Locally aggressive giant basal cell carcinoma of the head with focus on surgical treatment— a case report

Lokalnoagresivni gigantski bazocelularni karcinom vlasistra s posebnim osvrtom na kirurško liječenje – prikaz slučaja

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Summary

Introduction: Basal cell carcinoma is the most common non melanoma skin cancer. It accounts for approximately 80% of all skin cancers.

Case report: We presented a 62-year-old patient with a giant, deeply infiltrative, destructive lesion of the head which lasted for 15 years. Microbiological analysis showed contamination, computed tomography (CT) scan showed deep infiltration and bone destruction. The risks of operative treatment were numerous. The treatment was more complicated by infection, infiltrative spreading and the patient's comorbidity. Regardless, we decided on a wide surgical resection with pathohistological evaluation of the resection margins. The patient denied oncological treatment. After 10 years, there were no recurrent tumours.

Conclusion: Aggressive surgical treatment is the treatment of choice for giant basal cell carcinoma. In the case of giant locally aggressive and advanced neoplasms, when surgery is not appropriate or not possible, medical treatment becomes oncological.

Key words: non melanoma skin cancer, basal cell carcinoma, giant skin carcinoma

Sažetak

Uvod: Bazalno-stanični karcinom je najčešći nemelanomski maligni tumor kože. U prosjeku čini 80% svih malignih kožnih tumora.


Zaključak: Kirurški tretman je tretman izbora gigantskih, bazalno-staničnih karcinoma. U slučaju neoperabilnih gigantskih, lokalnoagresivnih i uznapredovalih bazalno-staničnih karcinoma, tretman izbora je onkološka terapija.

Ključne riječi: nemelanomski maligni tumor kože, bazocelularni karcinom, gigantski karcinom kože

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Introduction

There are 2 main types of skin malignancies: melanoma and nonmelanoma skin cancer. Non melanoma skin cancer includes basal cell skin cancer, squamous cell skin cancer and other rare types.\(^1\) Basal cell carcinoma (BCC) is the most common nonmelanoma skin cancer. The incidence of basal cell carcinoma is increasing. It is accounting approximately 80% of all skin cancers.\(^1\) This tumor is most associated with \(\omega\) radiation. Solar UVB radiation generally is considered to be the most important risk factor for the development of BCC. The other risk factors are light skin color, red or blonde hair color, and a family history of melanoma or sunburn reactions.\(^2\)

The tumor is slow growing but invasive and locally aggressive. Its metastases are very rare and have been reported in between 0.0028 and 0.55 of all BCC cases.\(^3\) BCC is classified into several basic types of which it is the most common nodular, superficial, nodulocystic, morpheic, metatypical, pigmented, and ulcerative.\(^4\)

Nodular and superficial type of BCC have a low risk for local recurrences, but morpheic, infiltrating and metatypical type are very destructive and with higher recurrence rate. That division of BCC is of big clinical importance.\(^5\)

Giant basal cell carcinoma (GBCC) is a BCC which is larger than 5cm in diameter. The occurrence rate of GBCC is approximately 0.5–1% out of all BCC types.\(^6\) Most often BCC are small tumors, mostly localized in the head and neck region.\(^7\)

In the treatment of giant locally aggressive and advanced neoplasms, metastatic or recurrent, when surgery is not appropriate or not possible, medical treatment becomes oncological. The most common treatment is oral hedgehog pathway and check point inhibitors.\(^8\)

There are two ways of hedgehog pathway treatment, which are approved by FDA.\(^9\) Vismodegib is the first hedgehog inhibitor approved by the FDA in 2012. An objective response rate (ORR) was 47.6% for locally advanced BCC and 30% for metastatic BCC at 12 months.\(^9,\)\(^10\) Sonidegib is the second oral HHI for the treatment of BCC, approved by the FDA in 2015. It is indicated for the treatment of locally advanced BCC that has recurred after surgery or radiation treatment or for the patients who are not candidates for surgery or radiation therapy. The research revealed an ORR of 56.1% with a median duration of response of 26.1 months and in 93.2% a 2-year survival rate for locally advanced BCC. An ORR of 7.7% was reported for metastatic BCC.\(^11\)

Immunotherapy of the advanced, non-melanoma skin cancer is gaining importance, because their high mutational burden index is high (MBI). Two anti-PD-1 antibodies, cemiplimab and pembrolizumab are approved.\(^12\)

PD-1 inhibitors produce persistent effects, with improved survival. Patients are capable to stop with therapy while they have benefits from treatment. PD-1 inhibitor therapy is well tolerated and safe among patients specifically with comorbidity.\(^13\)

Several case reports with anti-PD-1 agents\(^14\)\(^-\)\(^16\) and anti-CTLA-4 therapy\(^16\) revealed good responses in advanced disease. Seven patients received pembrolizumab plus vismodegib and nine patients received only pembrolizumab.\(^17\) The ORRs were 44% and 29% at 18 weeks, respectively. The authors concluded that combination therapy is not much better than monotherapy. The usage of pembrolizumab has been registered in 5 case reports more with complete or partial responses.\(^14\)\(^-\)\(^17\)

We present the case of locally aggressive and deep penetrating, extremely big basal cell carcinoma, located in the hairy part of head. The treatment options of such highly risked tumors must be carefully considered.

Case report

The Ethics Committee of the Zenica Cantonal Hospital allowed the data used in this case report and the patient gave us informed consent for the data and figures we used in this article also.

A 62-year-old patient arrived by car of the Emergency Medical Service to the Department of Emergency Medical Assistance (UB). On admission to UB he was somnolent, disoriented in time, space and towards persons, gave no answers to questions, could not perform more complicated requests, without pronounced lateralization in neurological findings, febrile (TT 39°C), eupnoic, normotensive, tachycardic (f 100/min). We obtained heteroanamnestic data that the patient had had a "head wound" for 15 years, which was bleeding occasionally. He bandaged the wound and hid it with a scarf. He had not consulted a doctor about this problem earlier.

He has been a diabetic on insulin therapy for many years. In the local finding we found a large ulcerated, deeply infiltrated tumor of the head, about 11cm in diameter, with purulent contents at the bottom, necrotic and gangrenous edges (Figure 1).

At the UB, we cleansed and bandaged the tumor, took wound swabs and made a computed tomography (CT) scan of the head. CT showed extensive and deeply infiltrative lesion that destroys the bone
After receiving adequate primary care and diagnostic processing at the UB, we transferred the patient to the Intensive Care Unit (ICU).

At the ICU, we connected the patient to vital functions monitoring and observed him intensively. In the laboratory findings, we found hypocalcemia, hypochromic anemia, metabolic ketoacidosis, and the level of glucose in the blood was from 8.5 to 12.5. Microbiological analysis of the wound swab showed contamination with *Staphylococcus aureus*. During the stay at the ICU, we prescribed appropriate antibiotic therapy, according to the antibiogram, and appropriate symptomatic therapy.

After the patient was stabilized, we started the surgery procedure. Following an appropriate positioning of the head, washing and limiting the operative field, we excised the tumor-infiltrated part of the skin. Then we osteoclastically removed the tumor-affected and severely softened bone down to the healthy tissue. We gradually removed the upper layer of the dura mater, which was also thickened and infiltrated by the tumor. After that, we opened the dura mater parasagitally on the left and allowed the spontaneous release of copious purulent content from the subdural space. We additionally washed it with saline and antibiotic solution. After establishing adequate hemostasis, we closed the defect with local transpositional flaps taken from the frontal and occipital regions. We covered the donor defect in that area with epidermal grafts according to Tirsch, which we took from the back of the left upper leg and lower leg. We did not reconstruct the calvaria and dura.

Postoperatively, we referred the patient to the ICU for postoperative treatment. In the further course, the flaps were without local signs of necrosis, as well as the epidermal graft. The patient was vitally stable, subjectively felt well. On the second day postoperatively, he was conscious, oriented, communicative, afebrile, eupnoic and the wounds were properly healed.

On the pathohistological examination we got the diagnosis of a giant basal cell carcinoma – metatypical type, with keratin pearls and infiltrative peripheral border. Locally aggressive, deeply infiltrated, ulcerated mass, resected in its entirety with clear resection margin at the end (Figure 3A-C). Separately delivered dura and bone were tumor-infiltrated with free resection margins at a distance of 5 mm at least.

After 15 days, the patient was discharged from the hospital to home treatment and care. About 30 days after the operation, the patient was ordered for a follow-up examination. During the control examination, the patient was in a normal state of consciousness and neurological findings. In the local findings there were no signs of infection and necrosis (Figure 4).

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(Figure 2).

**Figure 1** Preoperative image of the extensive and ulcerative BCC of the scalp (Department of Neurosurgery Zenica Cantonal Hospital)

*Slika 1. Preoperativna slika ekstenzivnog i ulcerativnog BCC vlasišta (Odjel Neurokirurgije Kantonalne bolnice Zenica)*

**Figure 2** CT scan of the head (bone window) (Department of Neurosurgery Zenica Cantonal Hospital)

*Slika 2. CT snimak glave (prozorzakost) (Odjel Neurokirurgije Kantonalne bolnice Zenica)*
Figure 3 This picture of a giant basal cell carcinoma demonstrating A) ulcerated surface, B) invasion of the fat by highly infiltrated trabeculae of basaloid cells, with the absence of peripheral palisading (C) and the area of squamous differentiation. Note the formation of keratin pearls (C) (H&E, original magnification ×20) (Department of Pathology Zenica Cantonal Hospital) Slika 3. Slika gigantskog bazocelularnog carcinoma koji pokazuje: A) ulceriranu površinu, B) invaziju masnog tkiva visoko infiltrativnim tračcima bazaloidnih stanica, bez izraže neperiferne palisadizacije C) aree skvamozne diferencijacije i keratinske perle (HE, ×20) (Odijel patologije Kantonalne bolnice Zenica)

The patient was recommended further treatment. But, due to his good physical condition, the patient refused oncological treatment. The locoregional status was satisfactory. Ten years after discovering the BCC lesion, the patient died due to a heart attack.

Figure 4 Appearance of the patient 30 days after the operation (Department of Neurosurgery Zenica Cantonal Hospital) Slika 4. Izgled pacijenta 30 dana nakon operacije (Odijel Neurokirurgije Kantonalne bolnice Zenica)

Discussion

Typical BCC lesions are small tumors with indolent behavior, located mostly at the skin which is exposed to the sun and UV light. The treatment of the BCC depends on the tumor characteristics which are based on their prognostic factors. The most important prognostic factors are size, site, tumor subtype, status of resection margins and prior treatment. In that regard, BCC are categorized in low and high risk tumor. The worst impact on tumor prognosis has large, long-standing lesions, infiltrating, morphetic or metatypical pathohistological subtype with an aggressive way of growth in the deeper lesion layers. Also, on the choice of treatments, a great influence is the medical condition of the patient, coexisting disease, and current medication. In addition, experience and the ability of the physician are undoubtedly significant.
The treatment of these large-dimensional tumors could be surgical and non-surgical. Surgical treatments are surgical resection, Mohs micrographic resection, radiotherapy and chemotherapy in unresectable tumors.18,19 Tumors located in the head area, especially large tumors, are in themselves classified as high-risk tumors20. High risk tumors require a more careful approach, primarily due to the volume and severity of the resection, but also the completeness of the excision. An aggressive surgical resection with tumor-free resection margins offers the best results and healing. The cure rates are averaging from 90% to 91%.20 In one study, the age of the patient, duration of the lesion and duration of the treatment were not significantly connected with the increased risk of relapse.21 Our patient arrived in our hospital's intensive care unit in a serious condition, with deep, infiltrative lesion on the head which had lasted for the last 15 years. The case was complicated by staphylococcal infection of the tumor surface in subdural space, and tumor infiltration of the dura of the upper sagittal sinus.

The risks of operative treatment were reflected in the possibility of intraoperative damage and thrombosis of the upper sagittal sinus, sepsis, damage of intracranial structures, liquefaction and postoperative necrosis of transplanted skin flaps. The case was more difficult due to the insulin-dependent diabetes.

There was a risk of closing the resulting defect with a skin flap due to the possibility of its infection and necrosis. Usually, the flaps are not applied to the infected substrate immediately but after a few days, when there is certainty that the infection has been cured.22 Wide excision of GBCC of the head and neck can consequently have large complex of soft tissue and bone defects and even in brain exposure. How the defect will be reconstructed depends on the extent of the defect. The large and complex defect in the head and neck area can be properly covered by the selection of free, regional, or local flaps.23 Nevertheless, after extensive removal of the tumor mass, removal of necrotic tissue and washing of the subdural space with an antibiotic solution, we decided to close the defect. The reason for such a decision was the general poor condition of the patient, the possibility of superinfection in an open wound with a more resistant strain, its spread towards the intracranial space, cerebrospinal fluid (CSF) and good blood circulation in the head. Our procedure, considering the postoperative course and rapid recovery of the patient, proved to be justified. After 10 years, there were no recurrent tumors and patient died due to a heart attack.

Metastatic BCC is very rare. It has been described in bone, lungs and axillary lymph nodes.24,25 In the case of BCC with pulmonary metastasis, after surgery, sonidegib, a hedgehog signaling inhibitor, was used as a first-line treatment and cemiplimab in the second act.24

In the treatment of giant locally aggressive and advanced neoplasms, metastatic or recurrent after surgery treatment and radiotherapy, then in case surgery is not appropriate or not possible, medical treatment becomes just oncological. The most common treatment is oral hedgehog pathway and check point inhibitors.8

Further investigation of immunotherapy, especially of PD-1 inhibitors is needed to define its optimal role for patients with this disease.

References

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