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ORIGINAL STUDY

Fluorescent border diagnosis and surgical treatment of the malignant process of external nose skin

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ABSTRACT

OBJECTIVE. The purpose of the study was to find out the diagnostic value of the Photolon® as a fluorescent visualization of the borders of malignant lesions of the external nose, with the aim of radical surgical removal of the tumor.

MATERIAL AND METHODS. During the period from 2016 until 2018, 30 patients with malignant neoplasms of the external nose were examined and operated on in the Otolaryngology-Head and Neck Department. During the study, patients underwent surgical removal of tumors by using a complex of anemic Klein's solution and fluorescent imaging of the lesion in 15 patients, while 15 patients were operated on without using Klein's solution and fluorescent imaging.

RESULTS. Observation in the postoperative period showed that, in the group of patients who underwent fluorescent imaging with adding anemic Klein's solution, the postoperative period was satisfactory, and no signs of recurrence were observed. In the group operated on without fluorescent imaging and without conducting anemic Klein's solution, after two years 4 (26.6%) patients were diagnosed with a superficial recurrence of skin cancer at the border of the cartilage and bone.

CONCLUSION. The authors provide suggestions for the effectiveness of the use of a complex of fluorescent imaging of the border of the tumor lesion and prophylactic anemic solution in the surgical removal of the tumor of the outer nose.

KEYWORDS: malignant neoplasms, external nose, Photolon®, fluorescent imaging.

INTRODUCTION

It is known that malignant diseases are one of the most important modern medical-biological and socio-economic problems in the world and, in particular, in Ukraine. In the register of Oncological Departments of Ukraine in 2019, there were 1,014,352 patients, including 356,928 men and 657,424 women. The leading place of cancer morbidity is occupied by non-melanoma skin cancers, unrelated to gender (20.8% of males and 17.1% of females)[1].

In recent years, there has been an increase in the number of superficial epithelial malignant neoplasms of the head and neck in all countries, especially the two most common carcinomas - basal cell carcinoma and squamous carcinoma. The incidence of these tumors is approximately 100 new cases per 100,000 population[1].

Differential diagnosis of chronic (precancerous) conditions of the nasal skin (actinic keratosis, Bowen's disease, cancer in situ) is quite difficult, so careful examination and follow-up is mandatory, especially in terms of changes in colors and sizes[2,3].

The issues of modern diagnosis of superficial neoplasms of the head and neck are relevant because the diagnosis in the late stages of skin cancer can lead to low survival of the patient and reduced quality of life. Unfortunately, at the stage of the early development of the disease, patients do not usually ask for medical help. But at this stage, the tumor can already be clinically indicated and acts aggressively[4-7]. Therefore, a skin tumor of the outer nose (nasus externus) with malignant signs should be surgically treated quickly, consisting in the excision of the tumor lesions or photodynamic therapy. Cryotherapy

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should be performed in the presence of residual tumors[8-11]. Today, in the world, there are two methods of surgical treatment of malignant skin tumors: 1. the removal of the tumor under visual control, taking into account the coefficient of radicalism; 2. the Mohs method.

Mohs surgery is a precise surgical technique used to treat skin cancer. During Mohs surgery, thin layers of cancer-containing skin are progressively removed and morphologically examined until only cancer-free tissue remains. This technique is known abroad as Mohs micrographic surgery and it is an improvement option for standard skin resection, the complete excision of the tumor with a small amount of surrounding healthy tissue at the same time. In our opinion, this method is more appropriate for removing the tumor of the body, where it is possible to mobilize and surgically remove a large section by using surrounding tissues to close the defects. The Mohs technique requires additional costs: an hour of surgery and a morphologist for additional morphological research.

All of the above confirms the need to find and implement modern preoperative diagnostic methods that help determine the characteristics of the tumor lesions (collection of medical history, assessment of objective clinical semiotics - dermatoscopy, cytological or pathomorphological examination, and the most important the tumor surgical removal)[5]. To date, the problem of sufficient visualization of the boundaries of the tumor lesions for the purpose of its radical excision is relevant. Today, the most effective and high-quality diagnosis of tumor lesions is fluorescent imaging, which is widely used by dermatologists and oncosurgeons in the process of photodynamic therapy and surgical removal. We used fluorescent imaging in a patient with surgical removal of an outer nose and ear tumor lesions. As a photosensitizer we used the drug Photolon®, registered in Ukraine (Figure 1), №UA / 11770/01/02 from 12.06.2017, order №651 from 12.06.2017, which was administered intratumorally (intra-focally).

Figure 1. Photosensitizer Photolon®.

The purpose of this research was to study the diagnostic informativeness of Photolon® as a fluorescent visualization of the border of malignant lesions of the external nose, for the purpose of radical surgical removal of the tumor.

MATERIAL AND METHODS

The study involved 30 patients with skin tumors of the outer nose. Of these, 13 were women and 17 were men, aged between 40 to 75 years. Treatment and research were performed in the ENT-Onco Department of the City Clinical Hospital №11, in Odessa, in the period 2016 - 2019. Patients were divided into two groups of 15 patients, depending on the form of the tumor growth and the method of objective visualization of the extent of the external nasal tumor spread during surgical removal. All patients underwent a comprehensive ENT and dermatological clinical examination: the study of the anamnesis (duration of skin neoplasms; changes in color, size and shape).

In both groups of patients, surgical removal was accompanied by a single morphological examination of the edges of the resection - the express method. The operation lasted one hour and 30 minutes and a morphological rapid study was performed.

The first group included 15 patients with the exophytic type of growth of neoplasms of the external nose skin, who underwent removal of the tumor within healthy tissues, without fluorescent imaging and anemic solution of 1% Lidocaine. The size of the tumor varied from 1x3cm to 8x10cm (Figure 2, Figure 3, Figure 4, Figure 5). Tumor biopsy results: in 6 patients (40%) the histotype was G1 at T2N0M0, in 7 patients (46.67%) - G2 at T3-4N0M0, and in 2 patients (13.33%) - G3 at T4N0M0 with wing cartilage defect nose. Surgical excision of the tumor was performed within healthy tissues, retreating 1.5 - 2

Figure 2. Highly differentiated skin cancer.

Figure 3. The patient's condition after removal of the exophytic tumor growth from the outer nose. The surgery ended with the complete removal of the outer nose.

Figure 4. Highly differentiated skin cancer.

Figure 5. Condition after the surgical removal of the tumor of the outer nose and face.

cm from the edges of the tumor with the simultaneous rapid examination. Express studies have shown the absence of malignant cells on the edges of the resection. The depth of excision was determined visually.

The second group consisted of 15 patients with endophytic and infiltrative growth of a neoplasm of the external nose; the size of the tumor was from 1x3 to 4 cm. The preoperative stage biopsies were performed by a gentle method in the area of nodular elements: in 8 patients (53.33%) - G1 at T2N0M0, in 6 (40%) - G2 at T2-3N0M0 and one patient, which amounted to 6.67%, with G3 at T4N0M0, with a large defect of the cartilage of the nasal wing. In order to fluorescently visualize the boundaries of the tumor lesion, pa-

tients used a photosensitizer Photolon® (Figure 1), which, by its action, accumulated selectively in the tumor tissue. Photolon® was administered intravenously at a dose of 1.0 to 3 mg/kg bodyweight for 3 to 5 minutes. The result was evaluated after 50 minutes. In order to prevent intraoperative metastasis and haemostasis, 5 minutes before surgery, Klein's anemic solution (1% Lidocaine solution + 2 - 3 drops of Adrenaline solution) was injected under the tumor base. The amount of Klein's solution depends on the area of the tumor lesion (on average, 5.0 to 10 ml was used). Klein's solution caused spasms of blood and lymphatic vessels, which in turn caused haemostasis. Next, the tumor lesion was removed taking into account the coefficient of radicalism within the color with a rapid study of the edges of the resection. The depth of excision was determined by the color zone of dark green.

Statistical processing of the study results was performed using the criterion of the ratio of two proportions ("z") and was performed using the program "Primer Biostatistics" (USA).

The technique of fluorescent imaging of tumor lesions was performed using some technical complexes LESA-01-BIOSPEC. As a radiation source to excite the fluorescence of the photosensitizer, we used the irradiation of He-Ne laser - 630 - 633 nm (Figure 6). The studies were performed at right angles to the object with a light touch of the optic fiber and the results were obtained by spot measurement of tissue spectra of the centers and periphery of the tumor. The healthy parts of the skin were visually analysed by the shape, magnitude and amplitude of the signal determined by the area of fluorescence intensity (S2) and the area S2/S1, which represents the coefficient of radicalism. In terms of indicators (S2/S1), the level of fluorescence of different parts of the skin (e.g., the center and periphery of the tumor and healthy skin) was assessed.

Additionally, studies of the entire lesion area were performed. For this purpose, we used a matrix LED illuminator (wavelength 665 nm, irradiation power 40 mW / cm2) with video surveillance.

Figure 7. Photolon accumulates in tumor cells and gives a dark green color over time.

Figure 8. The fluorescent visualization of the tumor lesion of the outer nose skin, purple in the area of the largest lesion, and crimson on the periphery.

RESULTS AND DISCUSSIONS

The differential criteria for the degree of accumulation of Photolon® was the color of the tumor lesion, which was observed 50 minutes after injection. The photon accumulated in the tumor cells and gave a dark green color, which in an hour became saturated and clearly defined the boundaries of the tumor lesion (Figure 7). If you illuminate the area of the tumor lesion with a laser beam, it acquires a deep purple color in the area of the largest lesion, and crimson on the periphery (Figure 8). Compared with imaging without irradiation, the boundaries of the tumor lesion did not change. Therefore, irradiation is not mandatory, it only confirmed the extent of the lesion. Then the colored borders of the tumor lesion were given with a pencil - diamond

green. And only after that, surgical excision of the tumor was performed along the outer contour of the border of diamond green and stained tissue along the tumor.

In both groups of patients, the result of the morphopathologic express study was negative - at the edges of the resection there was no non-neoplastic lesion. Only after that, if necessary, we performed a plastic cover of the defect.

The course of the postoperative period was without complications and was satisfactory in both groups of patients. On the 8th day, the sutures were removed.

In 3 patients (20%) of the first group with exophytic lesions of the external nose, the surgery ended with its complete removal, due to the spread of the tumor to the cartilage (cartilágines triangulares) and bone tissue (ossa nasalia) (Figure 2, Figure 3). Patients refused the plastic-reconstructive closure of the defect, remaining satisfied with the quality of life. Two years later, 4 patients (26.6%) from the first group were diagnosed with a superficial recurrence of skin cancer at the border of the cartilaginous and skeletal departments, up to 1.3 cm in size, star-shaped (Figure 9). The patients underwent surgical treatment with plastic closure of the defect with local tissues. The postoperative period passed without complications. Observation for 3 years showed no signs of recurrence and metastasis. 3-year survival rate in all patients was 100%.

Patients in the second group had no signs of recurrence and a satisfactory quality of life at the time of observation: 3 and 6 months, one year and three years.

According to the recurrence rate in the remote period, there was a significant decrease in differences in group №2 compared with group №1 ($Z = 2.091$, $P = 0.037$). Thus, malignant tumors of the external nose are a common and complex pathology, in which surgical treatment depends on the location, form of growth and morphology.

To reduce the number of diseases, it is important and necessary to do preventive work with healthy people on the danger of congenital endogenous factors that create the conditions for the development of malignant skin tumors. You should also have self-examinations and preventive medical examinations, especially after the summer period, and mandatory monitoring of precancerous conditions.

The course of superficial neoplasm of the external nose depended on the form of tumor growth. Endophytic and infiltrative growth are often complicated by the spread to cartilage and bone tissue, as well as metastasis to the brain, vision and lungs[12]. In such cases, it is necessary to carry out the expanded surgical interventions leading to postoperative defects and, as a result, it is necessary to carry out reconstructive plastic operations.

The obtained results will be useful for improving the quality of surgery and life of patients and can also be used in the selection of qualitative diagnosis of the extent of tumor lesions.

Figure 9. Clinical signs of recurrence of skin cancer of the outer nose.

CONCLUSIONS

1. Recurrence in the group of patients that had surgery without imaging using photosensitization "Photolon®" tumor boundaries was 26.67% (4 of 15 patients), which significantly exceeded the corresponding figure in the group of patients who underwent tumor removal under the conditions of this visualization (0 of 15 patients, z = 2,091; p = 0.037).
2. The effectiveness of surgical treatment with the visualization of tumor lesions of the outer nose skin without Photolon® was 73.3% (p> 0.05).
3. A color technique for determining the extent of tumor lesions in the second group of patients using a photosensitizer "Photolon®" and prophylactic anemic solution Klein was the most effective.
4. The color technique allowed to carry out surgical treatment according to the radical program in 100% of patients with malignant tumors of the external nose, regardless of the form of tumor growth (p <0.05).
5. There were no recurrences in the second group of patients after 3 years, while the quality of life was assessed as satisfactory.

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