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Photodynamic Therapy for Classic (Idiopathic) Type of Kaposi's Sarcoma (Case Report)

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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Case Report

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ABSTRACT

The author report a case of a patient with classic (idiopathic) type of Kaposi's sarcoma the third toe of the foot treated successfully with photodynamic therapy. Photosensitizer «Photolon» (RUE «Belmedpreparaty», Republic of Belarus) was injected intravenously at a dose of 2 mg/kg body weight. Photoirradiation was carried out 3 hour after the injection of photosensitizer with the use of a semiconductor laser «UPL PDT laser» («Lemt», Republic Belarus, λ=660±5 nm) with exposure dose of 100 J/cm^2 and power density of 0.38 W/cm^2. The effectiveness of treatment was assessed based on an analysis of clinical data. During the follow-up period of 3 and 6 months, no clinical signs of local recurrence in the photoirradiation area were detected.

Keywords: Kaposi sarcoma; photosensitizer; photodynamic therapy.

1. INTRODUCTION

Kaposi's sarcoma (KS) was first described in 1872 by Moritz Kaposi, a Vienna-based Hungarian dermatologist, as a rare multifocal angioproliferative tumor involving blood and lymphatic vessels in elderly men of Jewish origin (Kaposi, 1872) [1].

In 1994, Chang Y. and colleagues (Columbia University, New York, USA) identified human type 8 herpes virus (HHV-8, subgroup of 16 γ-

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herpes virus) in patients with various types of KS using a polymerase chain reaction [2].

The diagnosis of cutaneous KS is usually based on visible clinical findings. A histologic diagnosis is recommended (in all questionable cases). Histological findings in KS include spindle-shaped cells with vascular channels lined by abnormal endothelial cells assembled like a catch of fish. Extravasated erythrocytes, hemosiderin, and fibrosis can often be seen. Measuring the plasma levels of HHV-8 as a biomarker in KS has a very limited value in either diagnosis or prognostication [1].

There are 4 forms of Kaposi's sarcoma [3]: idiopathic (classical); endemic (African); AIDS-associated (epidemic) and immunosuppressive therapy-associated.

Cutaneous lesions are the most frequent clinical manifestations, but lesions in internal organs have also been observed. The initial stages of the disease is characterized by the appearance of spots or plaques with clear, irregular contours on the skin of the feet, shins, mucous membranes without subjective sensations. Patients may be noted for itching, burning and pain in the area of rashes, intensifying in the evening and at night. Eruptions have clear boundaries, increase in size, darken and turn into nodules of various sizes, thickened plaques or nodes with vascular crimson nodules, which can be located on the upper limbs, trunk, face, mucous membrane of the tongue and scrotum area [4].

At the moment, the development of new effective methods for treating patients with KS is very relevant. Patients with KS are given cytostatic therapy: herbal medicines (vinblastine, vincristine), alkylating compounds (cyclophosphamide, fotretamine), antimetabolites (methotrexate, pumite), liposomal (doxorubicin and daunorubicin). The maximum effect from its application comes in 5 months, and the average duration of remission is 4 months. The above chemotherapeutic agents affect skin and visceral manifestations of KS, inhibit cell growth and proliferation. The effectiveness of chloride propidium in combination with IFN-α2 (Viferon) and 49 IFN-α (Leukinferon) in the treatment of patients with KS has been demonstrated in a number of studies [3,5].

Kartashova M.G. reported, that for the treatment of SC are applied methods of local treatment (cryotherapy with liquid nitrogen, electron radiation and close-focus X-ray therapy). The author note that the effectiveness of these methods is about 80%. However, there is a high risk of local recurrence of the disease in the early observation period (3-6 months after treatment). The use of remote gamma-therapy and high-energy electron beam allows to improve the results of treatment [3].

At the moment, it is urgent to search for new methods of treating patients with cutaneous forms of Kaposi's sarcoma. These methods should be effective, characterized by good cosmetic results and minimal number of complications and adverse reactions. One of the promising directions in the treatment of this pathology is the photodynamic therapy (PDT). PDT is a treatment method which based on the significant increase of the cytotoxicity of drugs with photo irradiation of the tumor tissue. According to numerous studies of photochemical reactions include a direct interaction of excited molecules with the help of photo irradiation the photosensitizer (PS) on the substrate and forming transient radicals that react with oxygen. Interaction initiates a complex cascade of free radicals, such as singlet oxygen ($^1O_2$), hydroxyl radical ($^{\cdot}OH$), hydrogen peroxide (H_2O_2) and superoxide anion radical ($^{\cdot}O_{2-}$), causing the development of oxidative stress syndrome. As a result, PDT effectively induced tumor-cell apoptosis and necrosis. The two possible mechanisms might be:

- promoting mitochondria to release Cyto-C and activate Caspase-3, then to initiate apoptosis;
- destroying of microvessels, inhibition of angiogenesis and the induction of ischemia and anoxia of tumor cells, resulting in ischemic necrosis [6,7].

The aim of this study is to evaluate a safety and antitumor efficacy of PDT with chlorine-based PS photolon for treatment for patient with skin form of KS.

2. MATERIALS AND METHODS

2.1 Case Report

Patient B., born in 1954, in April 2013, appealed to the Department of hyperthermia and photodynamic therapy (N.N. Alexandrov National Cancer Center, Republic of Belarus) for medical

advice with the purpose of counseling and establishing an accurate diagnosis.

According to the patient, he considers himself ill about 1 year. At the time of the examination, the patient complained of the presence of tumor-like formations on the plantar part and the second toe of the right foot. Based on the analysis of clinical and morphological data (№ 12959-960 / 3 dated May 15, 2013) in 432 Minsk Military Hospital, the patient was diagnosed with KS.

2.2 Status Localis

There were two nodes of dark blue color with a diameter of 0.7 cm on the skin of the lateral surface of the right foot.

The patient was recommended to receive treatment with the use of PDT. The study was approved by local ethic committee. Patient signed informed consent to procedure in compliance with Helsinki declaration of 1964 (revised 2013).

2.3 PDT Session

PS «Photolon» (RUE «Belmedpreparaty», Republic of Belarus), which is a complex of chlorin e6 risodium salt with polyvinylpyrrolidone, was injected intravenously at a dose of 2 mg/kg body weight, in a darkened room. The tumor photoirradiation (PI) session was carried out 3 hour after the injection of PS with the use of a semiconductor laser «UPL PDT laser» («Lemt», Republic of Belarus, λ=660±5 nm). The exposure dose was 100 J/cm^2 and power density of laser radiation was 0.38 W/cm^2. The area of irradiation included a section of healthy tissue, retreating from the edge of the tumor to 5 mm.

Immediately after the PDT session, we detected the appearance of signs of hemorrhagic necrosis: the color of the pathological focus became black-brown, and insignificant exudation was revealed. The final formation of a necrotic scab with a clear border and the correct form in the zone of PI occurred 1 week after the treatment. The tolerability and safety of the PDT session was assessed based on the criteria CTCAE (Version 4.03) [8].

The effectiveness of treatment was assessed based on an analysis of clinical data. Performance criteria were as follows (according to WHO, 1979) [9]:

- complete regression (CR): absence of all signs of the disease, 100% resorption of pathological foci in 3 months after PDT;
- partial regression (PR): reduction of the total tumor size by 50% or more with subsequent stabilization established 3 months after the PDT session;
- stabilization of the process: no increase in the size of the tumor nodes, the appearance of new nodes or other signs of disease progression within 3 months;
- progression of the process: an increase in the total size of the tumor node by 25% or more, or the development of new foci.

3. RESULTS AND DISCUSSION

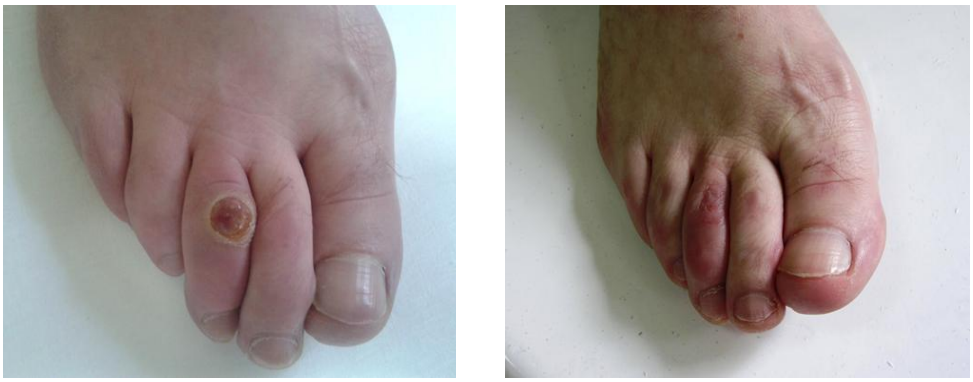
The PDT session was accompanied by a mildly expressed pain syndrome (grade I). There were no other complications and adverse reactions. The skin phototoxicity was not observed. At the control observation in 3 months in the zone of PI, we noticed the formation of a connective-tissue scar (Fig. 1).

At a follow-up examination 3 months after PDT, the patient had CR of the pathological focus. During the follow-up period of 3 and 6 months, no clinical signs of local recurrence in the PI zone were detected.

KS is a lympho-angioproliferative disease, having four variants: idiopathic (classical), endemic (African), AIDS-associated (epidemic) and immunosuppressive. Classical KS is characterized by single or multiple pea-sized bluishred macules on the distal portions of the lower extremities. The treatment of KS depends on the extent and the localization of lesions as well as on the clinical type of the disease. Modalities include surgical excision, chemotherapy, ionizing radiation, cryotherapy, laser irradiation, IFN-α2 (Viferon) + IFN-α (Leukinferon) and PDT.

At the moment, in the literature there are few research data on the use of the method of PDT in the treatment of skin symptoms of KS.

Prokofiev A.A. et al. reported about effective PDT with local administration of PS «Photoditazine» in the treatment of 16 patients with KS. There were no local recurrences at the time of observation up to 6 months [10]. The same authors described the case of the successful use of PDT in the treatment of the



A **B**

Fig. 1. Patient B., 60 years old

Clinical diagnosis: Kaposi's sarcoma of the third toe of the right foot, classic (idiopathic) type: A – state before PDT; B – state 3 months after PDT (exposure dose – 100 J/cm^2)

classic type of KS in the region of the glans penis in a patient of 60 years [11].

Kartashova M.G. et al. presented 5 cases of topical PDT with PS «Radachlorin» in the treatment of patients with a chronic form of idiopathic type of KS. PS was injected into the tumor in a volume of 0.5-1 ml/cm^2 (dose - 1.75-3.5 mg/cm^2). Photoirradiation (medical laser «LAMI», λ = 662±3 nm) was performed with exposure dose, which varied from 200 to 300 J/cm^2 , power density of 0.141 to 0.56 W/cm^2 and duration of one field – from 1.5 to 3 cm. During the follow-up period (9 months), local recurrences were not revealed [3].

Gelfond M.L. et al. presented case of topical PDT with PS «Photoditazine» in the treatment of patient with KS. Photoirradiation was performed 3 h.after PS administration at a dose 1.2 mg/kg with exposure dose of 400 J/cm^2. At control observation in 3 months the authors noted clinical stabilization of the process [12].

Park MY et al. published results of treatment of a patient with 6 foci of KS in the region of the lower limb. 20% methyl 5-ALA («Metvix») was injected directly into the tumor focus. PI was carried out at an exposure dose of 100 J/cm^2 at a radiation power density of 100 mW/cm^2 (λ = 580 and 740 nm). The authors note that after 4 treatment sessions a partial regression of pathological foci was noted [13].

Tardivo J.P. et al. studied the effectiveness of PDT (18 J/cm^2) with local administration of methylene blue and toluidine blue in the combined treatment of patients with KS. The author noted a good therapeutic and cosmetic result of the treatment [14].

Szeimies RM et al. reported on the successful experience of treatment of 6 patients with 30 skin lesions of KS by PDT with photosensitizing agent indocyanine green at a dose of 2.2 mg/kg. PI was produced by a diode laser (λ=805 nm, the exposure dose was 100 J/cm^2, and the radiation intensity was 3 W/cm^2). The authors noted the fact that the complete clinical regression of pathological foci (n = 27) was noted in all patients with the initial stages of the disease, in the case of the nodal form, only in 1 case out of 3 observations [15].

4. CONCLUSION

PDT with systemic administration of PS photolon has demonstrated its clinical effectiveness and can be recommended for the treatment of patients with KS restricted and common forms against a background of complex cytostatic therapy.

CONSENT

Author declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

ETHICAL APPROVAL

Author hereby declare that all medical and diagnostic issues have been examined and approved by the appropriate ethics committee (N.N. Alexandrov National Cancer Center, Republic Belarus) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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