A Study of Subclinical Extension of Basal Cell Carcinoma by Mohs Micrographic Surgery

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Background: Basal cell carcinoma (BCC) is the most common primary cutaneous neoplasm in Korea. Since the majority of BCCs occur on the head and neck and the goal of the BCC treatment is the complete removal of tumor, Mohs micrographic surgery is ideally suited for maximizing cure rate with minimizing tissue loss.

Objective: The purpose of this study is to evaluate the depth of excision as well as the lateral margins of BCC and to correlate these with the clinicopathologic aspects of the tumors.

Methods: Twenty patients with 21 BCCs (10 primary, 11 recurrent) diagnosed in the Department of Dermatology of Dong-A University Hospital from March, 1992 through December, 1993 were studied prospectively.

Results: 1. Sixty percent of tumors in primary BCCs in our series had a 2-mm maximal margin and 81.8% of recurrent BCC were eradicated with 4-mm or more lateral margin.
2. All the recurrent basal cell carcinomas (8 cases) measuring greater than 15-mm required more than 4-mm margin for the total removal.
3. More than 90% of BCC on the nose in our series required the removal of periosteum/perichondrium or the excision of whole layer.

Conclusion: Mohs micrographic surgery is an appropriate tool to use in proposing guidelines for the treatment of skin cancer because the most accurate method of determining the actual extent of skin cancer can be achieved.

Key Words: Basal cell carcinoma, Mohs micrographic surgery, surgical margins

Basal cell carcinoma (BCC) is the most common primary cutaneous malignant neoplasm in Korea. Since the majority of BCCs occur on the head and neck and the goal of the BCC treatment is the complete removal of the tumor, Mohs micrographic surgery is ideally suited for maximizing the cure rate with minimizing the tissue loss. Furthermore, it is an appropriate tool to

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Fig. 1. The visible clinical margin of the tumor and the surrounding normal skin at 2-mm increments were lined with gentian violet. The tumor was removed with a vertical excision along the 2-mm margin of normal appearing skin.

Fig. 3. Stages to be required for complete removal of BCCs by Mohs micrographic surgery. ■ and □ denote one stage (2-mm maximal margins) and two or more stages (more than 4-mm maximal margins), respectively.

the lateral margins of BCC and to correlate these with the clinicopathologic aspects of the tumors.

MATERIALS AND METHODS

Twenty patients with 21 BCCs (10 primary, 11 recurrent) diagnosed in the Department of Dermatology of Dong-A University Hospital from March, 1992 through December, 1993 were studied prospectively. All the patients were diagnosed by history, clinical appearance, and histopathologic findings. All cases were documented in terms of age, sex, duration, anatomic location, maximal tumor diameter, histopathologic type, number of stages required to eradicate the tumor, and safety margin/depth of excision as determined by Mohs micrographic surgery.

Six of the 20 patients (30%) were men, with a mean age of 57 years (range from 38 to 82 years). The distribution of the tumors was as follows: 13 (61.9%) on the nose, 5 (23.8%) on the cheek, and 1 each (4.8%) on the eyelid, the forehead and the postauricular area. Five (23.8%) of the tumors had primary closure and 16 (76.2%) had flaps for reconstruction. There was no recurrence during follow-ups ranging from 6 to 26 months.

Four histologic patterns by Lever's classification are identified: circumscribed, 9 cases (42.9%); infiltrative, 8 cases (38.1%); adenoid, 3 cases (14.2%); keratotic, 1 case (4.8%). By Sexton's classification, tumors were identified with the following patterns: nodular, 2 cases (9.5%); infiltrative, 4 cases (19.0%); superficial, 1 case (4.8%); micronodular, 2 cases (9.5%); nodular-infiltrative, 5 cases (23.8%); nodular-micronodular, 4 cases (19.0%); micronodular-infiltrative 2 cases (9.5%); nodular-micronodular-
Table 1. Safety lateral margins measured by Mohs micrographic surgery

<table>
<thead>
<tr>
<th>BCC</th>
<th>Number(percentage) of cases</th>
<th>Safety lateral margin</th>
<th>Sum of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2mm</td>
<td>4mm</td>
<td>6mm</td>
</tr>
<tr>
<td>Primary</td>
<td>6(60.0)</td>
<td>3(30.0)</td>
<td>1(10.0)</td>
</tr>
<tr>
<td>Recurrent</td>
<td>2(18.2)</td>
<td>6(54.5)</td>
<td>2(18.2)</td>
</tr>
<tr>
<td>Total</td>
<td>8(38.1)</td>
<td>9(42.9)</td>
<td>3(14.2)</td>
</tr>
</tbody>
</table>

Table 2. Vertical depth of invasion determined by Mohs micrographic surgery

<table>
<thead>
<tr>
<th>BCC</th>
<th>Number(percentage) of cases</th>
<th>Vertical depth of invasion</th>
<th>Sum of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Midsubcutis</td>
<td>or</td>
<td>Periosteum</td>
</tr>
<tr>
<td>Primary</td>
<td>4(40.0)</td>
<td>6(60.0)*</td>
<td>-</td>
</tr>
<tr>
<td>Recurrent</td>
<td>2(18.2)</td>
<td>7(63.6)</td>
<td>2(18.2)</td>
</tr>
<tr>
<td>Total</td>
<td>6(28.6)</td>
<td>13(61.9)</td>
<td>2(9.5)</td>
</tr>
</tbody>
</table>

*Five cases were located in the area of the nose and only one on the cheek.

infiltrative, 1 case(4.8%).

Preoperatively, the visible clinical margin of the tumor was marked in gentian violet under the operation light and its maximum diameter was measured. The surrounding normal skin was lined with gentian violet in 2-mm increments parallel to the clinical tumor margin.

The tumor was then excised using the modified Mohs micrographic surgery, fresh-tissue technique. Briefly, the tumor was removed en block with a vertical excision along the 2-mm margin of normal appearing skin, invariably with the entire upper fat(Fig. 1) but even deeper when vertical infiltration was suspected. For comparison, we used two methods for checking surgical margins: peripheral vertical and horizontal frozen sections and oblique peripheral sections(Mohs method)* (Fig. 2, A&B). We used instant photographs of surgical defect to aid accurate tissue mapping(Fig. 2, A).

Any residual tumor noted on microscopic examination was mapped and selectively excised. The processes were repeated until the entire tumor had been eradicated. Postoperatively, the lateral extent of the subclinical extension of the tumor into normal-appearing skin was calculated from the clinical tumor margins.

The greatest extents of lateral tumor invasion and vertical depth of tumor cells were recorded.

Safety lateral margin and maximal vertical depth data from initial and subsequent stages were considered as maximal subclinical extension.

RESULTS

Safety lateral margin and vertical depth of invasion according to primary and recurrent BCC

Sixty percent of the tumors in primary BCCs in our series required only one stage(2-mm maximal margin) and 81.8% of recurrent BCC were eradicated with 2 or more stages(4-mm or more lateral margin). One case of recurrent BCCs required 4 stages(8-mm margin) for the total removal(Table 1). A x² test for test for independence demonstrated a significant difference($X^2=3.884$, df=1, and p=.04) in the distribution of subclinical extension(group 1 : 2-mm margins, one stage ; group II : 4-mm or more margins, two or more stages) between primary and recurrent BCCs(Fig. 3).

Fifteen percent of recurrent BCCs were eradicated with the excision down to the mid-subcutaneous fat, and 63.6% required the excision extending to the muscular layer or periosteum/perichondrium. Four cases(40%) of primary BCCs were removed with the excision to the mid-subcutaneous fat and 6 cases(60%) down to the muscular layer or
Surgical depth according to anatomic location

Table 3. Surgical depth according to anatomic locations of BCCs

<table>
<thead>
<tr>
<th>Anatomic location</th>
<th>Midsubcutis</th>
<th>Surgical depth muscle or Perichondrium/ periosteum</th>
<th>whole layer Sum of cases to mucosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>1(1,0)</td>
<td>11(5,6)</td>
<td>1(0,1)</td>
</tr>
<tr>
<td>Cheek</td>
<td>3(1,2)</td>
<td>2(1,1)</td>
<td>-</td>
</tr>
<tr>
<td>Eyelid</td>
<td>-</td>
<td>-</td>
<td>1(0,1)</td>
</tr>
<tr>
<td>Forehead</td>
<td>1(1,0)</td>
<td>-</td>
<td>1(0,1)</td>
</tr>
<tr>
<td>Postauricle</td>
<td>1(1,0)</td>
<td>-</td>
<td>1(0,1)</td>
</tr>
<tr>
<td>Total</td>
<td>6(4,2)</td>
<td>13(6,7)</td>
<td>2(0,2)</td>
</tr>
</tbody>
</table>

*Numbers inside of ( ) means numbers of cases of primary and recurrent, respectively.

Table 4. Safety lateral margins according to tumor size of BCCs

<table>
<thead>
<tr>
<th>Tumor size (mm)</th>
<th>2mm</th>
<th>4mm</th>
<th>6mm</th>
<th>8mm</th>
<th>Sum of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>3(2,1)*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3(2,1)</td>
</tr>
<tr>
<td>10-14</td>
<td>3(2,1)</td>
<td>2(1,1)</td>
<td>-</td>
<td>-</td>
<td>5(3,2)</td>
</tr>
<tr>
<td>15-19</td>
<td>1(1,0)</td>
<td>5(1,4)</td>
<td>2(1,1)</td>
<td>-</td>
<td>8(3,5)</td>
</tr>
<tr>
<td>&gt;20</td>
<td>1(1,0)</td>
<td>2(1,1)</td>
<td>1(0,1)</td>
<td>1(0,1)</td>
<td>5(2,3)</td>
</tr>
<tr>
<td>Total</td>
<td>8(6,2)</td>
<td>9(3,6)</td>
<td>3(1,2)</td>
<td>1(0,1)</td>
<td>21(10,11)</td>
</tr>
</tbody>
</table>

*Numbers inside of ( ) means numbers of cases of primary and recurrent, respectively.

Surgical depth according to anatomic location

Sixty percent of BCCs located in cheek were eradicated with the excision down to the mid-subcutaneous fat and 40% down to the muscular layer but more than 80% of BCCs in the nose required the removal of the periosteum or perichondrium and even two cases of recurrent BCCs, each of which was located in the ala nasi and lower eyelid respectively, were eradicated with the excision of the whole layer to mucosal layer (Table 3). There was a significant difference ($\chi^2 = 5.716$, df=1, and p=0.02) in the distribution of categorized surgical depths (category I: midsubcutis; category II: muscle, periosteum/perichondrium or whole layer) between nose and cheek areas.

Safety lateral margin according to tumor size

To test whether the subclinical extension was independent of the tumor size, the distributions of our results among the following groups of tumor sizes were compared: 0 to 9mm, 10 to 14mm, 15 to 20mm, and greater than 20mm. A maximal 2-mm margin would have eradicated all 3 cases of BCC measuring 0 to 9mm, and 87.5% of tumors measuring 15 to 19mm, and 83.3% of tumors greater than 20mm require more than 4-mm margin for total removal. A $\chi^2$ test for independence demonstrated a significant difference ($\chi^2 = 8.809$, df=3, and p=0.04) in the subclinical extension among these groups (Table 4).

All the recurrent BCCs in our series measuring greater than 15mm required more than 4-mm margin for total removal. For recurrent cases, we investigated the difference in the safety lateral margin between two groups of tumor size (less than 15-mm and more than 15-mm maximal diameters) and the results (n=3, mean=2.7; n=8,
mean=5) were statistically significant ($\chi^2=6.519$, df=1, and $p=.01$).

Safety lateral margin according to histologic pattern

It is difficult to evaluate whether the subclinical extension was independent of the histologic pattern because the data were limited. But all the micronodular (2 cases) and nodular-micronodular-infiltrative (1 case) BCCs, by Sexton's classification, had 4-mm or more maximal subclinical extension and perietal/perichondral or deeper vertical invasion.

**DISCUSSION**

In Korea as well as other countries, BCC is the most common primary cutaneous malignant neoplasm, of which the prevalence rate was estimated to be more than one-third of the primary skin cancers. But incidence of skin cancer in Koreans is much less than in white people. Most BCCs are relatively innocuous and metastatic risk is negligible. We are inclined to use a traditional method for the complete cure of BCC, concerning ourselves with the cosmetic results and the patient morbidity. It easily recurs with such treatment because BCCs frequently extend beyond the clinically predictable borders. A recurrence of BCC is usually less dangerous than melanoma. But it is implicit in recurrence not only that subsequent therapy will cause sacrifice of more skin, but that the chance of successful eradication of the tumor decreases with each subsequent treatment. Occasional recurrent BCC can be extremely destructive and the chance of metastasis may increase.

Of the various methods for the treatment of BCC (i.e., curettage and electrodestruction, cryosurgery, radiation therapy, excisional surgery, and Mohs micrographic surgery), Mohs micrographic surgery is ideally suited for maximizing cure rate while minimizing tissue loss. About 5% of Mohs surgeons believe that all BCCs require Mohs surgery, but most would agree that this is an excessive use of resources, despite the extremely high cure rates obtained with this technique. This surgical method is not popular in Korea.

The American College of Mohs Micrographic Surgery and Cutaneous Oncology published a "position paper" outlining what it considered to be the necessary components of true Mohs surgery. They recommended tissue excision in thin layers, allowing the lateral and lower margins to be examined in the same plane under the microscope and "horizontally cut" frozen sections. Most articles on Mohs surgery state that the excision must be at about a 45° angle, so that the epidermis, dermis, and deeper tissue can be observed all in one plane. However we know of Mohs surgeons who use various combinations of peripheral 90° vertical and true horizontal sections to carefully check the margins (L.H. Goldberg, oral communication, January 1992). This can often result in a margin evaluation, which is equally thorough compared with oblique 45° sections, and is much easier to orient and interpret. The complete epidermal edge is often not present in 100% of the usual 45° obliquely sectioned margins. In our opinion, we learn by experience that 90° sectioning is much better for checking out the whole margins that completely encompass the neoplasm and for repair of the skin defect with a local flap.

Mohs surgery has already been used to study the subclinical extension of BCC. Burg et al. studied 72 BCCs and Salasche and Amonette studied 51 morphoeform and 50 primary BCCs by a similar fashion in measuring the radius of the tumor preoperatively and the radius of the defect postoperatively. The difference between the two measurements represented to them the subclinical extension. These two studies took no account of the tendency for the wound to expand once a full-thickness incision is made. This would result in falsely elevated values for the subclinical invasion of the tumors. Beirne and Beirne studied a series of 169 basal and squamous cell carcinomas by performing Mohs surgery and noting the number of stages necessary to achieve a tumor-free plane. Since the method utilized by these authors in determining the subclinical extension of tumor was limited by their estimation of 1 to 2 mm of normal skin excised for each stage of Mohs surgery without preoperatively marking, an error is introduced using Beirne and Beirne's formula for determining the necessary surgical margin. Recently, to arrive at a more accurate measurement, Wolf and Zitelli studied the subclinical invasion of 117 clinically well-defined BCCs in normal skin by preoperatively marking the surrounding normal-appearing skin at 2-mm increments. Utilizing this method, they recommended that to eradicate the entire cancer in more than 95% of cases which have a diameter...
less than 2cm, it is required to excise a minimum margin of 4-mm of normal skin. In 1991, Breuninger and Dietz described subclinical horizontal growth on the basis of a large series of 2,016 unselected BCCs (1757 primary, 250 recurrent) with the prediction curves of the probability of tumor-positive margins and recommended safety margins at first excision of BCCs that ensure tumor-free excisional margins in about 80% of cases. The margins studied were lateral margins only and the depths of invasion were not specially addressed.

Some Mohs surgeons recommended that morbidity and cosmetic results should be given more consideration, because a recurrence of BCC is usually less dangerous than melanoma and metastatic risk is negligible. But others who are over concerned with the repair of the defect and cosmetic considerations prior to starting a case often end up performing inadequate removal of tumors. Occasionally BCCs can be extremely destructive. The surgeon needs to balance these factors mentioned above, since they are contrary to each other.

At this point of time, it must be emphasized that one of the major advantages of the Mohs technique is its potential for maximal tissue conservation and the histologic control enables the surgeon to be confident that the tumor is gone, even when narrow margins are taken. Furthermore, substantial, though certainly not acceptable, rates of total tumor removal are attainable with smaller margins: 60% of tumors in primary BCCs in our series had a 2-mm maximal margin and 72.7% of recurrent BCCs were eradicated with up to a 4-mm margin (Table 2).

We propose guidelines of the first excision with 2-mm margin combined with meticulous Mohs surgical mapping at 2-mm increments in primary BCC and 3-mm or 4-mm margin according to anatomic location and tumor size in recurrent BCC.

Most previous reports deal with the subclinical lateral tumor extension of BCC, which almost always take place within the dermis, but did not specially address the vertical growth of tumor cells. Depth of excision plays a less important role in actual practice with local flap than the size of the surgical defect. Preserving the middle or deep dermis has an advantage only if the wound is to granulate by secondary intention. Brodland recommended that the depth of excision should be carried down to the mid-subcutaneous fat in skin with abundant fatty tissue, whereas deeper excision to the fascia, perichondrium, or periosteum is indicated where the subcutaneous layer is scant.

More than ninety percent of BCCs on the nose in our series required the removal of the periosteum/perichondrium or the excision of a whole layer to the mucosal layer (Table 3). Therefore, we would recommend guidelines of the first depth of excision down to the periosteum or perichondrium in BCC on the nose.

Most reports demonstrated the correlation of surgical margin with tumor size, which was also observed in our series. We recommend guidelines of the first excision with 4-mm lateral margin in recurrent BCCs measuring greater than 15mm.

The classification of BCC into differentiated and undifferentiated types is inadequate because of difficulties in its uniform application to therapy and its acceptance by dermatopathologists who attempted to define the histologic pattern correlated with adequacy of surgical excision and predicting recurrence. It was difficult for us to evaluate whether the subclinical extension was independent to the histologic pattern because the data were limited. But all the micronodular and nodular-micronodular-infiltrative BCCs, by Sexton's classification, in our series had 4-mm or more maximal subclinical extension and periosteal/perichondrial or deeper vertical invasion.

REFERENCES