ARTICLE

Small margin (up to 2 mm) excision of periocular basal cell carcinomas in the setting of a one-stop clinic — long-term outcomes at a minimum of 11 years' follow-up

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Abstract

Objectives To analyse the long-term outcome of small margin (up to 2 mm) excision of clinically well-demarcated primary periocular basal cell carcinomas (BCCs).

Methods Retrospective evaluation of 185 patients with excised well-demarcated primary BCCs at a minimum of 11 years following excision. All patients underwent tumour excision with maximum margins of 2 mm. Resulting defects were, if possible, closed directly. Reconstruction requiring flaps or grafts was delayed until receipt of the histological report, which was obtained in all cases.

Results Of 185 patients evaluated, 69 (37.3%) were still alive at the time of the study, at least 11 years post excision. One-stage excision and direct closure was performed in 60/69 patients (86.96%). In 9/69 patients (13.04%), excision was undertaken with reconstruction 4 days later, after receipt of the histopathology report. Histological assessment confirmed complete initial excision in 59/69 patients (85.5%) rising to 68 (98.6%) after two excisions. Mean follow-up was 13 years, with no recurrence in the living cohort. Three deceased patients had a recurrence, one of whose tumour was reported histologically as incompletely excised but declined further surgery, giving an overall recurrence rate of 3/185 (1.62%). For patients who completed treatment, the recurrence rate was 2 in 184 (1.09%). Six of the sixty-nine patients (8.7%) developed new tumours on the contralateral eyelid or the forehead.

Conclusions Primary, clinically well-demarcated periocular BCCs can be safely treated using small (up to 2 mm) excision margins in a one-stop setting with immediate reconstruction for those defects which can be closed directly without recourse to flaps or grafts.

Synopsis A retrospective study of 185 patients who had small margin (≤ 2 mm) excision of clinically well-demarcated primary periocular BCCs demonstrated a recurrence rate of 3/185 (1.62%) at a minimum of 11 years' follow-up.

Introduction

Basal cell carcinoma (BCC) is the most common malignant tumour of the eyelid in Caucasian populations, accounting for over 90% of cases [1, 2], and the incidence is expected to continue to increase [3]. BCCs are usually slow-growing tumours that do not metastasise but can lead to significant morbidity, including the need for exenteration in the case of orbital involvement (1.6% of cases in a large study [4]).

Treatment of periocular BCCs is typically with surgical excision, although other options include pharmacological therapy (including vismodegib and imiquimod) and radiotherapy [5]. Mohs' micrographic surgery (MMS) is often utilised and has a high cure rate, especially for primary BCC [6–8]. However, MMS requires significant human resources, both in terms of time and expertise, and in particular potentially involves two different physicians [9]. Intra-operative evaluation of frozen sections may offer a comparable cure rate to MMS [4, 10, 11], but involves significant intra-operative waiting time and therefore expense [9]. Direct excision with subsequent permanent section histological confirmation of margins also has a low recurrence rate, especially for nodular BCCs [4, 12–14], and may be the most cost-effective option in some cases [9]. In clinical practice MMS is

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invaluable for recurrent, medial canthal, and morpheaform BCCs [9]; however, a Cochrane Database systematic review in 2014 was unable to conclude as to the relative superiority of MMS or non-Mohs surgical excision of BCCs in terms of recurrence rate, complication rate, or cost-effectiveness [15].

Non-MMS excision of BCCs is commonly performed with 3–4 mm margins [12, 13]. This represents a significant tissue loss, particularly if the lid margin is involved, and in many patients leads to the removal of a significant volume of normal tissue [16]. Excision with 2 mm margins for primary well-demarcated nodular BCCs offers a low recurrence rate [13, 14], while preserving normal tissue. This can allow MMS to be reserved for more aggressive BCC subtypes and recurrent lesions.

In this study we report the long-term outcome (primarily the tumour recurrence rate) for patients following small margin (up to 2 mm) excision of primary, clinically well-demarcated, periocular BCCs in a non-Mohs setting in a one-stop clinic at a minimum of 11 years of follow-up. To the best of our knowledge, this represents the longest follow-up period reported in the literature.

Materials and methods

In our institution (Princess Alexandra Eye Pavilion, Edinburgh), a one-stop periocular lesion assessment and treatment clinic has been in operation since 1999. The details of all patients undergoing biopsy of lid lesions are recorded in a diary, along with the clinical diagnosis, site of the lesion, operating surgeon, initial follow-up plan, whether the lesion is primary or recurrent, if recurrent whether the primary surgery was performed in our unit or elsewhere, and, when reported, the histopathology result. All patients who underwent excision of a clinically well-demarcated, histologically confirmed primary BCC at least 11 years previously were included in the study.

A retrospective review of case notes and electronic patient records was conducted. All patients still alive at the time of the study were contacted via telephone or letter and invited for face-to-face review for research purposes. 35 of 69 patients (50.72%) attended for clinical examination, and were reviewed for any sign of tumour recurrence. The remaining 34 (49.28%) had photographs of their periocular region taken by either their opticians or their family, with the digital images forwarded to the authors for review. They were also asked about any history of subsequent surgery at the site of their previous excision.

All patients were treated under the care of the same consultant (MW), who performed all pre-operative marking. Excision was carried out by either MW or by his registrars under direct supervision.

Procedure of excision

For over 95% of patients, the margins of the tumour could be defined pre-operatively, often using the slit lamp [17]. Those patients in whom the clinical margins were unclear were referred for Mohs surgery. The skin was marked 2 mm beyond the margins of the tumour. Not infrequently, smaller excision margins were accepted if this allowed a canaliculus to be preserved or avoided a full thickness defect by employing a grey line split, as long as this allowed even a small clinically tumour-free margin.

Tumours were excised under local anaesthetic. If direct closure of the resulting defect was possible it was undertaken immediately after excision. If a more complex reconstruction was required (flap or graft) then the defect was dressed and the reconstruction scheduled for 4 days later following receipt of the histopathology result. If the histopathology indicated an incomplete excision then further resection was undertaken at 4 days, and after discussion with the patient the reconstruction was performed immediately following the second resection (Fig. 1).

Results

185 eligible patients were identified via case-note review, of whom 69 patients were still alive at the time of the study (37.3%). No patients had a cause of death related to BCC. The mean age of living patients at the time of follow-up was 74.9 years (minimum 46 years, maximum 99 years, median 77 years). Thirty-five patients were female (50.7%) and thirty-four were male (49.3%). Of the living patients, 60/69 (86.96%) had undergone one-stage excision and direct closure, and 9/69 (13.04%) had excision with delayed reconstruction as above. Histopathology confirmed complete initial excision in 59/69 patients (85.5%), increasing to 68 (98.6%) after two excisions. One patient who underwent one-stage excision and direct closure had a BCC that was reported histologically to be incompletely excised, but the patient opted for observation rather than further excision and remained tumour free. Mean follow-up was 13 years.

Of the 69 patients living at the time of the study, 8 had morphoeic BCCs, 1 had a multifocal BCC, 1 had a nodular cystic BCC, 2 had nodular BCCs, and 57 had no histological subtype data available. It is likely that the majority of patients in whom BCC subtype was not recorded had nodular BCCs. Lesion size data were available for 9 patients: 12 mm diameter × 1; 10 mm diameter × 1; 10 × 4 mm × 1; 7 × 5 mm × 1; 6 mm diameter × 3; 5 mm diameter × 2. Lesion locations are shown in Table 1.

No patient alive at the time of the study had a recurrence of their BCC. A review of the case notes and electronic records

Fig. 1 One-stop clinic typical patient pathway.

Table 1 Location of periocular BCCs.

Lesion location	Number of patients	Percentage
Lower lid	32	46.38
Medial canthus	22	31.88
Lower lid pericanalicular	6	8.70
Upper lid	5	7.25
Lateral canthus	4	5.80

of deceased patients identified three patients with BCC recurrence (1.62% of study population). One patient had a medial canthal BCC that was reported histologically as incompletely excised but declined further surgery, and had a recurrence at 17 months. Two patients had lower lid BCCs which were reported histologically as completely excised following initial excision, but recurred at 14 and 18 months. Six of the patients alive at the time of the study (8.7%) had developed new tumours on the contralateral eyelid or on the forehead.

Discussion

Our study demonstrates that a low recurrence rate (1.6%) can be achieved for primary well-demarcated BCCs with up to 2 mm clinical margin-controlled excision, with immediate direct closure in 86.96% of patients or delayed reconstruction ± further excision for larger tumours as described above. The histological clearance and recurrence rates in

this study are comparable with previous studies in the literature (Table 2).

In our study there were no cases of patients requiring a third excision to achieve histological clearance. By performing reconstruction at either the first or second visit we obviated the need for a third visit to the operating room for delayed reconstruction, and in most cases (86.96% of living patients) were able to provide the diagnosis, excision, and reconstruction at a single visit. This reduces the clinician, patient and operating room time required, and therefore cost in the short term. Using small margin excision as described in this study reduces the burden on the Mohs service, and allows for tissue-sparing excision in geographic areas where Mohs surgery is difficult to access. The similarity of recurrence rates in our study to others in the literature suggests that long-term morbidity and cost is unlikely to be increased by adopting this technique for primary well-demarcated lesions. The use of this excision technique would allow Mohs surgery or frozen section control to be reserved for tumours with poorly defined margins and/or recurrent lesions.

Of our three recurrences, two were reported histologically as completely excised (supporting the practice of following up patients even if histological clearance has been confirmed), and both had undergone excision and direct closure on the same day. Had we waited for histological confirmation before reconstruction these two patients would not have had more tissue removed (due to the histology report) but would have had a second theatre visit for reconstruction. The third patient in the group declined

Table 2 Comparison of histological clearance and recurrence rates in 12 studies.

Study	Technique	Cases	Mean follow-up (years)	Initial histological clearance (%)	Recurrence rate (%)
Current study (primary well-demarcated)	Up to 2 mm clinical margin $\pm$ 2 stage	185	13 (min 11)	85.5	1.62 (1.09)
Hsuan et al. [14] (primary nodular)	2 mm clinical margin, 2 stage	55	5.8 (min 5)	81.8	0
Hamada et al. [13] (all subtypes)	2–4 mm clinical margin $\pm$ 2+ stage	69	Min 5	84	4.35
Conway et al. [19] (primary, all subtypes)	4–8 mm clinical margin	31	6.4 (min 5)	90.3	9.7
	Frozen section control (3–4 mm)	114	6.9 (min 5)	–	0
Ho et al. [12] (all subtypes)	3 mm clinical margin, 2+ stage	385 primary	5	91.3	0.26
Wong et al. [4] (primary, all subtypes)	3 mm clinical margin	113	2.6	92.9	1.8
	Frozen section control (2–4 mm)	20	5	–	5
		423	2.6	–	0.71
		97	5	–	2.1
Pieh et al. [20] (primary, all subtypes)	Frozen section control	298	5.7	–	5.36
Giordano Resti et al. [10]	Frozen section control (2 mm)	89 primary	6 (min 2.5)	–	1.1
		21 recurrent		–	4.8
Gill et al. [11] (all subtypes)	Frozen section control	40 primary	6.4 (min 5)	–	0
		3 recurrent		–	0
Malhotra et al. [6] (all subtypes)	Mohs micrographic surgery	256 primary	5	–	0
		90 recurrent	5	–	7.8
Litwin et al. [7] (all subtypes)	Mohs micrographic surgery	63 primary	2.3 (min 1 month)	–	1.6
		25 recurrent		–	20
		13 unknown		–	0
Sin et al. [8] (all subtypes)	Mohs micrographic surgery	312 primary	2.5 (min 1 month)	–	0.3
		77 recurrent		–	6.5

further surgery in spite of a histology report showing that the tumour was incompletely excised. It was therefore likely that they would have a recurrence.

To our knowledge, this study represents the longest follow-up after periocular BCC excision in the literature. Notably, there were no late recurrences beyond 5 years, which is in keeping with the common practice of discharging patients after 5 years in the absence of recurrence. At a minimum of 11 years of follow-up, only 37.3% of patients were still alive. This high mortality rate is very relevant, as the goal for doctors treating patients with periocular BCC remains to provide not only very low long-term recurrence rates, but also low levels of morbidity, which small margin excisions promote.

Our study used direct clinical examination, where possible, to examine for late recurrence. This is likely to be more sensitive than patient-reported questionnaires as small recurrent lesions may be picked up by careful examination at the slit lamp.

Six of sixty-nine patients alive at the time of the study had a new BCC on the contralateral eyelids or the forehead. This underlines the importance of ensuring that patients know the signs of new BCCs and to seek review should they develop them.

Our study has several limitations. Firstly, as a retrospective study it was not possible to obtain all the data that we would like. We do not have complete data on the size of tumours excised, which is an important prognostic factor [18]. We also do not have a complete breakdown of histological subtypes. Secondly, although all patients were treated under the care of the same consultant, not all tumours were excised by the same surgeon. While this may more accurately reflect clinical practice, it does provide a potential source of inconsistency. Thirdly, it is possible that some patients who were deceased at the time of the study had undiagnosed recurrences of their BCCs. However, if these patients had clinically significant recurrences it is likely that they would have been re-referred.

As the Edinburgh one-stop periocular tumour clinic is part of the sole specialist oculoplastic service for the region, and maintains close links with the local dermatologists, it is highly likely that any recurrences would have been referred to us rather than to any other institution. Finally, it was not possible to examine all patients in person at a minimum of 11 years (35 of 69 (50.72%) patients examined in person), with reliance on digital photographs and patient- and family-reported history of recurrence in the remaining cases as described above.

Our study demonstrates that at a minimum of 11 years' follow-up, the rate of recurrence following up to 2 mm margin-controlled excision of primary well-demarcated BCCs remains low. There is a high incidence of mortality unrelated to BCCs following excision. Small margin excision can be considered in patients who present with BCCs with well-defined margins without recourse to Mohs surgery.

Summary

What was known before

- Basal cell carcinoma is the most common malignant tumour of the eyelid in Caucasian populations.
- Mohs micrographic surgery requires significant human resources.
- Non-Mohs excision of basal cell carcinomas is commonly performed with 3–4 mm margins, representing a significant tissue loss.

What this study adds

- A low recurrence rate can be achieved for primary well-demarcated basal cell carcinomas with up to 2 mm margin-controlled excision.
- A paradigm is presented that allowed 87% of patients to receive their diagnosis, excision, and reconstruction at a single visit.
- To our knowledge, this is the longest reported follow-up after periocular basal cell carcinoma excision in the literature (minimum 11 years), with data on long-term recurrence, mortality rate, and incidence of new basal cell carcinomas at other sites.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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