

PHOTODYNAMIC THERAPY OF PENILE CANCER

Yagudaev D.M.¹, Gens G.P.², Kadyrov Z.A.¹, Tikhonenko A.V.², Kalyagina N.A.³

¹Peoples' Friendship University of Russia, Moscow, Russia

²Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Moscow, Russia

³Prokhorov General Physics Institute of the Russian Academy of Sciences, Moscow, Russia

Abstract

In this article we submit the case report of a patient with cT1N0M0 penile cancer diagnosis. The patient underwent two courses of photodynamic therapy (PDT) using Fotoditazin photosensitizer (PS) and ATKUS-2 diode laser. The PS was administered at a dose of 1 mg/kg of body weight 2 hours prior to the PDT session. The irradiation parameters were: 662 nm laser wavelength, 200 mW/cm² power density and 250 J/cm² energy density. In the presented clinical observation, we demonstrated that PDT is an effective and safe treatment method in patients with non-invasive penile cancer. The use of photodynamic therapy allowed preserving the physiological urination, sexual function and achieving a good cosmetic effect.

Keywords: penile cancer, photodynamic therapy, fotoditazin.

For citations: Yagudaev D.M., Gens G.P., Kadyrov Z.A., Tikhonenko A.V., Kalyagina N.A. Photodynamic therapy of penile cancer, *Biomedical Photonics*, 2020, vol. 9., no. 1, pp. 42–46. (in Russian) doi: 10.24931/2413–9432–2020–9–1-42–46

Contacts: Tikhonenko A.V., e-mail: aptem_6007@mail.ru

ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ ПРИ РАКЕ ПОЛОВОГО ЧЛЕНА

Д.М. Ягудаев¹, Г.П. Генс², З.А. Кадыров¹, А.В. Тихоненко², Н.А. Калягина³

Российский университет дружбы народов, Москва, Россия

²Московский государственный медико-стоматологический университет им. А.И. Евдокимова, Москва, Россия

³Институт общей физики им. А.М. Прохорова РАН, Москва, Россия

Резюме

В данной статье представлено клиническое наблюдение за пациентом, имеющим диагноз: рак полового члена сТ1N0M0, которому было проведено 2 курса фотодинамической терапии (ФДТ) с использованием фотодитазина и диодного лазера «АТКУС-2». Фотодитазин в дозе 1 мг/кг массы тела вводили пациенту за 2 ч до начала сеанса ФДТ. Параметры облучения: длина волны излучения 662 нм, плотность мощности 200 мВт/см², плотность энергии облучения 250 Дж/см². В представленном клиническом наблюдении нами продемонстрировано, что ФДТ является эффективным и безопасным методом лечения у пациентов с неинвазивным раком полового члена. Использование ФДТ позволило сохранить физиологическое мочеиспускание, половую функцию и достичь хорошего косметического эффекта.

Ключевые слова: рак полового члена, фотодинамическая терапия, фотодитазин.

Для цитирования: Ягудаев Д.М., Генс Г.П., Кадыров З.А., Тихоненко А.В., Калягина Н.А. Фотодинамическая терапия при раке полового члена//Biomedical Photonics. – 2020. – Т. 9, № 1. – С. 42–46. doi: 10.24931/2413–9432–2020–9–1-42–46

Контакты: Тихоненко A.B., e-mail: aptem_6007@mail.ru

Penile cancer is a rare but aggressive malignancy. In 2017, penile cancer was diagnosed in 667 cases in Russia, which was only 0.24% of all newly diagnosed malignancies in men. However, over the past decade, the incidence of penile cancer has increased by more than

50%, especially in the over 55 age group. In the absence of specific treatment, the 5-year survival rate for this disease is 2.6% [1, 2].

In 95% of cases, penile cancer is a squamous cell carcinoma [3]. The main predisposing factors of penile cancer

are the presence of phimosis with chronic inflammation (up to 60% of cases) and human papillomavirus types 16 and 18 (up to 50% of cases) [4-6].

With adequate treatment, the 5-year survival rate of patients is up to 100% in stage I of the disease and up to 88% in stage II [7]. At these stages, it is possible to use organ-preserving operations that allow patients to maintain their sexual function and have natural urination.

Currently, the question of the most preferred method of treatment for penile cancer has not been solved due to the low prevalence of this disease. There are conflicting data in the literature on relapse-free 5-year survival in patients after organ-preserving and organ-resecting surgery in penile cancer, but the analysis of the results of most studies indicates a probability of local relapse in 50-55% of cases when the penis was preserved [8-10]. However, organ-preserving operations are the most preferable, since penectomy is associated with physical and psychological discomfort for the patient. It should be noted that the occurrence of relapses, subject to their timely diagnosis and treatment, does not have a negative impact on the survival of patients [10, 11].

According to current clinical recommendations, the choice of treatment tactics for malignant diseases is based on the localization, size and type of growth of the primary tumor, categories T, N, M, and degree of anaplasia G [1].

Photodynamic therapy (PDT) is one of the most promising methods of treating a range of oncological and non-oncological diseases. PDT is a technology based on a photochemical reaction that develops as a result of the interaction of laser radiation and a photosensitizer accumulated in pathological tissues.

Currently, PDT is effectively used for the treatment of urological diseases such as penile cancer, bladder cancer, benign prostatic hyperplasia, etc. PDT is also used in the complex treatment of purulent wounds of the scrotum and virus-associated diseases of the penis [12].

Experimental data indicate that the main factors of tumor destruction in PDT are the following components: damage and death of tumor cells, destruction of the microcirculatory bed of the tumor, inflammatory response and immune response of the body [13].

In April 2019, patient K., aged 42, was hospitalized to the Central Clinical Hospital No. 2 named after N. A. Semashko with a referral diagnosis of penile cancer.

For several years before that, the patient had noted the presence of a slight scarring of the foreskin. In February 2018, he first noticed the appearance of redness of the balanus, and visited a urologist at his place of residence, where he was diagnosed with balanoposthitis and prescribed conservative therapy. The patient underwent the prescribed treatment, but it was not effective.

In early 2019, the patient noted progression of the disease which appeared as a space-occupying lesion on the balanus and the foreskin. The patient was repeatedly consulted by the urologist. With a referral diagnosis of penile cancer, he was hospitalized to the Central Clinical Hospital No. 2 named after N. A. Semashko.

Upon admission, his local status included scarring of the foreskin, on the balanus, closer to the coronal sulcus; two lesions, up to 15 mm in diameter of bright red color with an exophytic component up to 5 mm, with a partial transition to the inner leaf of the foreskin, were observed; no infiltration of the spongy body was observed, the urethra was intact, and the inguinal lymph nodes were not changed (Fig. 1).

A biopsy of the neoplasm was performed, which was described as a result of histological examination as a fragment of mucosa with the growth of a moderately differentiated squamous cell cancer with a tendency to keratinization. In a comprehensive examination, which included MRI of the pelvic organs, CT of the abdominal cavity and chest, no data for the damage of regional lymph nodes or the presence of distant metastases were found in the patient.

Taking into account the stage of the disease and the absence of tumor dissemination signs, the oncological council decided to resort to a combined organ-preserving treatment: PDT of the penis with subsequent circumcision.

The patient underwent PDT with the use of Photoditazine (OOO "VETA-GRAND", Russia, registration certificate No. ЛС 001246 dated 18.05.2012) and an "ATKUS-2" diode laser (AO "Poluprovodnikovyie Pribory", Russia). 2 hours before irradiation, the patient was administered Photoditazine, at a dose of 1 mg/kg of body weight. During the manipulation, the focus was affected by laser radiation with a wavelength of 662 nm, a power density of 200 mW/cm², and an irradiation energy density of 250 J/cm².

Due to the presence of two lesions, the session was conducted with the use of a polypositional method. At the second stage of combined treatment, the patient underwent circumcision. The surgical material was sent for morphological examination. According to the histological conclusion, the tissue featured a growth of moderately differentiated squamous cell cancer with a tendency to keratinization, with an invasion into the subepithelial base of up to 1 mm, and a negative surgical margin.

The immediate effect of this technique was observed after PDT: a demarcation line began to form, and hemorrhagic necrosis of the affected tissues appeared (Fig. 2).

On the day after the surgery, the demarcation line was clearly visualized. A skin slough formed on the right half of the balanus (Fig. 3).

The post-surgery period proceeded smoothly. At the control examination after 1 month, the patient







Рис. 1. Клиническая картина до операции **Fig. 1.** Clinical picture before the operation





Рис. 2. Клиническая картина после операции **Fig. 3.** Clinical picture after the operation



Рис. 3. Клиническая картина, 1-е сутки после операции **Fig. 3.** Clinical picture, 1 day after the operation



Рис. 4. Клиническая картина, 25-е сутки после операции Fig. 4. Clinical picture, 25 days after the operation



Рис. 5. Клиническая картина, контроль через 2 мес **Fig. 5.** Clinical picture, control after 2 months



Рис. 6. Клиническая картина, контроль через **1** мес после **2**-го курса ФДТ

 $\textbf{Fig. 6.} \ \textbf{Clinical picture}, control \ \textbf{1} \ month \ after \ the \ second \ \textbf{PDT} \ course$

showed good healing of the postoperative defect on the right (Fig. 4). A control cytological study was performed from the zone of the worst healing. Conclusion: cells of the squamous epithelium with signs of inflammation.

During the control examination after 2 months, the patient showed complete healing of the surgery area, without visible cosmetic defects. However, on the left side of the balanus, a modified area measuring 5 mm in diameter was observed (Fig. 5). To exclude the continued growth of the tumor, a cytological study was performed. No data were obtained for the presence of tumor cells. The clinical situation was discussed at the oncological council. Taking into account the clinical picture and high aggressiveness of the penile cancer, it was decided to administer a second course of PDT.

The patient underwent a repeated course of PDT with the use of the method described above. During a control examination 1 month after the second course, a complete regression of the neoplasm was confirmed, and no cosmetic defects were observed (Fig. 6).

In our account of the clinical observation, we have demonstrated that PDT is an effective and safe method of treatment in patients with non-invasive penile cancer. This method does not involve any serious operational risks.

The use of PDT allowed for the preservation of physiological urination and sexual function, and it also produced a good cosmetic effect.

REFERENCES

- Klinicheskie rekomendacii. Rak polovogo chlena. Ministerstvo zdravoohraneniya Rossijskoj Federatsii [Clinical recommendations. Penile cancer. Ministry of Health of the Russian Federation]. 2017. 23 p. (in Russ.)
- Al'-Shukri S.H., Korneev I.A., Giorgobiani T.G., Ageev M.N., Batmaev D.B. Penile cancer, *Urologicheskie vedomosti*, 2013, vol. 3, no. 1, pp. 28–32. (in Russ.)
- Matveev B. P., Matveev V. B., Halaf'yan E. A., Volkova M. I. Regional metastases in penile cancer: what is the optimal treatment tactic?, Urologiya, 2004, no. 4, pp. 19–23. (in Russ.)
- Bleeker M. C., Heideman D. A., Snijders P. J., Horenblas S., Dillner J., Meijer C. J. Penile cancer: epidemiology, pathogenesis and prevention. Prevention, World J. Urol., 2009, vol. 27, no. 2, pp. 141–150.
- Maden C., Sherman K.J., Beckmann A.M., Hislop T.G., Teh C.Z., Ashley R.L., Daling J.R. History of circumcision, medical conditions, and sexual activity and risk of penile cancer, *J. Nat. Canc. Inst.*, 1993, vol. 85, no. 1, pp. 19–24.
- Halaf'yan E. A., Volkova M. I., Gurariy L. L., Zaharova T. I., Romanov V. A. Penile cancer prediction factors, *Onkourologiya*, 2005, no. 3, pp. 55–60. (in Russ.)
- 7. Mobilio G., Ficarra V. Genital treatment of penile carcinoma, *Curr. Opin. Urol.*, 2001, vol. 11, pp. 299–304
- 8. Soria J.C., Fizazi K., Piron D., Kramar A., Gerbaulet A., Haie-Meder C., Perrin J.L., Court B., Wibault P., Théodore C. Squamous cell carcinoma of the penis: multivariate analysis prognosticfactors

ЛИТЕРАТУРА

- 1. Клинические рекомендации. Рак полового члена/Министерство здравоохранения Российской Федерации 2017. 23 с.
- Аль-Шукри С.Х., Корнеев И.А., Гиоргобиани Т.Г. и др. Рак полового члена//Урологические ведомости. – 2013. – Т. 3, № 1. – С. 28–32.
- 3. Матвеев Б.П., Матвеев В.Б., Халафьян Э.А., Волкова М.И. Регионарные метастазы при раке полового члена: какова оптимальная тактика лечения?//Урология. 2004. № 4. С. 19–23.
- Bleeker M.C., Heideman D.A., Snijders P.J. et al. Penile cancer: epidemiology, pathogenesis and prevention. prevention//World J. Urol. 2009. Vol. 27, No. 2. P. 141–150.
- Maden C., Sherman K.J., Beckmann A.M. et al. History of circumcision, medical conditions, and sexual activity and risk of penile cancer//J. Nat. Canc. Inst. 1993. Vol. 85, No. 1. P. 19–24.
- 6. Халафьян Э. А., Волкова М. И., Гурарий Л.Л. и др. Факторы прогноза при раке полового члена//Онкоурология. 2005. № 3. C. 55–60.
- Mobilio G., Ficarra V. Genital treatment of penile carcinoma//Curr. Opin. Urol. – 2001. – Vol. 11. – P. 299–304
- 8. Soria J. C., Fizazi K., Piron D., et al. Squamous cell carcinoma of the penis: multivariate analysis prognostic factors and natural history in monocentric study with aconservative policy//Ann. Oncol. 1997. Vol. 8. P. 1089–1098.
- 9. Харченко В.П., Каприн А.Д., Титова В.А. и др. Лучевая диагностика и комплексное лечение рака полового члена//Вопросы онкологии. 2006. Т. 52, № 3. С. 315–321.



- and natural history in monocentric study with aconservative policy, *Ann. Oncol.*, 1997, vol. 8, pp. 1089–1098.
- Harchenko V.P., Kaprin A.D., Titova V.A., Pan'shin G.A., Milenin K.N. Radiation diagnosis and complex treatment of penile cancer, Voprosy onkologii, 2006, vol. 52, no. 3, pp. 315–321. (in Russ.)
- Gotsadze D., Matveev B., Zak B., Mamaladze V. Is conservativeorgan-sparing treatment of penile carcinoma justified?, *Europ. Urol.*, 2000, Vol. 38, pp. 306–312.
- 11. Koch M.O., Smith J.A.Jr. Local recurrence of squamous cell carcinoma of the penis, *Urol. Clin. North Amer.*, 1994, vol. 21 (4), pp. 739–743
- 12. Yagudaev D.M., Engay V.A., Alferov A.S., Ayvazyan D.R., Purtskhvanidze V.A. Radiation diagnosis and complex treatment of penile cancer, *Lazernaya meditsina*, 2015, vol. 19, no. 1, pp. 37–39. (in Russ.)
- 13. Oleinick N.L., Morris L., Varnes M.E.The peripheral benzodiazepine receptor in photodynamic therapy with the phthalocyanine photosensitizer Pc4, *J. Photochem. and Photobiol.*, 2002, vol. 75 (6), pp. 652–661.

- 10. Gotsadze D., Matveev B., Zak B., Mamaladze V. Is conservativeorgan-sparing treatment of penile carcinoma justified?//Europ. Urol. – 2000. – Vol. 38. – P. 306–312.
- Koch M.O., Smith J.A.Jr. Local recurrence of squamous cell carcinoma of the penis//Urol. Clin. North Amer. 1994. Vol. 21 (4). P. 739–743
- 12. Ягудаев Д.М., Енгай В.А., Алферов А.С. и др. Фотодинамическая терапия как органосохраняющий метод лечения рака полового члена//Лазерная медицина. 2015. Т. 19, № 1. С. 37—39.
- 13. Oleinick N.L., Morris L., Varnes M.E.The peripheral benzodiazepine receptor in photodynamic therapy with the phthalocyanine photosensitizer Pc4//J. Photochem. and Photobiol. – 2002. – Vol. 75 (6). – P. 652–661.