

Analysis of selected recurrence risk factors after treatment of head and neck basal cell carcinoma

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Abstract

Introduction: Basal cell carcinoma (BCC) is the most common type of non-melanoma malignant skin tumors. Eighty-five percent of all cases are located on the skin of the head and neck. The risk of recurrence after surgery is estimated at 5–15%.

Aim: To evaluate the selected risk factors for recurrence after surgical treatment of head and neck BCC at the Department of Head and Neck Surgery in the Greater Poland Cancer Centre of the Poznan University of Medical Sciences.

Material and methods: A retrospective analysis was made of patients treated at the Department of Head and Neck Surgery in the Greater Poland Cancer Centre of the Poznan University of Medical Sciences in 2007–2012 for BCC of the head and neck region. The study covered 312 patients: 198 males (63%) and 114 females (37%), aged 32–96 years.

Results: In the study group of 312 tumors, recurrence after initial treatment in this Centre was diagnosed in 18 patients (9%), whereas in patients who were previously operated elsewhere, recurrence was found in 22 cases (17%). The nodular type was the most common BCC type in the study group and concerned 175 patients (56%). The most numerous group (114; 37%) in this study group comprised patients with external nose and cheek tumors.

Conclusions: The importance of preoperative biopsy to assess the histological type as a routine treatment of patients with BCC is essential. Ultrasound evaluation to assess the exact size and depth of tumor invasion should also be implemented.

Key words: basal cell carcinoma, recurrence, surgery.

Introduction

Basal cell carcinoma (BCC) is the most common non-melanoma malignant skin tumour [1, 2]. It originates from the epidermal or progenitor cells of the hair follicle, which resemble the basal cell layer of the epidermis. The cancer is characterized by a high local malignancy and a high (tenfold) risk of a second primary cancer to occur [3]. Histologically, it is divided into nodular, superficial, morpheaform, infiltrative or mixed types (Table 1).

Eighty-five percent of BCC cases are located on the skin of the head and neck [4], which results from the exposure to UV sunshine, the main risk factor [5]. Other risk

factors include radiotherapy and immunosuppression (risk being 10 to 20 times higher in patients after organ transplants) [6–9].

Basal cell carcinoma is the most commonly diagnosed cancer in the world. The BCC prevalence is constantly growing, which may likely be caused by increased UV radiation associated with destruction of the ozone layer, increased outdoor physical activity and dress code changes [10]. The geographical distribution of BCC incidence is, above all, conditioned by the duration of sunshine exposure. The highest incidence occurs in Australia (1041 per 100,000 population in males and 745 per

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Table 1. Basal cell carcinoma characteristics

Nodular	Microscopic characteristics: clusters of cancerous cells of different size and shape, showing a palisade-like arrangement at the circumference Location: head and neck Risk factor: UV exposure Note: the most common histological type
Superficial	Microscopic characteristics: irregular clusters of cancer cells attached to atrophic epidermis, rarely penetrating down into the dermis Location: trunk Risk factor: intensive short exposure to sunshine Notes: more commonly diagnosed in women and young people
Morpheaform	Microscopic characteristics: strips of atypical basaloid cells sunk in a thick fibrous bed Location: head and neck Risk factor: UV exposure Note: represents approximately 6% of all BCC cases, very aggressive growth
Infiltrative	Microscopic characteristics: atypical basaloid cells arranged in several layers of thick longitudinal strips without circumferential palisade-form cells Location: head and neck Risk factor: prolonged UV exposure Note: represents approximately 4.8% of all BCC cases, aggressive growth

100,000 population in females) versus Germany, a country of the lowest incidence (53 per 100,000 population in males and 46 per 100,000 in females) [11]. In Poland, BCC incidence is estimated at 69.8 per 100,000 population [12].

In the United States, the total number of BCC and squamous cell carcinoma (SCC) of the skin (ratio 3 : 1) is higher than the number of all other cancers. One in three cancers diagnosed in the world is skin cancer [13]. The incidence of BCC is still increasing. It has tripled in the last 30 years [14]. Vries *et al.* [15] reports an expected increased incidence of BCC to be maintained at least until 2015.

Over the two recent decades, the mean age of BCC patients decreased as sun bed tanning has been more and more popular with young people [16].

The risk of recurrence after surgery is estimated at 5–15%. It depends, among other things, on the severity of the disease, its location, histological type of tumor and surgical technique primarily used [17]. The BCC treatment approaches include wide surgical resection, Mohs micrographic surgery, radiotherapy, photodynamic therapy, local treatment (e.g. imiquimod), cauterization and cryotherapy [1]. It is believed, however, that classic surgical excision should be the gold standard for the treatment

of basal cell carcinoma of the head and neck, especially when radical resection is possible.

Aim

The aim of this study is to evaluate the selected risk factors for recurrence after surgical treatment of head and neck basal cell carcinomas at the Department of Head and Neck Surgery in the Greater Poland Cancer Centre of the University of Medical Sciences in Poznan.

Material and methods

A retrospective analysis was made of patients treated at the Department of Head and Neck Surgery in the Greater Poland Cancer Centre of the Poznan University of Medical Sciences in 2007–2012 for basal cell carcinoma of the head and neck region. The study included 312 patients: 198 males (63%) and 114 females (37%), aged 32–96 years (median age 73 years) (Table 2).

Results

Results are presented in Tables 3–10. In the study group of 312 tumors, 204 (65%) were patients with pri-

Table 2. Patient characteristics (*n* = 312)

Variables	Tumor location						Total
	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	
No. of patients	114 (37%)	82 (26%)	52 (17%)	36 (12%)	18 (6%)	8 (3%)	312 (100%)
Female	46 (41%)	21 (26%)	29 (44%)	14 (39%)	2 (12%)	2 (25%)	114 (37%)
Male	68 (59%)	61 (74%)	25 (46%)	22 (61%)	16 (88%)	6 (75%)	198 (63%)
Patients in primary treatment	72 (63%)	62 (75%)	40 (77%)	16 (44%)	8 (44%)	4 (50%)	204 (65%)
Patients in recurrence treatment	42 (37%)	20 (25%)	12 (23%)	20 (56%)	10 (66%)	4 (50%)	108 (35%)
Mean follow-up [months]	57	27	22	19	28	26	

Table 3. The BCC classification according to TNM – all patients

	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	Total
T1	27 (24%)	24 (30%)	21 (39%)	7 (19%)	0	0	79 (25%)
T2	32 (28%)	39 (47%)	11 (20%)	18 (50%)	2 (11%)	2 (25%)	104 (33%)
T3	36 (32%)	16 (20%)	15 (28%)	6 (17%)	12 (77%)	4 (50%)	89 (28%)
T4	19 (16%)	3 (3%)	7 (13%)	5 (14%)	4 (22%)	2 (25%)	40 (14%)
All	114 (100%)	82 (100%)	54 (100%)	36 (100%)	18 (100%)	8 (100%)	312 (100%)

Table 4. BCC classification according to TNM – recurrences

	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	All
T1	2 (9%)	1 (12%)	0	0	0	0	3 (7.5%)
T2	8 (35%)	2 (22%)	0	1 (25%)	0	1 (100%)	12 (30%)
T3	7 (30%)	4 (44%)	1 (100%)	1 (25%)	1 (50%)	0	14 (35%)
T4	6 (26%)	2 (22%)	0	2 (50%)	1 (50%)	0	11 (27.5%)
All	23 (100%)	9 (100%)	1 (100%)	4 (100%)	2 (100%)	1 (100%)	40 (100%)

Table 5. BCC histological types – all patients

	Nose and cheek	Auricle	Lips	Ocular	Scalp	Forehead	All
Nodular	68 (60%)	44 (54%)	28 (52%)	21 (59%)	10 (55%)	4 (50%)	175 (56%)
Superficial	4 (4%)	5 (6%)	10 (19%)	4 (11%)	2 (11%)	0	25 (8%)
Morpheaform	14 (12%)	11 (13%)	5 (9%)	5 (14%)	1 (6%)	2 (25%)	38 (12%)
Infiltrative	11 (10%)	4 (5%)	7 (13%)	3 (8%)	3 (17%)	1 (12.5%)	29 (9%)
Mixed	17 (14%)	18 (22%)	4 (7%)	3 (8%)	2 (11%)	1 (12.5%)	45 (15%)
All	114 (100%)	82 (100%)	54 (100%)	36 (100%)	18 (100%)	8 (100%)	312 (100%)

Table 6. Treatment results – local recurrence by location

Location	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	Total
Recurrence after primary treatment	11 (15%)	5 (8%)	0	1 (6%)	1 (12.5%)	0	18 (9%)
Recurrence after recurrence treatment	12 (23%)	4 (16%)	1 (8%)	3 (14%)	1 (10%)	1 (25%)	22 (17%)

Table 7. Treatment results – local recurrence by location and gender

	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	All together
Female	46	21	29	14	2	2	114
Recurrence	8	3	0	1	0	0	12 (10%)
Male	68	61	25	22	16	6	198
Recurrence	15	6	1	3	2	1	28 (14%)

Table 8. Treatment results – local recurrence after primary treatment by BCC histological type

	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	All
Nodular	5	1	0	0	1	0	7
Superficial	0	0	0	0	0	0	0
Morpheaform	3	2	0	0	0	0	5
Infiltrative	2	2	0	1	0	0	5
Mixed	1	0	0	0	0	0	1
All	11	5	0	1	1	0	18

Table 9. Treatment results – local recurrence after recurrence treatment by BCC histological type

	Nose and cheek	Auricle	Lips and chin	Ocular	Scalp	Forehead	All
Nodular	5	1	0	1	1	0	9
Superficial	1	0	0	0	0	0	1
Morpheaform	3	1	1	1	0	0	6
Infiltrative	2	2	0	1	0	1	6
Mixed	0	0	0	0	0	0	0
All	12	4	1	3	1	1	22

marily diagnosed basal cell carcinoma, while the other 108 (35%) presented for treatment with a recurrence of the disease. After initial treatment in this clinic, recurrence was diagnosed in 18 patients (9%), whereas in patients who were previously operated elsewhere, recurrence was found in 22 cases (17%).

Of the 312 patients, 114 were women (37%) in whom, after surgical treatment, 12 recurrences (10%) were diagnosed. Among the 198 males (63%), recurrence after treatment was found in 28 cases (14%) (Table 7).

In 278 cases (89%), the surgical specimen was removed by conventional surgery. In this group tumor recurrence was diagnosed in 38 patients (14%). CO₂ laser was used in 34 patients (11%), followed by a relapse of two of them (6%) (Table 10).

The nodular type was the most common basal cell carcinoma type in the study group and concerned 175 patients (56%). Recurrence was observed in 16 of them (40%). The second most common type was a mixed type (45 patients (15%), one recurrence (2%)). Further types were the morpheaform (38 patients (12%), 11 relapses (28%)); infiltrative (29 patients (9%), 11 recurrences (28%)) and superficial type (25 patients (8%), one recurrence (2%)).

Seventy-nine patients (25%) were referred to our institution in stage T1 tumor according to TNM classification, 104 (33%) in stage T2, 89 (28%) in stage T3 and 40 patients (14%) in stage T4. Stage T3 tumors were most associated with tumor recurrence (14 patients; 35%), followed successively by T4 (12 patients; 30%), T2 (11 patients; 27.5%) and T1 (3 patients; 7.5%) (Tables 5, 8 and 9).

The most numerous group (114; 37%) in our study group were patients suffering from basal cell carcinoma of the external nose and cheek. A local recurrence of BCC was found in 11 patients (15%) who received primary treatment (pBCC) and a second recurrence was found in 12 (23%) patients treated due to the recurrence (rBCC). The mean follow-up time was 57 months (Table 5). Of 82 patients with auricle tumors, a local cancer recurrence was observed in 5 (8%) cases, rBCC in 4 patients (16%) (follow-up was 17 months) (Table 5). Of 52 patients with primary BCC of the lip and chin region, none was found to have a local recurrence. Of the 36 (12%) patients with tumor in the ocular region, a recurrence after primary treatment was found in one case, rBCC in 3 cases (14%). Among the 18 patients (6%) with scalp tumor, a recur-

Table 10. Treatment results – local recurrence by surgical technique used

	Classic surgery	CO ₂ Laser	All
Cases	278	34	312
Recurrence	38	2	40
% of recurrences	14	6	13

rence after primary treatment was diagnosed in 1 patient, after secondary treatment also in 1 patient (Table 5). The smallest group consisted of patients with forehead BCC (8 patients, 3%). A relapse was found in 1 patient with a previously diagnosed recurrence.

Discussion

Basal cell carcinoma is the most common cancer among Caucasians characterized by high local malignancy, and also a high rate of recurrence. Therefore, it is a significant social problem. For this reason, the authors undertook the analysis of selected risk factors for recurrence after treatment of BCC.

Analysis of 312 patients diagnosed with BCC of the head and neck was conducted. Of these, 204 (65%) patients were patients with primary BCC (pBCC), and 108 patients (35%) were referred from other centers with a diagnosis of recurrent BCC (rBCC). In this study, a recurrence after surgery of rBCC was found in 22 patients, representing 17% of the total group of patients operated due to the recurrence. This result is inferior compared to patients treated primarily (18 cases, 9%). According to the literature, previously treated BCC is a strong risk factor for subsequent relapses. Sartore *et al.* [17] reported a 23% recurrence rate in patients previously treated versus 18% in patients who have not been treated before. Similar results were reported by Sliverman *et al.* [18] (11.6% in a group of 135 patients). In their publication, Rowe *et al.* [19] showed the recurrence incidence of 17.4% for patients after rBCC surgery.

The head and neck BCC incidence rate is higher in men due to a more extensive exposure to sunshine. Women, on the other hand, tend more to use clothes covering the head and neck region. The above gender-specific distribution of the disease is reflected in publications by Yaldiz *et al.* [20] and Bastiaens *et al.* [21] where men accounted

for 62.8% and 54% of cases, respectively. Similarly in our study, men represented the majority of the population (198 patients, 63%). The male : female (M : F) rate was 1.74 : 1. In contrast, Zhang *et al.* [22] found a M : F rate of 1 : 1.1, but their study group consisted of 60 cases only. In this study, the local recurrence rate in the female population was estimated at 10% (12 patients). In men, the number of treatment failures was 28, that is 14%. More favorable treatment results in women may be accounted for by their taking more care of their looks and seeking medical aid earlier. Sartore *et al.* [17], contrary to the above correlation, did not demonstrate in their report any relationship between gender and incidence of the basal cell carcinoma recurrence.

Classical surgery with intraoperative microscopic assessment of margins is a gold standard in treatment of head and neck basal cell carcinomas. This is due to high efficacy and low cost of the procedure [23]. We do not perform Mohs surgeries in our centre. However, Mosterd *et al.* [24] demonstrated that although the incidence of local recurrences after treatment using conventional surgical techniques is higher than in the Mohs method, the difference is not statistically significant. In this study after classical surgical resection, 38 recurrences were noted, both for patients presenting with primary BCC (pBCC) and recurrent BCC (rBCC), constituting a 14% recurrence rate for procedures performed in that fashion. In contrast, a cancer recurrence in the 34 patients treated with CO₂ laser was found in 2 patients (a 6% recurrence rate). Iyer *et al.* [25] showed a recurrence rate of 3.2% in their group of 61 patients treated using laser techniques.

The most commonly diagnosed histological type of BCC at the Greater Poland Cancer Centre was the nodular type (175 patients, 56% of all cases), followed by the mixed type (45; 15%), morpheaform type (38; 12%) and infiltrative type (29; 9%). Our results are in good agreement with the analyses by Bastiaens *et al.* [21] (1280 nodular types out of 1960 specimens studied) and Betti *et al.* [26] (1008/1774). Seven cases (39%) of the local recurrence after primary treatment of BCC nodular type were found. This number is inferior to recurrences after infiltrative and morpheaform BCC types (5 and 5 patients, respectively; 55%). Considering a lower number of patients with originally diagnosed infiltrative and morpheaform BCC subtypes, these should be assumed to be characterized by a stronger tendency to relapse. With regard to treatment of patients presenting with recurrent BCC, the proportions of the above subtypes were similar (9 patients; (40%), 6 and 6 patients, respectively (54%)). Our results are consistent with reports by Bartos *et al.* [27], who showed that 54% of all recurrences in their study sample were more aggressive subtypes. Sartore *et al.* [17] also identified the highest proportion of local failures to occur in patients with infiltrative and morpheaform BCC.

In terms of the stage of the disease, the largest group presenting was formed by patients with stage T2 tumors (104; 33%). On the other hand, patients with stage T3 (14; 35%) and T4 (12; 30%) had the highest incidence of tumor recurrence. It is postulated that the larger size tumors may make consistent effective radical surgical excision more difficult.

The most numerous group of BCC patients treated in this Centre were those suffering from basal cell carcinoma of the external nose and cheek. The second in order were patients with BCC of the auricle (82 cases; 26%). In the study by Janjua *et al.* [28], patients with tumors of the nose and cheek region also represented a clear majority (97 cases out of 171 patients). Similar results were reported by Chow *et al.* [29], Aandani and Ganatra [30]. As in the reports by Ocanha *et al.* [31] and Farhi *et al.* [32], this study found the highest number of local recurrences following primary surgical treatment for tumors of the nose and cheek (11 cases; 15%) and auricle (5 patients; 8%). This is most likely caused by the complex anatomy of those regions and consequent difficulty in achieving sufficient radicality of the procedure.

In conclusion, BCC is characterized by a high risk of recurrence, which should lead to careful treatment planning. In order to improve the results of treatment, preoperative evaluation using high-frequency ultrasound (HF USG) could be implemented in the assessment of the depth of the tumor infiltration. A reliably useful correlation between the size of the tumor assessed by USG and histopathological examination has been demonstrated [33]. Preoperative biopsy with histopathological evaluation may lead to a wider extension of free surgical margins when histological type suggesting a greater risk of recurrence (invasive, morpheaform) is found. Similarly, wider free margins in excising the tumor should be applied when treating the recurrence. More cautious and hence, wider margins must also be incorporated for lesions located in the nose and cheek region. Periodic and long-term follow up is extremely important not only to assess the occurrence of a possible relapse, but also to address the fact that patients with BCC are at an increased risk of developing a second primary lesion.

Certain limitations of this study are present. The authors analyzed only some of the risk factors. In the evaluation of the recurrence risk other factors may be important such as the degree of sun exposure in childhood, alcohol and tobacco abuse, profession, treatment with immunosuppressive drugs and many others, which were not analyzed. It should be noted that a number of risk factors in one patient could potentially multiply the risk of recurrence – no such analysis has been performed.

Conclusions

An important clinical problem in the treatment of basal cell skin cancer of the head and neck region is the

high percentage of local failures. The importance of pre-operative biopsy to assess the histological type as a routine treatment of patients with BCC is essential. Ultrasound evaluation to assess the exact size and depth of tumor invasion should also be implemented. Regular and systematic check-ups at specialized outpatient clinics are very important. The authors propose a scheme every 6 months during the first year after surgery and then every 12 months or in the event of an alarming lesion.

Conflict of interest

None declared.

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