Occurrence of Subclinical Tumor in Excised Facial Subunits

Pearson G. Lang, MD; Irenee M. Duncan, MD; Marcelo Hochman, MD

Objective: To determine the incidence of subclinical tumor in excised facial subunits in patients undergoing reconstruction after Mohs surgery.

Design: The study group comprised 45 patients who had their Mohs defects repaired by a facial plastic surgeon at a tertiary care center (university hospital). In the group, there were 74 biopsy-proved cutaneous neoplasms of the face. The median age of the group was 67 years. Nineteen patients (42%) had multiple tumors. There were 63 basal cell carcinomas (85%) and 11 squamous cell carcinomas (15%). Forty-seven tumors (64%) were primary and 27 (36%) were recurrent. Reconstruction of the defects was based on the principle of aesthetic subunits. Excised subunits were examined by the Mohs surgeon. Further excisions were performed, as necessary, if tumor was present in the subunit.

Results: Five patients (11%) had subclinical basal cell carcinomas in their excised facial subunits. Four patients underwent further resections.

Conclusions: In patients with severe sun damage, recurrent tumors, and a history of skin cancer, clinically normal tissue excised during the reconstruction of their Mohs defects may contain subclinical tumor. Consequently, when these “high-risk” patients undergo reconstruction, excised facial subunits should be submitted for pathologic examination.

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Basal Cell Carcinoma (BCC), especially recurrent BCC, often demonstrates extensive subclinical growth with fingerlike extensions. This infiltration is particularly common in the midface, where BCCs often behave more aggressively and recur more frequently. An “iceberg” phenomenon, in which tumor strands invade deeply and widely within the perichondrium and periosteum and along fascial and embryonic fusion planes, may occur. Before a surgical defect is reconstructed, it is imperative that the entire tumor be removed. Flaps and scar tissue can delay the detection of buried tumor, so that by the time it is clinically apparent, the spread of the tumor can be quite extensive.

Mohs micrographic surgery (MMS) provides a precise surgical treatment for locally aggressive, invasive cutaneous neoplasms. The theoretical cure rate for MMS is 100% provided that the tumor cells grow in a contiguous fashion. Reported 5-year cure rates for primary and recurrent BCCs are 99% and 94%, respectively. Five-year cure rates are equally high (98%) for small squamous cell carcinomas (SCCs). Local recurrence or tumor persistence after MMS is considered rare, with technical errors accounting for the majority of cases. The previous mode of therapy, tumor biology, and patient characteristics may account for the remainder of recurrences.

Although recurrences may occur after MMS, because of the excellent 5-year cure rates for both primary and recurrent BCCs and small SCCs (<2.0 cm) immediate reconstruction of Mohs defects has become quite acceptable. Basing the reconstruction on the principle of aesthetic subunits yields the best cosmetic results. The face can be divided into topographical units (ie, forehead, eyelids, cheeks, nose, lip, mentum, and auricles), and the nose can be further subdivided into smaller subunits (ie, dorsum, sidewall, tip, soft triangles, alae, and columella). Excising the entire subunit involved by the defect offers superior cosmetic results by permitting placement of scars in the borders of subunits. The additional tissue removed at the time of reconstruction is usually discarded. As observed in the patients described herein, subclinical tumor

From the Departments of Dermatology (Dr Lang) and Otolaryngology–Head and Neck Surgery (Dr Duncan), Medical University of South Carolina and The Facial Surgery Center (Dr Hochman), Charleston, SC.
may be present in this subunit tissue despite clear margins as determined by MMS.

METHODS

The study group comprised 45 patients who were referred to the Mohs surgeon (P.G.L.) at the Medical University of South Carolina, Charleston, for MMS for biopsy-proved skin cancers and who had their resultant defects repaired by a facial plastic surgeon (M.H.).

All patients underwent MMS. The gross tumor was removed, and a Mohs layer was excised. This layer was further subdivided, and the resulting specimens were color coded for orientation. Lines were drawn on the skin to show the source of the specimens, and a map of the wound was drawn. The gross tumor was sent for vertical sectioning using a frozen-section technique with hematoxylin-eosin staining, and the Mohs specimens were sent for horizontal sectioning using the same technique and staining method. The open wound was pressure dressed with antibiotic ointment. The Mohs surgeon examined all specimens microscopically. Additional Mohs layers were excised, as needed, to create a tumor-free wound.

Reconstruction of the defect was based on the principle of aesthetic facial subunits. Additional tissue was excised so that the defect encompassed an entire aesthetic subunit. The subunit specimen(s) was sent to the Mohs surgeon with a map showing the relationship of the tissue to the Mohs defect and its orientation. The tissue was subdivided and color coded for orientation. A map was drawn. The specimens underwent routine fixation, paraffin embedding, and horizontal sectioning with hematoxylin-eosin staining. The specimens were then evaluated under the microscope by the Mohs surgeon for the presence of tumor. The spatial relationship between subclinical tumor within a subunit and the Mohs defect was determined. Further resections were performed as necessary if the subunit specimens demonstrated tumor. When tumor was present in the subunit, the Mohs surgeon conducted a retrospective review of the original Mohs specimens to assess the slides for quality and the possibility of overlooked tumor.

RESULTS

The median age of the patients at presentation was 67 years (age range, 29-83 years). There were 22 men and 23 women. All patients had a history of long-term sun exposure. Nineteen patients (42%) had multiple tumors at presentation. A total of 74 biopsy-proved tumors were treated, of which 63 (85%) were BCCs and 11 (15%) were SCCs. Forty-seven (64%) tumors were primary and 27 (36%) were recurrent. Fifty-seven (76%) of the tumors were located on the nose (Table). The average preoperative tumor diameter was 1.17 cm (88%, <2.0 cm; 12%, >2.0 cm). The average Mohs defect diameter was 2.45 cm. The median time delay to reconstruction was 10.8 days (range 1-43 days).

Facial subunit specimens from 5 patients (11%) contained subclinical BCC. The median age of these patients was 66 years (age range, 47-70 years). Four of the patients were male and 1 was female. Two of 4 patients who presented with recurrent BCCs had multiple tumors at presentation. One patient presented with a single recurrence of BCC that had developed in the region of a previous flap. The fifth patient, who was immunocompromised after undergoing a cadaveric renal transplantation, presented with multiple primary BCCs. The tumors were located on the nose in 4 of the 5 patients and in the temporal region in 1 patient. In these 5 patients, the average preoperative tumor diameter was 1.16 cm (4 tumors, <2.0 cm; 1 tumor, >2.0 cm). The average number of Mohs stages required was 4.4 (range, 2-9 stages). The average diameter of the Mohs defects was 3.24 cm. The median time delay to their reconstruction was 14.6 days (range, 1-40 days).

The 4 patients with nasal tip and/or dorsum defects underwent reconstruction with staged paramedian forehead flaps, and the patient with a temporal defect underwent reconstruction with a cervicofacial advancement flap and a split-thickness skin graft to the superior aspect of the defect. The corresponding subunits that were excised included the nasal tip in 4 cases and a wide temporal area excision in 1 case.

In all 5 patients, the excised subunit tissue contained foci of BCC. In 1 patient, the tumor was located in the center of the subunit specimen and the surrounding tissue was clear of tumor; therefore, no further intervention was deemed necessary. In the remaining 4 patients, the tumor was located near the margins of the specimen(s). Consequently, MMS was offered to these 4 patients. One patient refused further surgery. The other 3 patients underwent MMS, with clear margins being obtained. In 2 of these patients, an additional tumor was discovered.

The Mohs surgeon reviewed the original Mohs specimens from the 5 patients. On review, all the specimens and slides were of good quality and the negative margins remained negative. The histologic findings were reassessed, and the spatial relationship of the presenting and subunit tumors was determined using the maps. Four of the original tumors demonstrated superficial multicentric or aggressive and infiltrating patterns. Only the immunocompromised patient had a tumor with a nodular growth pattern. Two of the subunit tumors demonstrated an aggressive/infiltrating histologic pattern similar to that of the presenting tumor and were contiguous with the Mohs defect. Two of the subunit tumors demonstrated a different histologic pattern from the presenting tumor and were not contiguous with the Mohs defect. The fifth patient had 2 tumors in the subunit: one was histologically similar to the pre-
senting tumor and was contiguous with the Mohs defect, and the second was different histologically and not contiguous with the defect.

There were no recurrences in these 5 patients during a 4-year follow-up period. However, another patient in the series did develop a BCC in the lateral edge of the paramedian forehead flap 9 months after reconstruction despite close scrutiny of the donor skin at the time of reconstruction. This patient had presented with an aggressive growth-pattern primary BCC of the nasal dorsum. The Mohs defect, which measured 2.5 × 2.0 cm, had been reconstructed with a staged paramedian forehead flap. The flap donor skin was clinically normal in appearance at the time of reconstruction. The patient subsequently underwent Mohs excision of the lesion in the flap and of the forehead donor region. Basal cell carcinoma was present in both areas.

**COMMENT**

In our study, 5 patients (11%) demonstrated subclinical tumor in excised facial subunits after clear Mohs margins. An issue, then, is whether all excised subunits should be examined for subclinical tumor or whether a subset of patients can be identified in whom the incidence of subclinical tumor would be higher.

As discussed earlier, MMS is quite capable of tracing out subclinical extensions of BCC. Therefore, a skin cancer occurring at or near a prior site of MMS represents either a new primary tumor or the persistence or recurrence of the prior cancer. Iatrogenic “skip” areas created by a prior biopsy or previous treatment may be a mechanism of persistence.7 Perineural tumor involvement is also known to demonstrate skip lesions that may be missed despite complete microscopic excision.1 Two patients in this study demonstrated subunit carcinoma adjacent to clear Mohs margins, and these loci of tumor were histologically similar to the Mohs tumor. However, perineural or lymphatic involvement was not noted, nor was scar tissue or inflammation present. Whether these foci represented another primary tumor or an incompletely excised tumor is not clear; however, review of the original slides revealed complete sections and no evidence of overlooked tumors. It is possible that they could have represented disconnected foci of tumor created by previous treatment.

True tumor multifocality may explain the appearance of multiple tumors in a given area or the development of tumor adjacent to previously treated sites. Three patients in this study demonstrated loci of BCC in the subunit not adjacent to the edge of the Mohs defect and with different histologic patterns. Scar tissue and inflammation were not present in these specimens, nor was perineural or lymphatic involvement seen.

In a very large study, Karagas et al13 showed that the estimated risk of subsequent primary BCC and SCC developing in patients with previous nonmelanoma skin cancer was 35% at 3 years and 50% at 5 years. This risk was higher among patients who were male and older than 60 years and who had severe actinic damage and more sun-sensitive skin. The total number of previous skin cancers was strongly associated with the risk of the development of subsequent skin cancer.

The 5-year risk for a patient with one previous skin cancer developing another skin cancer is 27%, which increases to 49% with a history of 2 previous skin cancers. The risk, when there have been more than 4 previous lesions, is greater than 73%. In our series, all patients had a history of long-term sun exposure. Four of the 5 patients with positive subunits were male, and 4 patients had recurrent BCC. Two of the 5 patients had multiple tumors at presentation. We did not have data on the total number of previous skin cancers or documented information on the patients’ skin types; however, because many of the patients had multiple tumors, one can assume that many of these patients were fair complected. When this study was initiated, we had no inkling as to what its outcome might be. Based on our data, one might conclude that in our patient population a higher-than-expected recurrence rate could be anticipated after MMS; yet this has not been our experience. Repeated review of our long-term statistics has shown 5-year cure rates of 98% or more. The patients in our study had surgical defects of significant size, but other than that, there was no bias in their selection for referral for reconstruction or for their inclusion in this study. However, in all likelihood, there probably was some bias regarding their referral for Mohs surgery; ie, often, the more difficult cases are referred for Mohs surgery. Therefore, many of the patients in our study, especially those with tumor in their cosmetic units, may not typify most patients with skin cancers of the head and neck, but would be better classified as “high-risk” patients. Thus, for the “average” or “low-risk” patients (ie, those with a single primary tumors and without a history of skin cancer), it may not be necessary to routinely submit cosmetic subunits removed at the time of reconstruction for pathologic examination. However, based on our experience, we suggest that in patients with recurrent tumors (ie, high-risk patients) or a history of multiple skin cancers and significant actinic damage the donor site be closely scrutinized for tumor lest it be transferred into a tumor-free wound and that the excised subunit(s) be submitted for pathologic examination.

**CONCLUSIONS**

We have found that clinically normal facial subunit tissue excised during the reconstruction of Mohs defects may contain subclinical carcinoma in up to 11% of patients despite negative Mohs margins. Thus, in high-risk patients with severe sun damage, recurrent tumors, and a history of multiple skin cancers, it is prudent to submit excised subunits for pathologic examination.

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Corresponding author: Pearson G. Lang, MD, Department of Dermatology, Medical University of South Carolina, 96 Jonathan Lucas St, Suite 623, Charleston, SC 29425 (e-mail: watersa@musc.edu).

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