Basal Cell Carcinoma: Analysis of Factors Associated With Incomplete Excision at a Referral Hospital in Southern Spain

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Practice Points

- Basal cell carcinomas with adjacent severe elastosis as well as those with infiltration of the deeper dermal layers are associated with a greater risk for incomplete excision.
- Basal cell carcinomas associated with moderate to severe elastosis are difficult to delimit and therefore a careful demarking of the borders should be performed to avoid incomplete excision.

Basal cell carcinoma (BCC) is the most prevalent malignancy, with excision as the best therapeutic approach. Incomplete excision of nonmelanoma skin cancer is a clinical indicator of the surgical technique performed. This retrospective study of 300 patients with BCC assessed the rate of incomplete excision in a tertiary referral hospital in southern Spain and its relationship with tumor location as well as histologic and surgical features.

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Basal cell carcinoma (BCC) is the most prevalent malignancy, with 200 to 600 cases per 100,000 individuals in the white population and 3.5 cases per 100,000 individuals in the black population worldwide.[1] Excessive exposure to UV radiation as well as heavy and sporadic UV exposure in adulthood have been found to be major etiologic factors, as they lead to DNA alterations that increase the risk for BCC.[2] Despite the success of multiple treatment modalities (eg, imiquimod cream 5%, cryotherapy, laser excision), surgical resection remains the gold standard, with reported cure rates ranging from 95% to 99%.[3,4] Surgical resection is more cost efficient and allows for histologic examination.[2-4]

Incomplete excision of nonmelanoma skin cancers including BCC is a clinical indicator of the surgical technique performed. This study assessed the rate of incomplete excision in a tertiary referral hospital in the southern Mediterranean region of Spain and its relationship with tumor location as well as histologic and surgical features.

Materials and Methods

A retrospective study of patients presenting between January 1, 2010, and December 31, 2010, was conducted. Using the hospital's electronic pathology records, medical records of specimens containing the terms *skin* in the specimen field and *basal cell carcinoma* in the diagnosis field were identified. Patients with concomitant or a history of cutaneous squamous cell carcinoma were excluded. Reexcision of incompletely excised lesions; punch, shave, or incisional

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biopsies; and palliative excisions also were excluded. A trained pathologist from the hospital reviewed the specimens. The lesions were classified as incompletely excised when the specimen showed positive margins at the sides and/or the bottom. Furthermore, all specimens were evaluated to obtain information regarding the lesion depth, presence of necrosis, and surgical margins. The specimens were classified according to the BCC differentiation pattern: superficial, nodular, micronodular, morpheic. Basal cell carcinomas with mixed features were classified according to the most predominant subtype. Elastosis also was graded (grade 0=absent; grade 1=papillary dermis; grade 2=middle reticular dermis; grade 3=deep reticular dermis). From the surgical records, additional information was obtained regarding the site and size of the lesion, method of wound closure, and type of anesthetic used, which indirectly signifies the complexity of the lesions. Lesions that require local anesthetic generally are easier to excise compared to lesions that require general anesthetic, as the latter lesions typically are larger or are located in complex anatomic areas. Therefore, the type of anesthetic may be a potential factor for positive surgical margins.

Statistical Analysis—For statistical analysis, a multivariate logistic regression analysis was performed with the categorical variable *incomplete excision* (yes or no) as the outcome variable using SPSS version 15 software. All the variables initially considered in the study were included in the final statistical model; no variables were excluded. $P<.05$ was considered significant and all tests were 2-tailed.

Results

A total of 323 specimens from 300 patients were included in the study. One BCC was present in 282 patients, 2 BCCs in 13 patients, and 3 BCCs in 5 patients. The incidence of incomplete excision was 14.6%. Table 1 summarizes the results from the multivariate statistical analysis.

Patient Demographics—The mean (standard deviation [SD]) age was 72.98 (10.72) years (range, 37−89 years). Of 300 patients, 165 (55%) were women and 135 (45%) were men. There were no statistically significant differences in the rate of incomplete excision with regard to sex ($P>.05$).

Lesion Site—The majority of the evaluated lesions were located on the head (70.0%), with the nose as the most frequent site. We found a statistically significant difference in the rate of incomplete excision in the head versus other locations such as the trunk, neck, and limbs ($P=.008$; 95% confidence interval, 0.005−0.445). Although no statistical differences were obtained, it was noted that the sites with the greatest risk for incomplete excision were the inner canthus (23.1%), auricular region (18.2%), and periocular region (17.2%). The rate of incomplete excision in the facial area is summarized in Table 2.

Lesion Size—Of the specimens evaluated, 212 lesions measured less than 10 mm in diameter, 89 measured 10 to 20 mm, and 22 were larger than 20 mm. Lesions larger than 20 mm or between 10 to 20 mm had a significantly higher rate of incomplete excision ($P=.014$ and $P=.001$, respectively) than lesions measuring less than 10 cm.

Tumor Depth—There were 247 lesions with a depth of 0 to 3.0 mm, 63 lesions with a depth of 3.1 to 6.0 mm, and 13 lesions with a depth of more than 6.0 mm. The mean (SD) tumor depth was 2.64 (1.34) mm. Tumors deeper than 6.0 mm showed a significantly higher rate of incomplete excision compared to those that measured 3.0 mm or less ($P=.025$). Statistical significance was not observed for tumor depths ranging from 3.1 to 6.0 mm ($P=.311$).

BCC Subtype—The most prevalent subtype was nodular BCC (n=248), followed by morpheic BCC (n=33), superficial BCC (n=28), and micronodular BCC (n=14). The rate of incomplete excision was 13.7% for nodular BCC, 15.1% for morpheic BCC, 17.9% for superficial BCC, and 14.3% for micronodular BCC. There were statistically significant differences in the rate of incomplete excision for morpheic and superficial BCC compared to nodular BCC ($P=.001$ and $P=.01$, respectively); this outcome was not observed for micronodular BCC ($P=.57$).

Necrosis—Necrosis was observed in 148 of the specimens evaluated. This feature did not affect the rate of incomplete excision ($P=.96$).

Elastosis—According to the scale used to rate tumor elastosis, 78 lesions were classified as grade 0, showing no elastosis, while 109, 80, and 56 lesions were classified as grades 1, 2, and 3, respectively. Statistically significant differences were found for incomplete excision and the grade of elastosis. Specimens with grades 2 and 3 were more likely to be incompletely excised compared to specimens without elastosis (grade 0)($P=.001$ and $P=.0001$, respectively); however, lesions classified as grade 1 (papillary dermis) showed no differences in margins affected by tumoral cells compared to lesions classified as grade 0 ($P=.45$).

Surgical Margins—Surgical margins ranged from 1 to 10 mm (mean [SD] margin, 2.04 [1.31] mm). Margins greater than 10 mm were not found. In BCCs located on the head, the mean (SD) margin was 1.98 (1.37) mm and in the other locations it was 2.43 (1.65) mm.

Table 1.

Multivariate Statistical Analysis[a]

Covariable	Odds Ratio	*P* Value (95% CI)
Lesion site		
Head vs other locations (eg, trunk, neck, limbs)	1.8	.008 (0.005-0.445)
Lesion size		
<10 mm		
10−20 mm	1.2	.001 (1.01-1.32)
>20 mm	2.4	.014 (1.62-3.31)
Tumor depth		
<3.0 mm		
3.1−6.0 mm	1.3	.311 (0.57-2.21)
>6.0 mm	1.9	.025 (1.61-2.34)
BCC subtype		
Nodular		
Morpheic	2.1	.001 (1.55-2.58)
Superficial	2.2	.01 (1.33-2.83)
Micronodular	1.2	.57 (0.16-1.9)
Necrosis		
Presence vs absence	1.02	.96 (0.56-2.3)
Elastosis[b]		
Grade 0		
Grade 1	1.89	.45 (0.35-3.82)
Grade 2	1.36	.001 (1.13-1.78)
Grade 3	2.21	.0001 (1.74-2.78)
Method of surgical closure		
Direct		
Flap	0.84	.23 (0.34-1.28)
Skin graft	0.92	.38 (0.76-1.19)
Anesthesia		
Local vs general anesthetic	1.08	.42 (0.22-1.89)

Abbreviations: CI, confidence interval; BCC, basal cell carcinoma.

[a]For each covariable, the category reference is listed first (except for lesion site and anesthesia).

[b]Grade 0=absent; grade 1=papillary dermis; grade 2=middle reticular dermis; grade 3=deep reticular dermis).

Table 2.

Rate of Incomplete Excision on the Face

Facial Area	Complete Excision, n	Incomplete Excision, n (%)[a]
Inner canthus	10	3 (23.1)
Auricular region	27	6 (18.2)
Periocular region	24	5 (17.2)
Cheek	20	4 (16.7)
Scalp	20	4 (16.7)
Nose	44	7 (13.7)
Outer canthus	15	2 (11.8)
Forehead	14	1 (6.7)
Temple	14	1 (6.7)
Chin	5	0 (0)
Total	193	33 (14.6)

[a]Rate of incomplete excision.

Tumor Invasion and Infiltration—The lateral margin was infiltrated by tumoral cells in 20 specimens and the deep margin was infiltrated in 22 lesions. No nerve invasion was observed. The ratio of deep to lateral margin involvement was 1 to 1.

Method of Surgical Closure—Direct closure was the most frequent repair method, which was used to close 285 excisions. Flap repair was used to close 26 excisions and skin graft was used in 12 excisions. No statistical correlation was observed between the rate of incomplete excision and the method of repair ($P>.05$).

Anesthesia—Local anesthetic was used in 292 patients and general anesthetic was required in 8 patients. There were no differences in the rate of incomplete excision between local and general anesthetic ($P>.05$).

Comment

This study aimed to establish the rate of incomplete excision of BCC lesions in a tertiary referral hospital in southern Spain and to identify factors associated with this outcome. In prior retrospective studies, the reported incidence of incomplete excision of BCC ranged from 6.3% to 25%.[5-15] In our study, the overall rate of incomplete excision was 14.6%, which is compatible with the reported literature (Table 3).

San Cecilio University Hospital is a tertiary referral hospital with a catchment area that includes the surrounding metropolis of Granada, a province on the southern Mediterranean coast of Spain. According to the Granada Cancer Registry, BCC is quite prevalent, with an annual incidence of 240 cases per 100,000 men and 110 cases per 100,000 women.[31] The patients at our tertiary referral hospital typically present with complex tumors that are beyond the therapeutic capacity of the primary physician. The 14.6% rate of incomplete excision reported in this study is in part a reflection of the complexity of lesions treated in our hospital, as complex lesions are associated with greater incidences of incomplete excision.

Basal cell carcinomas located on sites other than the head demonstrated a lower risk for incomplete excision compared to BCCs on the head. Within the head area, the inner canthus, auricular region, and periocular region were particularly difficult to treat, while the other locations in the head had average proportions of incomplete excision. This finding is consistent with other published studies.[7,8,17,22,32] A possible explanation may be the proximity of vital structures and cosmetic considerations that often are taken into account when treating lesions on the face. The average surgical margin was slightly lower in BCCs on the head compared to those in other locations (1.98 vs 2.43). Head lesions constituted 70.0% of all BCCs excised in our hospital. This figure is similar to those reported in some centers, such as the Peter MacCallum Cancer Centre (East Melbourne, Australia),[22] but is lower than the rates of 80% to 90% reported at other centers.[7,17]

Most of the BCCs (65.6%) in our study were less than 10 mm in diameter; overall, 34.4% were larger than 10 mm. Tumors that were larger than 20 mm were more likely to be incompletely excised compared to lesions that were less than 10 mm. This outcome is consistent with published reports stating that the risk for subclinical extension increases with tumor size.[15] We found that BCCs measuring 10 to 20 mm had a higher risk for positive margins than tumors less than 10 mm.

Regarding the histologic subtype, morpheic and superficial BCCs were significantly more likely to be incompletely excised ($P=.001$ and $P=.01$, respectively). This finding is consistent with results from other reports in the literature.[17,22,33,34] Morpheic BCC

usually presents as yellowish white, flesh-colored lesions with induration and borders that are not sharply demarcated. These characteristics contribute to the difficulty in delineating accurate surgical margins. Superficial BCCs spread within the epidermis and show poorly demarcated margins, which contributes to a higher rate of incomplete excision. Micronodular BCC is a histologic form of BCC that has no distinctive clinical characteristics and was not found to be a risk factor of incomplete excision in our study.

Table 3.

Reported Rates of Incomplete Excision

Reference (Year)	Total No. of Lesions	Incomplete Excision, %
Lawrence et al[16] (1986)	58	17.2
Kumar el al[17] (2002)	757	4.5
Bisson el al[18] (2002)	100	4.0
Thomas et al[19] (2003)	71	2.8
Hsuan et al[20] (2004)	55	18.2
Bhatti el al[21] (2006)	900	14.0
Su et al[22] (2007)	1214	11.2
Griffiths et al[23] (2007)	1539	8.0
Farhi et al[24] (2007)	362	10.3
Twist[25] (2009)	124	1.6
Macbeth et al[26] (2009)	1419	14.0
Hansen et al[27] (2009)	6881	6.4
Sherry et al[28] (2010)	3006	3.2
Malik et al[29] (2010)	1832	14.0
Santiago et al[30] (2010)	947	9.5

One particularly interesting finding in our study was the positive correlation between incomplete excision and the depth of the tumor invasion. In the same way that larger lesions have a greater risk for incomplete excision, we found that the depth of invasion also was an independent risk factor for incomplete excision. Thick tumors (>6.0 mm) showed a statistically higher rate of incomplete excision compared to thinner lesions (≤3 mm)(P=.025). This outcome might be considered a confounding factor for incomplete excision, whereby the thicker tumors would predominate in high-risk areas such as periorbital or periauricular areas. However, of 13 BCCs that were greater than 6.0 mm in our study, only 2 were located on the face (forehead and nose), 3 were located on the scalp, 1 on the neck, 3 on the arms, and 4 on the back. Large and infiltrative BCCs, which are more likely to be completely excised,[15,22] have an asymmetrical infiltration of the deeper layers of the dermal tissue.[33] This feature results in a greater risk for incomplete excision. Therefore, this invasive growth in depth may be a contributing risk factor for incomplete excision in BCCs independent of size and infiltration. This finding is interesting from a surgical perspective because deep margin involvement often is more concerning, as the reexcision of deep margins is more difficult and recurrences are only detectable in later stages.

Guidelines suggest that surgical margins should be 3 mm for nonmorpheic BCCs less than 20 mm in diameter and 10 mm for morpheic and infiltrative BCCs as well as BCCs greater than 20 mm in diameter to allow for complete excision.[35] In our study, small BCCs (≤20 mm) accounted for 93.2% of all excisions, but only 12.3% of these lesions were excised with 3-mm margins or greater. Although large BCCs (>20 mm) accounted for 6.8% of all excisions, only 9.0% of these lesions were excised with 10-mm margins or greater.

In the majority of BCCs (88.2% [285/323]) in our study, the repair method used was direct closure, which was related to small lesions. The method of surgical closure was not a factor related to incomplete excision; however, in other studies, graft repair has been found to be associated with a higher percentage of incomplete excision.[22] This method of closure was required in only 12 lesions in our study.

Necrosis is a histologic feature that is present in some BCCs. We analyzed the presence of this feature in our study sample and found that it was not correlated with a higher incidence of incomplete excision. In the same way, the presence of elastosis was measured and classified in 4 possible grades. We observed that the presence of grades 2 and 3 elastosis was associated with higher rates of incomplete excision. Solar elastosis is the deposit of altered elastin in the dermis. Elastotic changes of the dermis are thought to be an indicator of cumulative sun exposure, which is associated with the risk for developing BCC. Solar elastosis of the face presents as yellowish skin and is associated with atrophic and dyschromic changes. All these changes add difficulty in delineating the borders of the lesion, particularly in lesions with severe elastosis, and may explain our finding. In the same way, lesions with grade 1 elastosis are easier to demark; in our study, these lesions were associated with a similar rate of incomplete excision as tumors without elastosis (grade 0).

The choice of anesthesia depends on tumor and patient factors. There were no statistical differences in the rate of incomplete excision associated with local versus general anesthetic. Results from other studies are consistent with our finding.[22]

It is important to note that Mohs micrographic surgery is not available in our clinic. This technique offers the highest cure rates and allows for the removal of the neoplastic tissue with minimal removal of surrounding healthy tissue, causing less functional and aesthetic damage.[36] In southern Spain, the performance of Mohs micrographic surgery is about to be generalized. Therefore, it is important that this technique is made available to dermatologic surgeons because it can deliver excellent curative and aesthetic results when effectively used. Despite not having this technique available in our clinic, we still have achieved a considerable incomplete excision outcome.

Our study includes a few limitations. First, we did not consider the variations in experience among the surgeons of our clinic. Second, this is the first study analyzing the rate of incomplete excision of BCCs at our hospital, so it may be interesting to compare the figures obtained in our work with the results of future studies conducted at the same center.

Conclusion

This study retrospectively analyzed the surgical therapeutic results in BCCs excised at a tertiary referral hospital in southern Spain. We observed incomplete excision rates similar to those reported in other studies. Notwithstanding, a better marking of the correct surgical margins, particularly in lesions with surrounding moderate to severe elastosis, in addition to the application of Mohs micrographic surgery in those lesions likely to recur should be performed to improve our findings.

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