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CLINICAL STUDY

5 Years review of periocular basal cell carcinoma and proposed follow-up protocol

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Abstract

Aim **(1) To investigate the recurrence of periocular basal cell carcinoma (BCC) reported as completely excised on histology. (2) To identify risks associated with recurrence. (3) To recommend a rational follow-up protocol.**

Methods **This is a cohort study by case note review of consecutive patients undergoing excision of periocular BCC between 2000 and 2006 at University Hospitals of Leicester. All lesions were excised with 3 mm clinical margin and the defect reconstructed only after the excision margin was declared clear.**

Results **A total of 413 episodes of surgical excision were recorded for 270 patients over the 7-year period of 2000–2006. All of them have 5 years follow-up. Mean age 73.7 (± 12.5). In all, 67% were nodular BCC and 45.4% located in the lower eyelid. The main outcome measure was the recurrence rate. None of the patients with primary nodular BCC suffered recurrence. The recurrence rate for primary morphoeaform BCC following complete excision is 3.8%. In total, 8.1% of patients had several lesions simultaneously whereas 7.8% patients had BCC in multiple locations subsequently (metachronous). Three patients who had previously recurrent BCC (rBCC) treated elsewhere or not using this method had orbital/lacrimal drainage system involvement requiring exenteration.**

Conclusion **We recommend that patients with a single, completely excised primary solid or nodular BCC can be discharged after one 6-monthly review, although they should be instructed to monitor for the development of further lesions. The incidence of recurrence for primary morphoeaform BCC is 3.8% and for rBCC is 3.6% over 5 years and these patients should stay under review for this period.**

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Introduction

Basal cell carcinoma (BCC) is the most common periocular skin cancer affecting mainly Caucasians. In the UK, 53 000 new cases of BCC are estimated every year and figures are continuing to rise on a yearly basis. More worrying, the largest increase in incidence is seen in the 30–39 year age groups.[1]

Traditionally, 5 years of clinical follow-up for periocular (high-risk site) BCC is recommended to ensure early detection of recurrence[2] or new primary lesions.[3] Primary BCCs (pBCCs) recur <10% of the time, with two-thirds recurring in the first 3 years.[4,5] However, the studies are relatively dated, use a wide variety of techniques with different methods of excision margin control,[5,6] and none describe the histological processing of the specimens.

In the light of increasing incidence of BCC and limited resources in the UK health-care system, it is not always possible to follow every patient for 5 years post excision. A national survey with self-completion questionnaire showed variability in follow-up. In all, 27% of respondents reported that they would not review further after excision of a 'well-defined' BCC from inside a central 'T' area on the face; 37% reported that they would review on one occasion; and 36% reported that they review more than once.[7]

Follow-up of excised BCC constitutes a large workload in oculoplastic follow-up clinics. Although we acknowledge that there is always a risk of recurrence with all types BCC, it is in

our experience that the majority do not recur and therefore do not require follow-up over a long period of time. To examine this hypothesis, we conducted a study to look at 5 years' complete follow-up of periocular BCC in Leicester.

We aimed to investigate the recurrence of histologically proven completely excised BCC and to identify risks associated with recurrence in order to recommend a follow-up protocol.

Materials and methods

A detailed retrospective analysis was undertaken of the medical records of all patients who underwent excision of periocular BCC between 2000 and 2006 in Leicester Royal Infirmary. Incision biopsies were excluded. All of them have complete 5 years follow-up. Data collected included demographics, location and nature of lesion, histology, evidence of recurrence, time since last excision, and duration of follow-up.

At our centre, a two-stage procedure is used. The first stage is excision with a 3 mm margin from the perceived edge of lesion subjected to rapid turnaround paraffin section. The second stage involves reconstruction a few days later when the histology results are available. If the margins are clear, then reconstruction is performed. If involved, then further excision is undertaken with either a frozen section or paraffin examination until a clear margin is obtained, followed then by reconstruction.

Two patients who declined further excision are excluded from the study.

Histological technique

Routinely a rapid paraffin technique is used in which the sample is processed with a turnover of 24–48 h. The specimen is received in formalin within 1–2 h of surgery and is therefore not necessarily fixed. The whole of the excised tissue is blocked out in a bread slice manner with the end slices being levelled $\times 3$ towards the resection margins. The blocks are then processed overnight (Leica ASP 300 processor, Nussloch, Germany) in the conventional manner and are ready for examination the following morning. This differs from the traditional method in that modern processors will take unfixed material so there is no need to wait for tissue to be fixed before cutting the blocks. Standard H&E slides are prepared and examined by conventional microscopy. If the end blocks are involved by tumour, they are reversed 180 degrees so that the resection margin can be seen *en face.*

In regards with frozen section, we adopt the *en face* or bread-loafing technique depending on the width of the re-excision of the involved margin: if narrow the whole tissue is sectioned *enface*, if wider than about 3 mm then the whole sample is cut in bread loaf manner. The frozen section findings are confirmed with subsequent routine paraffin preparation of the specimen. Since 2009 we have provision for Mohs', which is sparingly used given the long waiting list for it and restrict its use to post radiotherapy or recurrent morpheaform type.

Results

During the 7-year period 2000 to 2006 at the University Hospitals of Leicester (tertiary referral centre), there were 413 BCC excised from 270 patients; 140 female and 130 male. Mean age 73.7 ± 12.5 (range 28–99) and the median age 77. Histologically, the majority were nodular BCC (277 or 67.1%), 20 (4.8%) were multifocal/superficial, 39 (9.4%) of the infiltrative/morpheaform type, and 2 (0.5%) described as micronodular. Focal squamous differentiation was seen in 1 patient (0.2%) and 74 (17.9%) were of mixed pattern histology. As expected, the majority (45.4%) were located on the lower eyelid, 18.6% on the medial canthus, 11.4% on the upper eyelid, 5.8% on the temple, 4% on the cheek, and 2.4% on the brow. All patients had 5 years follow-up. A total of 385 are primary cases whereas 28 were recurrent cases referred from elsewhere or before such techniques was adopted in our unit.

None of the patients included in the study had Gorlin syndrome nor were they immunosuppressed.

In order to achieve complete clearance of the BCC, some patients required several attempts at excision. In 36 out of 413 lesions (8.7%), more than one procedure was required before complete excision was confirmed histologically. Table 1 shows the percentage of each histological subtype requiring more than one excision to achieve clearance.

As we do not calculate recurrent tumours sent from other units where primary excision methods are different, there is only one case of recurrence in our group leading to incidence of 0.26% (1/385). Table 2 showed characteristics of recurrent BCC (rBCC). None of the patients with primary nodular BCC suffered recurrence, but the recurrence rate for primary morpheaform/infiltrative BCC is 1/26 (3.8%).

Eighteen patients had two lesions, three patients had three lesions, and one patient had four lesions and above; an incidence for multiple lesions in a simultaneous setting of 22/270 (8.1%). Simultaneous BCC can be of different histological types. BCC also occurred in multiple locations subsequently (metachronous lesions) in 21/270 (7.8%) of patients.

Three patients had extensive lesions involving orbit that required exenteration. All of these were recurrent lesions referred from other units and were of the aggressive morpheaform or infiltrative subtype. All three patients are still alive at the time of writing this paper.

Table 1 Percentage of patients with each histological subtype requiring more than one excision to achieve clearance

Histological type of BCC	*Percentage requiring extra excision*
Nodular	5.8 (16/277)
Mixed	10.8 (8/74)
Infiltrative/morpheaform	20.5 (8/39)
Multifocal	15 (3/20)
Micronodular	50 (1/2)

One patient had 10 lesions from the age of 52 onwards attributed to excessive sunbed use.

Discussion

We present here the largest series of BCC excised with non-Mohs' rapid paraffin technique. Our series is unique in that clinical follow-up is used as opposed to questionnaire, which may be subject to bias.[8] The reported recurrence rate in current literature is 1–3% in pBCC and 5–7% for rBCC.[8–10] Our incidence of 0.26% with pBCC improves on this. Table 3 showed recurrence rates of previous studies that have 5 years follow-up results.

Although recently Mohs' micrographic surgery has been hailed as the best method of removing BCC with minimal recurrence,[8,11–13] it may be too costly[14] and time consuming to be used for all periocular BCC.[15] In addition, it may not be available in every hospital. It is reassuring that our technique of excising BCC and examining with rapid turnover paraffin techniques, occasionally combined with fresh-frozen section control, achieves results comparable to another recent study.[16]

Close communication between the surgeon and the pathologist enables accurate orientation of the specimen in relation to a map of the lesion[12,17] facilitating clearance. In general, we require a clear histological margin of >0.1 mm for nodular BCC and >1 mm for morpheaform/infiltrative subtypes. Cases with a narrow histological clearance margin are discussed at the skin cancer multi-disciplinary meeting.

In all, 8.7% (36/413) of the tumours required more than one excision to achieve complete excision, which is not surprisingly lower than with the 2 mm margin used by Hamada *et al*[16] (22.7%). Periocular tumours frequently extend well beyond the obvious clinical margin,[18–20] and the subtle extension of infiltrative and morpheaform BCC is probably one of the main reasons for their recurrence.[21] An average of 7.2 mm of subclinical tumour extension was found in 51 morpheaform BCC in one study as compared with 2.1 mm of extension in 138 well-circumscribed periocular lesion.[22] In our study, 20.5% of the morpheaform BCC required more than one surgical excision to achieve complete clearance.

Guardiano *et al*[23] attempted to use dermoscopy to improve yield and did not find the evidences supportive.

Table 2 Characteristics of recurrent basal cell carcinoma

Patient	*Type of BCC*	*Location*	*Number of excisions at same site previously*
A	Infiltrating, morpheaform	Upper eyelid	4
B	Morpheaform	Medial canthus	0

Fluorescein confocal mosaicing microscopy[24] and multispectral polarized light imaging[25] show promising results but are still largely experimental.

We choose a two-stage approach to ensure all lesions are completely excised, obviating the uncertainty of possible incomplete excision when customary 3 mm or 4 mm margins are used and simultaneous closure of wound is undertaken.[26] We opt for ensuring complete excision for all our BCC as reports show recurrence rates varying between 30 and 50% for incompletely excised BCC depending on the length of follow-up.[27] Recurrence can be difficult to diagnose in the periocular area as the recurrent tumour may arise in the deeper margins and can spread subdermally or into the orbit. The treatment of a recurrent tumour can induce greater morbidity and cost than immediate re-excision of incompletely excised tumours.[28] Therefore, most guidelines on the management of BCC recommend re-excision of incompletely excised tumours whereas acknowledging that this is not always achieved in practice.[27,29,30] Most of our patients are happy to attend the surgery twice knowing that their tumour will be completely excised. The effort to ensure complete initial excision is 'rewarded' in the low recurrence rates in this study. In addition, the two-stage procedure facilitates planning of the appropriate theatre time for the reconstruction.

For those lesions in which complete clearance is not achieved with the first excision, fresh-frozen section may be used for margin control if it is just one margin and not of morpheaform, as it has been used widely with proven efficacy.[20,31] It is rapid (<2 h) and allows the defect to be reconstructed in the same theatre session once the margin is confirmed clear. With frozen section, the pathologist dissects a 0.5 to 1.0 mm margin of tissue for cryosectioning.[12] All fresh-frozen section are further analysed in formalin subsequently as the literature suggests frozen section may be more prone to inaccurate interpretation than formal paraffin section. Difference between the findings on fresh-frozen section and formal histology section was noted in two of our patients. One was because the section, which contained BCC had been trimmed through leading to a negative paraffin results. In another case, the lesion was multifocal and the fresh-frozen section was negative whereas the paraffin section was positive. A further excision was undertaken in this case.

Table 3 Recurrence rate of previous studies

Year of study and author	*Study sample (patients, lesions)*	*Excision method*	*5 Years follow-up recurrence rate (primary BCC)*	*5 Years recurrence rate (recurrent BCC)*
Mohs[11]	1414 Lesions (1124 primary, 290 recurrent)	Mohs (fixed tissue and fresh tissue techniques)	0.6%	7.6%
1992–2001 Wong *et al*[12]	97 Lesions (primary lesions)	En face frozen section control	2.1% (2/97)	4.4% (2/21 lesions)
Glatt *et al*[46]	81 Cases	Frozen section (FS)	2.5% (5 year)[a]	
1993–1996 Malhotra *et al*[8]	346 Patients	Mohs' surgery	0% (cases are not consecutive, 5 years follow-up based on questionnaire, there are significant proportion of loss to follow-up, which involved older and infiltrative lesions)	7.8% (7/90)
1994–1997 Hamada *et al*[16]	55 Patients	2 mm excision, further 2 mm re-excision if necessary	0% (primary nodular)	
2000–2006 Our results	428 Lesions, 270 patients	3 mm excision and check for histology clearance, further excision with paraffin/FFS control	0.26% (overall), 0% (primary nodular), 3.8% (primary morpheaform)	3.8%

[a] 5 years recurrence rate without differentiating primary BCC and recurrent BCC.

Three cases (3/413 or 7.3%) had extensive recurrent disease involving orbit at presentation to our unit and required exenteration. All were aggressive infiltrative, morpheaform disease. Two patients presented with ocular dysmotility and one with a mass fixed to bone. None of these patients have died of disease or show intracranial spread. Our series is consistent with the reported literature incidence of 0.8 to 3.6%.[32–37]

In this study, recurrence for pBCC is very uncommon once the excision is histologically complete.[16,38] Our single case of recurrence of pBCC in 6 years of study was in a case of morpheaform BCC in the medial canthus, which required more than one excision. We therefore propose that those with pBCC with non-aggressive (nodular) histology could be discharged after one 6-monthly follow-up, once complete excision is confirmed, but advised to monitor for new lesions elsewhere. However, patients with infiltrative, morpheaform, micronodular, mixed, or rBCC should be followed-up for at least 5 years. Recurrent BCC confirmed by biopsy often has a mixture of scar tissue and basaloid cells, making pathologic identification of margins difficult.[32] In addition, recurrent eyelid BCC often exhibit more aggressive biological behaviour associated with a less favourable prognosis and a worse outcome.[39,40]

Although we agree as with others that follow-up is of value for some patients, it is not possible in the modern NHS with limited capacity and resources. Equally, a large proportion of patients do not wish to be followed-up[41] and in some clinics there is a high rate of non-attendance.[42] Prolonged follow-up of all patients with periocular BCC[12,43,44] is both costly and inconvenient. Our views concur with the current evidence-based recommendations from the BAD (British Association of Dermatologists) guidelines advising that long-term hospital-based follow-up after treatment of BCC for patients other than those with Gorlin's syndrome is neither necessary nor recommended.[45]

The retrospective nature means that tumour size, which was not constantly documented has not been assessed as a risk factor for recurrence.

In conclusion, we found no episodes of recurrence after proven complete excision of primary nodular BCC during 5 years follow-up period. rBCCs and high-risk primary infiltrative/morpheaform lesions need to be followed-up for at least 5 years as they are more likely to recur and progress extensively. We therefore recommend that patients with primary nodular BCC be discharged after one 6-monthly follow-up once complete excision is confirmed and wound healing satisfactory. However, all patients should be advised to monitor for new lesions elsewhere and seek medical attention if any suspicious lumps are identified.

Summary

What was known before

- All periocular BCC was routinely followed-up for 5 years to detect recurrence or identify new lesions.

What this study adds

- There is low risk of recurrence after complete excision of primary nodular BCC and hence patient can be discharged for self-monitoring after one satisfactory 6-monthly post-operative review. rBCCs and high-risk primary infiltrative/morpheaform lesions need to be followed-up for at least 5 years as they are more likely to recur and progress extensively.

Conflict of interest

The authors declare no conflict of interest.

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