

RECURRENT PERIOCULAR BASAL CELL CARCINOMA. A CASE REPORT

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SUMMARY

Aim: We present the management of a severe case of recurrent periocular basal cell carcinoma, orbital invasion and exenteration.

Case report: The present case is of a recurrent basal cell carcinoma in a 84-year-old male presenting with non-healing lesion above right eyelid. A tumor excision was performed in May 2014. Histopathology revealed a basal cell carcinoma (dg. C44.1 ICD-10-CM) with positive margins. The re-excision of the lesion was performed. After two years, there was a local recurrence and orbital invasion. Indication for external curative radiation therapy. Plastic surgery of the upper eyelid. Orbital exenteration was indicated in January 2018. After another year, a recurrence of the tumor was once again noted. Histopathology revealed a basal cell carcinoma (dg. C44.1 (TNM 7, pMx, pNx, pTx)). The patient was indicated for external radiotherapy. There were no indications for biological treatment. After another year, a progression of the local finding was noted.

Conclusion: Basal cell carcinoma (BCC) is the most common non-melanoma skin cancer of the periocular region. Primary treatment of basal cell carcinoma is surgical. Advanced lesions require extensive surgical interventions and other available treatment modalities. In some cases, mutilating surgery – exenteration of the orbit is inevitable. Despite a relatively small percentage of invasive diseases today, advanced stages may still occur; either as a result of the patient's late presentation, inadequate initial therapy aimed at maintaining critical periorbital structures, or due to high tumor aggression. The case report highlights necessity of radical resection of primary tumor with histological examination.

Key words: basal cell carcinoma, periocular tumors, tumors eyelashes, orbital exenteration

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INTRODUCTION

Basal cell carcinoma (BCC) is the most common tumour of the eyelids and periocular region. The incidence of BCC of the eyelids (C44.1 ICD-10-CM) is gradually increasing worldwide. Basal cell carcinoma represents 90 % of malignant tumours of the eyelids, predominantly in the male population [1,2]. It has its specifics around the eye. It occurs very often in the sixth, seventh and eighth decades of life, but in 10 % of cases it can also appear between the ages of 20 and 40 years. The aetiology is mainly related to exposure to solar radiation in people with pale skin. This fact is based on extensive studies including Europe, Australia and North America [3]. More than 50 % of BCC of the eyelids occur in the lower lid and medial canthus. Metastases of the BCC are rare, but aggressive behaviour is characteristic. Orbital invasion is described in 1.6–2.5 % of cases [4]. The primary treatment of BCC is radical surgical resection with negative

resection margins [4,5,6]. Radiotherapy is widely used in the treatment of BCC. Chemotherapy, cryotherapy, photodynamic therapy or biological treatment are not often indicated [4,6]. In large, recurrent or complicated cases, it is necessary to proceed to mutilating procedures, such as orbital exenteration [4,7].

CASE REPORT

In May 2014, a patient born in 1930 was sent to the Department of Ophthalmology, Central Military Hospital – Faculty Hospital Ružomberok, for a suspected tumour in the region of the right supercilium. The patient's personal and family medical history was insignificant. From the ocular history: in 2009 cataract surgery bilaterally, in 2012 YAG laser capsulotomy bilaterally. Other ocular diagnoses included visual field disorder, synchysis scintilans. Central visual acuity in the right eye was 5/10, central visual acuity in the left eye was

5/15. The patient described a non-healing and bleeding lesion in the right eyebrow persisting for more than two weeks. A physical examination determined a rigid bordered formation up to 2 cm, whitish in colour in the right supercilium on the lateral side; the edge was solid. The centre on the surface was covered with a crust. We suspected a tumorous process – basal cell carcinoma. The patient was sent to the plastic surgery department for a biopsy and histology of the lesion.

On 30 May 2014, a biopsy of the lesion was taken. The wound was closed by individual sutures. In the evening, the patient was brought for treatment by the emergency services due to significant bleeding from the surgical wound. Revision of the wound was performed, the bleeding was stopped and two individual stitches were added. The patient was sent to outpatient care in a stable condition. The diagnosis of infiltrative type basal cell carcinoma was histologically confirmed. However, the sample had positive resection margins. The patient was indicated for re-excision of the lesion in July 2014 at the centre where the primary tumour excision had been performed. After one week, the wound was healed per primam. The result of the histology from re-excision confirmed the diagnosis of basal cell carcinoma (without definition of edges). The patient did not attend further follow-up examinations.

A further two years later, on 2 March 2016, the patient reported to the surgical department. He described frequent bleeding from the wound, a non-healing lesion on the right upper eyelid. From the surgical department he was sent to us to assess the local finding. On physical examination, we found a bleeding infiltrating tumour of the upper eyelid, with ulceration of size 1 cm and semiptosis of the upper eyelid. Due to the location of the tumour, we sent the patient to the plastic surgery department for resection of the tumour. The patient was then sent to the Department of Oncology, Central Military Hospital – Faculty Hospital Ružomberok, in order to consider the subsequent procedure for histologically verified basal cell carcinoma.

An X-ray of the chest was performed at the oncology outpatient clinic in order to rule out infiltration of the splanchnocranium and superciliary arch. Magnetic resonance imaging (MRI) of splanchnocranium was added to exclude overgrowth into the retrobulbar space.

The conclusion was of no metastases, but there was local infiltration of the orbit of 2 cm in depth. Exposure on a linear accelerator was indicated. The patient's family preferred the centre in Žilina, where the patient had family, and so in June 2016 the patient was sent to the workplace of Department of Oncology in Žilina. External radiotherapy was applied in a curative dose.

On 7 July 2016, following radiotherapy, central visual acuity of the right eye was 3/50. Objectively we found thickening and exulceration on the skin of the right eyelid. The patient opened the ocular aperture to approximately 4 mm spontaneously, without exophthalmos, there

was chemosis of the conjunctiva, the cornea was without keratopathy. MRI of the right orbit was performed repeatedly, without demonstrable intraorbital invasion. The following were performed: *Incisio et excisio conjunctivae l.dx., tarsoraphia partialis l.dx.*, histologically - free margins of tumour cells. After a further week, central visual acuity of the right eye is preserved to counting fingers in front of the eye. On the cornea, the defect interferes with the surface layers of the stroma, with a size 4 x 7 mm, the local finding did not show improvement after surgery. Due to non-compliance, hospitalisation was proposed, but the patient refused.

In January 2017, the patient reported to the ophthalmological department due to right eye pain. Central visual acuity had deteriorated to light without projection, the right eye was hypertonic with anterior uveitis and corneal ulcer. Osmotic diuretic treatment, local antibiotics, antiglaucomatic and re-epithelialisation treatments were administered, with an improvement in the local finding.

In June 2017, a recurrence of basal cell carcinoma was detected in the palpebral groove of the upper eyelid. Central visual acuity was without light perception. The upper eyelid was deformed, stiff resistances with ulcerated surface were present, lengths up to 20 mm. The patient was repeatedly examined at the Department of Ophthalmology, Faculty of Medicine and UNB, Ružinov Hospital, in Bratislava. Exenteration of orbit was indicated.

In August 2017, the patient again reported to the ambulance of ophthalmology in Ružomberok, due to tearing and pain of the right eyeball and eyelid. We determined that the patient had not reported for the operation in Bratislava. The lesion of the upper eyelid was complicated by a large loss-making exulcerated defect with a superficial crust. The eyeball was immobile, fixed, abundantly vascularised.

The patient had been repeatedly included in the operational programme. Orbital exenteration was performed on 9.1.2018 (Figure 1. A, B) at the Department of Ophthalmology, University Hospital in Ružinov, perioperatively and postoperatively without complications (Figure 2. A, B). After healing (Figure 3.) an individual epithesis of the left eyelid was produced (Figure 4. A, B). The patient was then released, with a check once every 1–2 weeks.

In May 2018, upon a physical examination, the zygomatic region was hyperaemic, with hard oedema and pathological secretion. The patient was hospitalised at the Department of Ophthalmology in Ružomberok. Broad spectrum antibiotics were prescribed generally. After cultivation of *Staphylococcus aureus* - with an excellent effect on antibiotic treatment.

In February 2019, a recurrence in the supraorbital arch was detected. At the Department of Otorhinolaryngology and Cervicofacial Surgery in Ružomberok, a biopsy of the lesion was taken. Computer tomography of the paranasal sinuses (CT PND) was performed. Skeletal infiltration could not be excluded. Histologically confirmed basal cell carcinoma (C44.1, TNM 7, pMx, pNx, pTx) was



Figure 1. (A, B) Perioperative presentation - right orbital exenteration (01/2018)



Figure 2. (A, B) Postsurgical presentation of the orbital exenteration – 2 months (03/2018)

detected. The patient's condition was consulted with an oncologist. Due to the age and location of the finding, it was assessed as inoperable. Repeat irradiation was indicated. Proton therapy (PBT) with Pencil Beam Scanning was not approved due to age; repeat irradiation was contraindicated by Cyber Knife stereotactic technology. Consideration of biological therapy by means of a clinical oncologist was recommended.

On 16.9.2019, a repeat irradiation by external radiotherapy (ERT) 18x3Gy was performed at the centre in Žilina. Biological therapy was not indicated. MRI was without recurrence – pathology in clinical remission. The patient attended regular follow-up examinations. In October 2020, recurrence of basal cell carcinoma was detected again. The skin of the area of the orbit was reddened, swelling, with uncovering of the eye socket, on the surface with crust and purulent scum. The patient was examined by a dermatologist through a melanoma commission, and also sent for health assessment to the Department of



Figure 3. Postsurgical presentation of the orbital exenteration – 4 months (04/2018)



Figure 4. (A, B) 4 months after tumor resection and completed reconstruction by epithesis in the frame of glasses (04/2018)

Ophthalmology, University Hospital in Ružinov. Due to the general condition and age of the patient, palliative therapy was indicated.

DISCUSSION

Non-melanoma skin cancer of the eyelids represents 5–10 % of all skin tumours. Basal cell carcinoma is the most common malignant tumour of the eyelid, accounting for 80–90 % of cases. Squamous cell carcinoma (SCC) represents 3.4–12.6 %, sebaceous carcinoma 0.6–10.2 %, melanoma and Merkel cell carcinoma less than 1 % [1,2]. BCC of the eyelids in the Slovak Republic (SR) in the last statistically processed year 2008 was approximately 3926 cases in both sexes together, of which 275 were localised on the eyelids [3]. Basal cell carcinoma (BCC) is the most common malignancy in the periocular region. Dependency on gender, age, and tumour incidence have been demonstrated in several studies. Most commonly found in patients between the sixth and eighth decades of life, the median age was 62 years (46 % were at least 65 years of age), with a slight predominance in the male population with 61 % [2,4,5,6]. The predominance of men suggests that men are at greater risk than women, possibly also due to late arrival and delay in diagnosis. The most common localisation of basal cell carcinoma is the area of the lower eyelid, medial and lateral canthus [6,7,8].

Risk factors for the development of basal cell carcinoma are described in several studies. These include older age, male gender, Caucasian population. The 5-year cumulative risk of new BCC in patients with at least one BCC is 41–45 %, compared to a 5 % risk in the Caucasian population without BCC. The most important risk factor is exposure to ultraviolet radiation, light skin colour, proximity to the equator. Other factors influencing the development of BCC are exposure to ionising radiation, patient immunosuppression, HIV seropositivity, smoking or genetic burden [2,9].

Clinical manifestations of periorbital lesion may be re-

latively subtle. BCC is most often manifested as erythema, induration, palpable lesion, recurrent bleeding or cystic nodule. Typically, it has a pearly, waxy, or translucent character. However, the lesion is often painful. Patients are often without symptoms or subjective difficulties. A study by Lebowitch describes 35.7 % of lesions attached to the bone. Limited mobility of the eyeball may be a significant clinical finding, incidence is from 30–76.5 %. These patients often present symptoms such as diplopia, of which 35.7 % of patients had only a visual or palpable lesion with no fixation to the bone or manifestations in the orbit. The study showed that patients with obvious clinical signs such as epiphora or keratopathy did not complain of any pain. Another late clinical symptom is strabismus, which may be accompanied by a head nerve injury and invasion of the bone. These invasions are often completely without symptoms, without orbital signs and even without visual disturbance until late in the disease [4,10,11].

The primary therapeutic modality of BCC is surgical resection. Due to tumour localisation, tissue-sparing methods are often used, which increase the risk of recurrence [10]. The integrity of the eyelids and their function is important for protecting and maintaining eyeball function. The shape of the tumour, the distance from the edge and its diameter are important for choosing the best surgical technique. BCC in the field of the medial and lateral canthus therefore has a significantly higher risk of intraorbital and perineural overgrowth. The need for orbital exenteration in basal cell carcinoma may be significantly higher if the lesion includes a medial canthus [4]. Data on relapses following basalioma surgical treatment vary depending on the operating technique used. The incidence of relapses in patients treated without the use of Mohs micrographic surgery or "en-face" frozen incision perioperatively ranged from 1.8–39 %, in the case of longer observation of patients the proportion of relapses increased [11,12,13,14].

The recurrences after excision are caused by several

factors. Depending on the stage and location, the incidence of BCC recurrences is approximately 95 % after treatment. The incidence rate after primary surgery is 1–5 % per annum. Mohs micrographic surgery was considered the best method of removing BCC with minimal recurrences [15,16]. The most common cause of recurrence is non-compliance with the recommendation for radical basalioma excision 0.3–1 cm from the clinically visible edges of the tumour [16].

Long-term cancer, as well as recurrent or incompletely excised tumours, are considered contributing factors to aggressive, invasive lesions. In addition to insufficiently radical procedure, another supporting factor for incomplete excision is that basalioma can spread subclinically even a few centimetres from a clinically obvious tumour.

Based on biological behaviour, we generally distinguish between indolent (superficial and nodular) and aggressive types (infiltrative, micronodular and metatypical) basal cell carcinoma of the skin. The result of tumour histology and subtype has been clearly demonstrated as a prognostic factor for the invasive and malignant potentials of BCC [4,15].

Following incomplete excision, recurrent malignant tumours or impossibility of surgery, a high dose rate (HDR) of brachytherapy is applied in the treatment of non-melanoma lesions [17,18]. In the past, especially in the 1970s, standard external radiotherapy was used as monotherapy (mostly ⁶⁰Co) in the treatment of basaliomas in the lower eyelid area and inner corner. This method has been surpassed due to postradiation cicatricial changes in the surrounding area. However, in some cases this treatment is still considered highly effective [18]. Local pharmacological treatment, including the imiquimod immunomodulator, is less successful and is not used widely in localisation near the edge of the eyelid, outer or inner corner [19]. Chemotherapy was also applied in the past in the treatment of BCC, but unsuccessfully [20].

Vismodegib is an orally available Hedgehog pathway inhibitor with a small molecule. Hedgehog pathway signalling via smoothed transmembrane protein

(SMO) leads to activation and nuclear localisation of glioma-associated oncogene (GLI) transcription factors and to the induction of Hedgehog target genes [21]. Indications for treatment are very limited. According to a study published in the American Journal of Ophthalmology, vismodegib therapy for periocular and orbital BCC is effective, and the side effects are mostly manageable [22]. A study by Harmeet describes the effectiveness of vismodegib in the treatment of periocular and orbital BCC in about half of all cases [23]. The optimal treatment protocol and duration are still unknown, and it is necessary to seek individual therapeutic practices that will lead to maximum therapeutic effect and minimal adverse reactions [22,23].

In several patients we proceed to orbital exenteration due to the failure of previous therapeutic modalities. Given that recidivism after exenteration can be up to 50–75 %, it is very important not to underestimate the timely management of these lesions [24].

We can define several determinants of recurrent periocular basal cell carcinoma and severe course of the disease. Factors that cannot be influenced include age, male gender, Caucasian population [2,4,5,6]. Factors that can be influenced are ionising radiation, tumour localisation [6,7,8,9]. Long-term cancer, histologically confirmed aggressive BCC type, positive resection margins after primary excision and non-compliance of the patient determine the course of the disease [15,16].

CONCLUSION

Within the context of onco-ophthalmology, increased attention must be given to periocular malignant tumours. Advanced findings lead to mutilating operations that pose a serious aesthetic problem. The case report highlights the importance of early diagnosis, radical resection, multidisciplinary co-operation, lifetime dispensation of a patient with early recidivism. Multidisciplinary and patient co-operation in the field of cancer is essential, improving early diagnosis, treatment and survival of patients. Patient management requires an individualised approach.

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