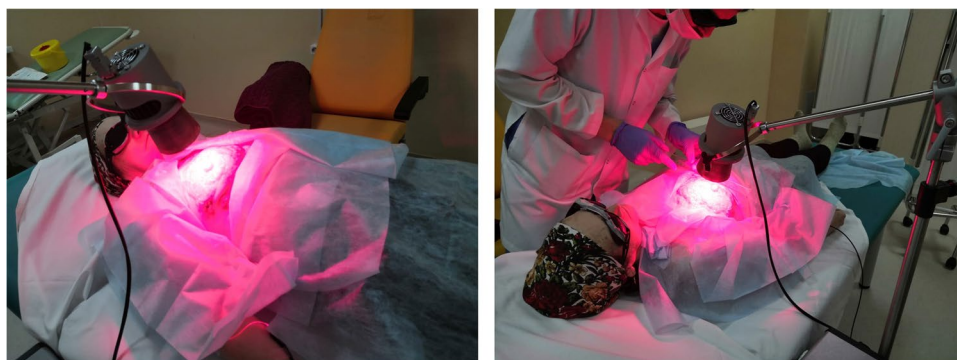
Patient K., 69 years old, was diagnosed with cancer of the left breast in October 2015. T2N3M0. Stage IIIC. Complex treatment was carried out: 2 courses of neo-adjuvant chemotherapy + radical mastectomy + remote radiation therapy summation of the focal dose 30gr + 4 courses of adjuvant chemotherapy. Histological conclusion: infiltrating carcinoma with therapeutic pathomorphosis 2st., metastases of regional lymph nodes (19 of 21).

In October 2018, the progression of the process was established. After verification of the diagnosis, (infiltrating G2 carcinoma. RE—4 points; RP-4 points; Her 2 neu 3+ , Ki67-20%) palliative hormone and targeted therapy was prescribed. Against the background of ongoing treatment until November 2019, there is a progression of the process: continued growth of skin metastases and the metastatic foci in the lungs (according to CT). Taking into account the ineffectiveness of the therapy, the deterioration of the general condition, the severity of the concomitant pathology, and the conducting of antitumor therapy were stopped. In the period up to February 2020, the patient repeatedly received supportive treatment in the palliative care department.

In March 2020, the patient requested assistance at the center for photodynamic therapy at Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan. Local status: on the anterior wall of the chest and abdominal cavity, multiple moderately painful irregularly shaped masses with a bleeding surface, dense consistency, immobile, and with indistinct borders protruding above the skin level from 0.5 to 2.5 cm are determined. The area of lesions is 1400 cm² (Fig. 1). Considering the volume of metastatic skin lesions, palliative multi-course PDT was recommended.

Fig. 1 Status before PDT



Fig. 2 Fluorescencediagnostics**Fig. 3** PDT session

The mechanism of photodynamic therapy is based on the three non-toxic components, which produce the desired effects within pathological tissues only by mutual interactions between: • the photosensitizer (PS); • light with the appropriate wavelength; and • oxygen dissolved in the cells [15]. There are two main mechanisms of the photodynamic reaction. Both are closely dependent on oxygen molecules inside cells. The first stage of both mechanisms is similar. A photosensitizer, after entering the cell, is irradiated with a light wavelength coinciding with the PS absorption spectrum and is converted from the singlet basic energy state S^0 into the excited singlet state S_1 because of the photon absorption. Part of the energy is radiated in the form of a quantum of fluorescence, and the remaining energy directs a photosensitizer molecule to the excited triplet state T_1 — the proper, therapeutic form of the compound (Scheme 1) [16, 17].

The photosensitizer was diluted on 0.9% sodium chloride solution at a dose of 1.5 mg/kg and administered intrave. A Photolon® photosensitizer was used for the PDT session. Moleculously. After 3 h, intravenous laser irradiation of blood was performed on the Lakhta-Milon device with an output power of 0.1 W and an exposure time of 30 min. Before the PDT session, a fluorescent diagnosis was performed (Fig. 2), in which non-visual foci

**Fig. 4** Immediately after PDT

of skin lesions were detected. The device “Lakhta-Milon” and the LED medical device “LATUS-T-FARA” were used for PDT. Polypositional treatment of the affected areas was carried out, and the energy density of one irradiation position was 150 J/cm². The power density of the laser radiation is 200 MW/cm². The total laser exposure time is 100 min (Fig. 3).



Fig. 5 Condition in 2 weeks after PDT: necrotic scab of the tumor area

2 Results and Discussion

During PDT, the patient noted moderate pain, which was relieved by the administration of non-steroidal anti-inflammatory drugs. Immediately after the end of the PDT session, a change in the color of the formations to dark purple was noted, and bleeding stopped (Fig. 4.). The patient passed the PDT session satisfactorily, no adverse reactions were detected.

At the control examination in 2 weeks after the treatment, the mass of a necrotic scab with the formation of fibrin films was noted (Fig. 5).

After a month and 1.5 months, the pronounced effect was observed in the form of a decrease in both the area and volume of the tumor lesion of the skin (Fig. 6). As a result of the treatment, a partial regression of the tumor was obtained. On examination, the scar in the area of PDT is pale pink, and the continued growth of the tumor is determined in the form of separate areas of infiltration along the anterior edge of the scar. Subjectively, the patient notes a significant improvement in well-being, sleep and appetite. The assessment of the quality of life before and after treatment using the QOL-CS questionnaire also confirms the improvement of physical and mental well-being.

It is planned to continue PDT procedures on a monthly basis until the full effect is obtained.

Fig. 6 Condition in 1.5 months after PDT



3 Conclusion

Thus, the given clinical example demonstrates the possibility of using PDT for the treatment of skin metastases of patients with breast cancer. The method proved to be highly effective and at the same time safe. This technology should be included as a technique of choice to the guidelines for the treatment of malignant tumors.

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Declarations

Research Involving Humans and Animals Statement The permission of the local ethics committee was obtained by the management departments of Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan.

Informed Consent Informed consent was signed by patient before the procedure.

Conflict of Interest The authors declare no competing interests.

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