

# FATAL PROGRESSION OF SQUAMOUS CELL CARCINOMA 10 YEARS AFTER CADAVERIC KIDNEY TRANSPLANTATION

I.N. Dymkov<sup>1, 2</sup>, A.V. Smirnov<sup>1</sup>, A.D. Perlina<sup>3</sup>, K.G. Tailer<sup>2</sup>, I.V. Alexandrov<sup>1, 2</sup>

<sup>1</sup> Volgograd State Medical University, Volgograd, Russian Federation

<sup>2</sup> Volgograd Regional Center of Urology and Nephrology, Volzhsky, Russian Federation

<sup>3</sup> Vladimirsky Moscow Regional Research Clinical Institute, Moscow, Russian Federation

Various research has shown that non-melanocytic malignant skin lesion is one of the most common post-kidney transplant neoplasms. Multiple lesions and a more aggressive clinical course are more common in kidney transplant patients than in the general population. This paper presents a case of malignant skin neoplasms in a patient 10 years after cadaveric kidney transplantation. The patient received standard 3-component immunosuppression with satisfactory graft function (serum creatinine level remained at 157–178  $\mu\text{mol/L}$ ). Scalp neoplasm was removed. Histological examination revealed a morphological picture characteristic of basal cell carcinoma with squamous differentiation. Subsequently, a relapse of the skin neoplasm of the temporal region, as well as new lesions in the frontal region and the skin of the anterior chest wall, were discovered. Despite surgical treatment and close-focus x-ray radiation, the disease rapidly progressed and eventually led to death. Squamous cell carcinoma can progress very rapidly in patients after solid organ transplantation, despite ongoing combination treatment. Perhaps in such cases, it is worth cancelling immunosuppressive therapy completely and removing the kidney graft in order to control progression of the malignant tumor process.

**Keywords:** skin neoplasms, squamous cell carcinoma, kidney transplantation, immunosuppression.

## INTRODUCTION

After solid organ transplantation and long-term immunosuppressive therapy, patients have a higher risk of developing skin infectious and oncological complications.

There are reports confirming the risk of developing skin cancer in this group of patients [6]. It is noted that increased risk of skin cancer in kidney-transplant recipients receiving immunosuppressive therapy is proportional to therapy duration and dosage. In addition to immunosuppressive therapy, other risk factors of skin cancer include exposure to ultraviolet (UV) radiation, childhood sunburn episodes, presence of solar keratoses, presence of pre-transplant tumor lesions, and male.

## OBSERVATION DESCRIPTION

In 1999, 37-year-old patient S., started having increased blood pressure up to 200/120 mmHg. An examination in 2002 revealed changes in the general urine analysis (proteinuria, erythrocyturia). After a follow-up examination, he was diagnosed with chronic glomerulonephritis. The patient did not visit a nephrologist. In connection with progression of chronic renal failure since the end of August 2004, renal replacement therapy by long-term hemodialysis was started.

Having secured a suitable cadaveric donor, an operation was performed in January 2005 – cadaver kidney

allograft, with immediate graft function. The starting immunosuppressive therapy regimen was three-component (cyclosporine, mycophenolate mofetil, methylprednisolone) without monoclonal and polyclonal antibody induction. The postoperative period was uneventful, the patient was discharged for outpatient treatment on day 20 after surgery.

Due to development of transplant nephropathy in 2007, manifested by elevated creatinine levels to 278  $\mu\text{mol/L}$  and moderate albuminuria, cyclosporin was converted to tacrolimus, with a positive clinical effect; blood plasma creatinine stabilized at 156–167  $\mu\text{mol/L}$ .

By the end of 2010, the patient was hospitalized for 2-sided community-acquired pneumonia. After an antibiotic therapy course, without changing the immunosuppression regimen, he was discharged after radiographic verification of resolution of the pneumonia.

The follow-up period was uneventful; graft function was satisfactory, serum creatinine level remained at 157–178  $\mu\text{mol/L}$ .

At the next visit to the clinic in 2015, skin neoplasm was detected in the left temporal region. The neoplasm was removed. Histological examination revealed a morphological picture of basal cell carcinoma (BCC) exhibiting squamous differentiation, as well as focal areas of keratin pearls showing keratinization (Fig. 1).

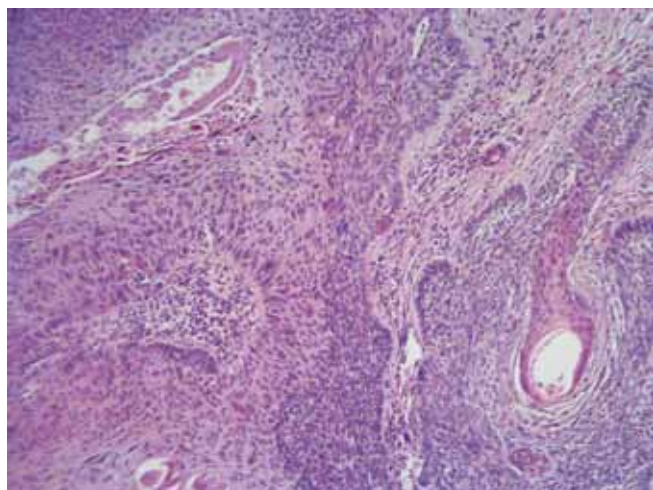


Fig. 1. Patient S. 57 years old. Morphological picture of BCC exhibiting squamous differentiation; presence of keratin pearls showing keratinization. Hematoxylin and eosin stain.  $\times 100$

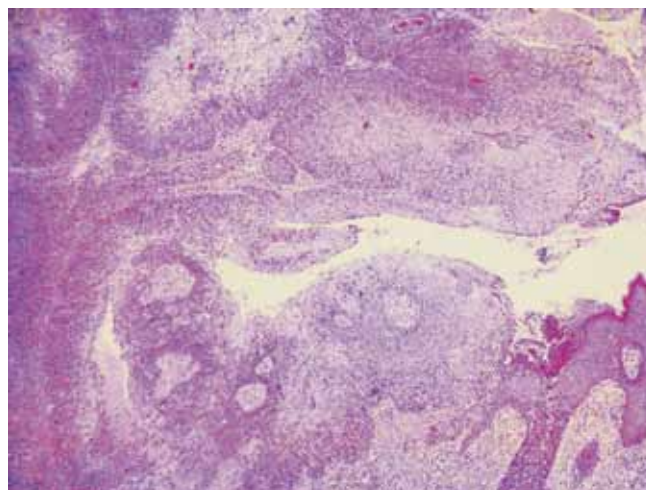


Fig. 2. Poorly differentiated squamous cell carcinoma. Hematoxylin and eosin stain.  $\times 100$



Fig. 3. CT scan of the skull. Progression of the process into the soft tissues of the parietal region with destruction of skull bones

*The postoperative period was uneventful. The patient was discharged for regular medical checkup by an oncologist at the patient's place of residence.*

*In March 2018, temporal skin neoplasm recurred, and new foci were found in the frontal region, the anterior thoracic wall. Wide excision of all skin neoplasms from the base was performed. Histopathological examination confirmed squamous cell carcinoma (SCC) (Fig. 2).*

*The postoperative period was uneventful. Due to progression of oncological process, a course of close-focus x-ray radiation was carried out, dosage 3–5 g/day, course 50–80 g.*

*Nevertheless, in July 2018, the process progressed into the soft tissues of the parietal region, destroying the skull bones (Fig. 3, 4). A biopsy of the parietal soft-tissue tumor was performed. Histological examination revealed a poorly differentiated SCC.*

*Despite ongoing therapy, the disease progressed, resulting in death three years after onset of the disease.*

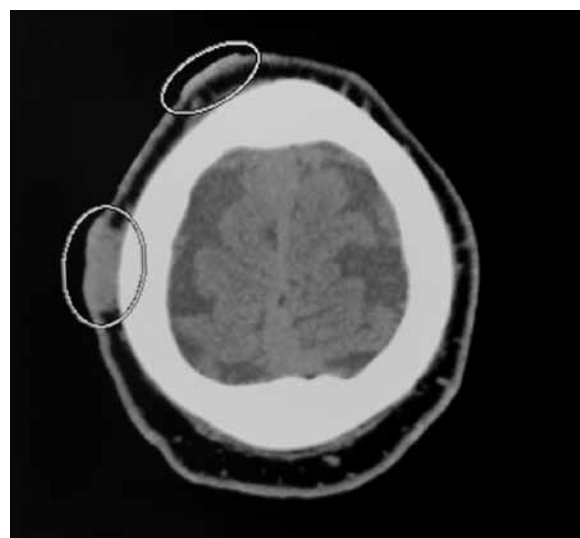


Fig. 4. CT scan of the skull. Progression of the process into the soft tissues of the parietal region with destruction of the skull bones

## DISCUSSION

Numerous data indicate that non-melanocytic skin cancer is one of the most common neoplasms in kidney transplant recipients [8, 9]. Multiple lesions and a more aggressive clinical course are more common in kidney transplant recipients than in the general population [1, 2].

The risk of developing skin cancer varies by geographic region. In particular, Australia has the highest incidence.

Sun exposure is one of the main risk factors for non-melanoma skin cancer (NMSC) in kidney recipients. So according to Joanna Sułowicz et al., of all 53 NMSC lesions diagnosed in 25 of 486 patients with a transplanted kidney, 34 (64.2%) were located on the face, which is the area most exposed to ultraviolet radiation.

In a study by Imko-Walczyk on a population of kidney transplant recipients from Gdańsk in Poland, location of skin cancers was similar to that observed in the general population (76% of SCCs and 72% of BCCs were related to the head and neck regions) [6].

The researchers found that NMSC occurrence increased with duration of immunosuppression and was 20.7% at 5 years, 37.35% at 10 years, and 53.08% at 15 years post-transplantation [5].

Most publications contain reports that SCC incidence prevails over that of BCC [4, 7].

Squamous cell skin cancer is a tumor originating from the squamous epithelium. It has a higher degree of malignancy than other skin tumors, and usually transforms from some precancerous diseases.

## CONCLUSION

It is quite difficult to reliably assess the risk factors for development and progression of malignant skin tumors in our patient.

Nevertheless, the Volgograd Oblast is a region with a fairly high UV load, which, of course, can have an additional effect on patients at risk, particularly after solid organ transplantation. The first signs of the disease were noted 7 years after conversion of immunosuppressive therapy from cyclosporine to tacrolimus.

Surgical and radiation treatments for SCC of the skin on the background of immunosuppression in a transplant recipient was accompanied by rapid progression despite treatment, resulting to death. Perhaps, in cases

of rapid progression of malignant skin lesions in kidney transplant recipients, complete withdrawal of immunosuppressive therapy with high chances of graft loss in an attempt to save the patient's life may be the alternative solution.

*The authors declare no conflict of interest.*

## REFERENCES

1. Bernat Garcia J, Morales Suárez-Varela M, Vilata JJ et al. Risk factors for nonmelanoma skin cancer in kidney transplant patients in a Spanish population in the Mediterranean region. *Acta Derm Venerol.* 2013; 93: 422–427. doi: 10.2340/00015555-1525.
2. Etzkorn JR, Parikh RP, Marzan SS et al. Identifying risk factors using a skin cancer screening program. *Cancer Control.* 2013; 20: 248–254. doi: 10.1177/107327481302000402.
3. Mudigona T, Levendov MM, O'Neill JL et al. Incidence, risk factors, and preventive management of skin cancers in organ transplant recipients: a review of single- and multicenter retrospective studies from 2006 to 2010. *Dermatol Surg.* 2013; 39: 345–364.
4. Urwin HR, Jones PW, Harden PN et al. Predicting risk of nonmelanoma skin cancer and premalignant skin lesions in renal transplant recipients. *Transplantation.* 2009; 87: 1667–1671. doi: 10.1097/TP.0b013e3181a5ce2e.
5. Moloney FJ, Comber H, O'Lorain P et al. A population-based study of skin cancer incidence and prevalence in renal transplant recipients. *Br J Dermatol.* 2006; 154: 498–504.
6. Imko-Walczyk B. The assessment of the risk of cancer and their possible prevention in patients after kidney transplantation. Doctoral thesis. Gdańsk, Poland; 2009. <http://pbc.gda.pl/dlibra/doccontent?id=4847&from=FBC>. Polish.
7. Kauffmann HM, Cherikh WS, McBride MA et al. Post-transplant *de novo* malignancies in renal transplant recipients: the past and present. *Transplant Int.* 2006; 19: 607–619. doi: 10.1111/j.1432-2277.2006.00330.
8. Kazanceva IA, Gurevich LE, Bobrov MA. Rare clinical cases of “combined” skin carcinomas in cadaver renal allograft recipients. *Almanah klinicheskoy mediciny.* 2018; 4 (46): 367–373. (in Russ).
9. Vatazin AV, Dutov VV, Zulkarnaev AB, Fedulkina VA, Krstich M. Infectious complications after kidney transplantation. *Urology.* 2013; 3: 107–111. (in Russ).

*The article was submitted to the journal on 9.01.2020*