The Significance of Positive Margins (Known and Unknown) at the Conclusion of Mohs Surgery in the Orbital Region

*James R. Boynton, M.D., 'Mark F. Rounds, M.D., 'Vito C. Quatela, M.D., and 'Marc D. Brown, M.D.

*Department of Surgery, The Geneseo Hospital, and Departments of *Ophthalmology, 'Otolaryngology and 'Dermatology, Strong Memorial Hospital, Rochester, New York, U.S.A.

Summary: The Mohs fresh tissue technique has provided a high rate of cure in cases of malignant tumors in the orbital region. However, in some patients, tumor may persist after Mohs surgery if margins are falsely negative or if the Mohs surgeon elects to terminate the procedure with known positive margins. We report six patients who had residual tumor present in the periorbital region after Mohs surgery. These patients have a serious prognosis associated with subsequent morbidity. Accurate communication between the Mohs surgeon and subsequent treating surgeons, combined with aggressive tumor management, may help to minimize morbidity and improve mortality.

Key Words: Exenteration—Mohs surgery—Tumor recurrence.

Complete removal of periorbital malignancies, including basal cell carcinomas, is extremely important. Nowhere in the body are cutaneous tumors more dangerous nor are the functional and cosmetic sequelae of excess tissue removal more damaging than in the eyelid. The Mohs fresh tissue technique has proven to be an effective way of ensuring complete tumor excisions, providing a cure rate of 97–98%. In certain cases, however, resection margins may be (a) positive for residual cancer at the conclusion of Mohs surgery or (b) falsely negative for tumor. The significance of incomplete tumor removal at a Mohs setting as it relates to subsequent prognosis has not been widely documented. We describe six patients (eight Mohs procedures) who had residual tumor after a Mohs procedure. In three cases, the initial procedure was terminated with known positive margins, whereas in three cases, it was thought that the patient was tumor free. We emphasize the importance of aggressive management in these cases, including diligent postoperative follow-up. These patients also illustrate the morbidity and reconstructive dilemmas associated with treatment of large periorbital tumors.

CASE REPORTS

Case 1

A 67-year-old woman underwent Mohs surgery to remove a 3 × 4-cm squamous cell carcinoma from the left eyebrow region. The final slides at the time of the original surgery showed residual skin cancer at the deep margins, which were at the level of peristomeum. A skin graft and flap repair were carried out at another hospital. Three months after the original Mohs surgery, she was referred for corneal exposure. Examination showed the left upper lid to be retracted and bound to the superior orbital rim (Fig. 1). The left upper lid retraction was repaired with a retroauricular skin graft. At the time of surgery, friable tissue beneath the superior orbital rim was excised. Histopathologic examination of this specimen revealed squamous cell carcinoma. The pa-
FIG. 1. Case 1. Vertical shortening of left upper eyelid after reconstruction after Mohs procedure was terminated with known positive margins.

Patient returned to the original reconstructive surgeon, who performed additional tumor resection and another skin graft. She was again seen by us 8 months after that procedure. There was incomplete closure of the upper lid. She was taken to the operating room to undergo another skin-grafting procedure to lengthen the medial one-third of the left upper lid. Dissection in the involved area of the lid revealed friable tissue, which proved to be squamous cell carcinoma on frozen-section examination. The visible tumor was removed and reconstruction deferred.

Eighteen months after the initial Mohs surgery, after insertion of tissue expanders beneath the scalp (Fig. 2), she underwent orbital exenteration, removal of the frontal bone, and wide soft-tissue excision. Calvarial bone grafts were placed in the orbital and frontal defects (Fig. 3) and covered with large flaps made possible by the previously placed tissue expanders. These flaps subsequently failed to survive, and a free-flap procedure was performed (Fig. 4). She remains free of tumor 7 years after the initial Mohs procedure.

Case 2

A 71-year-old woman underwent Mohs surgery to remove a 4 × 5-cm basal cell carcinoma from the right eyebrow region. The final slides showed tumor to be present at the deep margins of resection, which included the periosteum. The patient underwent additional tumor resection and reconstruction elsewhere. She was referred to us 1 year after the original procedure with the upper lid tethered to the superior orbital rim (Fig. 5). At the time of surgery for scar excision and skin grafting, firm tissue was found beneath the orbital rim extending posteriorly into the orbit. Biopsy revealed basal cell carcinoma. She later underwent exenteration of the right orbit and removal of the frontal bone. A flap covered the frontal defect, and the orbit was left open. Six months later, biopsy of ulcerated areas at the periphery of the flap reconstruction was positive for basal cell carcinoma. She has subsequently undergone three repeated local excisions of recurrences by the original reconstructive surgeon. She was last seen by us 3 years after the initial Mohs surgery, at which time she was not free of disease (Fig. 6).

Case 3

A 76-year-old woman was seen with a 7 × 4-cm basal cell carcinoma involving the left lower eyelid and medial canthus. The final slides after three stages of Mohs surgery revealed no tumor.

Two days later, reconstruction of the surgical defect (Fig. 7) was performed with a semicircular flap laterally and retroauricular and supraclavicular skin grafts.

Nine months after the original Mohs surgery, abnormal soft tissue beneath the skin-grafted area was excised and proved to be recurrent basal cell carcinoma.

Three weeks later, the patient underwent extensive resection of the recurrent cancer, including the entire lower eyelid, the inferior 180° of bulbar conjunctiva, all of the inferior orbital soft tissues between the medial and lateral rectus muscles, the inferior orbital rim, and the orbital floor. In addi-

FIG. 2. Case 1. Scalp tissue expanders in place before surgery to remove residual tumor.
tion, a left partial rhinectomy and a left partial maxilloectomy were carried out.

Frozen-section examination of the orbital soft tissue revealed no tumor to be present at any of the deep margins.

Four months after the last surgical procedure, the patient died of cardiac complications unrelated to her head and neck problems.

Case 4* 
A 64-year-old white woman was seen with a cutaneous mass involving the nasal bridge and left medial canthus. Biopsy revealed a malignant fibrous histiocytoma.

Seven tissue sections were excised during two stages of Mohs micrographic surgery. Tumor-free margins were obtained.

Nine months later during repair of cicatricial ectropion of the left lower eyelid, abnormal subcutaneous tissue in the medial canthus proved to be malignant fibrous histiocytoma.

The following month, the patient underwent three stages of Mohs surgery. Ten tissue sections were taken, and margins positive for tumor were found laterally adjacent to bulbar conjunctiva, deep on the periorbital at the medial canthus, and adjacent to the nasal bridge (Fig. 8).

Two months later, the patient underwent a block resection at the medial canthus, including the nasal bone to just past the midline, the lacrimal sac, and ethmoid air cells posterior to the sac but anterior to the anterior ethmoidal artery. The conjunctiva was dissected from the limbus between the 6 and 12 o’clock positions medially, and the medial rectus muscle was detached from the globe. The medial rectus was severed at the level of the anterior ethmoidal artery, and the orbital tissues medially were excised as part of the first block resection. In an effort to avoid exenteration, orbital tissue between the superior and inferior rectus muscles and medial to the optic nerve was excised to the apex of the orbit, along with the posterior ethmoid sinus mucosa and medial wall of the orbit (Fig. 9). Frozen sections revealed no additional tumor in the last resected specimens.

Postoperatively, the left eye maintained 20/100 vision. It was, however, fixed in lateral gaze. A significant upper lid ptosis prevented diplopia (Fig. 10). The patient remained tumor free for 5 years until she died of pulmonary problems.

Case 5
A 65-year-old man was referred for extensive morpheaform basal cell carcinoma.

Two stages of Mohs surgery were carried out, and peripheral margins were clear. Residual cancer

*This case has been previously reported:
was noted on the deep margin at the medial canthus. The Mohs procedure was terminated, with a plan to excise the residual tumor at the time of reconstruction (Fig. 11). Four days later, the patient underwent additional tumor excision and reconstruction. Tissue at the medial canthus, including the caruncle, orbicularis, upper and lower canaliculi, and a portion of the lacrimal sac, was excised. Frozen-section examination of this specimen revealed basal cell carcinoma in the superficial portion of the specimen. The deep and peripheral margins were clear. Three separate additional pieces of tissue were excised deep to the previous specimen. These contained no tumor. Reconstruction of the lower eyelid was performed with an auricular cartilage graft covered with a “bucket handle” skin flap from the upper lid and skin grafts taken from behind both ears.

Except for intermittent epiphora, the patient did well for the next 2 years (Fig. 12) until he died of causes unrelated to his periocular skin cancer, 9 years after his initial surgery.

Case 6

A 68-year-old man was seen with a 2-cm basal cell carcinoma in the left medial canthus. The patient underwent a three-stage Mohs micrographic procedure with a resulting defect measuring 2.5 × 1.3 cm. The patient was seen again 2.5 years later, at which time a 4-mm nodule was noted at the medial lower eyelid. Biopsy revealed nodular basal cell carcinoma. This occurred at the edge of the canthal defect, which had previously granulated and therefore was thought to represent a recurrence. A four-stage procedure was performed, resulting in a 1.3-cm defect.

Eight months later, another recurrence of the basal cell tumor was noted in the medial portion of the left upper lid. A deep resection of the medial canthus, including the lacrimal sac, was performed in the major operating room. Margins were checked by the Mohs method and were clear. The patient has remained tumor free for 1 year.

DISCUSSION

Four patients in this series were known to have residual tumor at the conclusion of a Mohs surgery. Three patients experienced later recurrence of tumor after Mohs surgery with clear margins. One patient (case 4), who initially had recurrence after clear margins, underwent a second Mohs surgery, which was terminated with known positive margins. Another patient (case 6) also experienced two recurrences after clear margins, and a third Mohs procedure is believed to have removed all of the tumor. Of the four cases with known residual tumor, two were successfully treated by us with aggressive tumor excision and preservation of the eye. Two patients were treated elsewhere and experienced recurrence requiring subsequent exenteration of the orbit. One of these has remained free of tumor, whereas the other has apparently incurable disease (see Table 1).

Although cure rates of 93–98% have been cited using the Mohs technique (1,2), a number of problematic cases such as we describe have also been reported. These include cases in which margins were falsely negative as well as instances of known residual tumor. Mordick et al. (3) reported on 53 head and neck cases of Mohs surgery. Five patients had recurrences. In three of these, the Mohs procedure was terminated with known positive margins. One required exenteration for extirpation of a medial canthal basal cell carcinoma, and one underwent frontal bone excision, only to experience later recurrence. Folberg et al. (4) described three patients with eyelid sebaceous cell carcinoma treated by Mohs resection. All three had undetected residual tumor, and two developed recurrence requiring exenteration.

The advantages of the Mohs micrographic procedure for removing skin cancer have been clearly articulated (5) and include a high cure rate, decreased morbidity, tissue conservation, and other practical treatment considerations. However, the limitations and disadvantages of the technique have received less attention. The Mohs procedure may involve two separate surgeries, and this adds cost and inconvenience for the patient. In many cases, conventional frozen sections can be an efficient effective guide to tumor removal. Although not the main subject of our article, this deserves mention.

Large tumors may present difficulties in an outpatient setting, where most Mohs procedures are done. When the resection reaches a bony surface, the Mohs surgeon usually terminates the procedure. Similarly, when a vital structure such as the eye is encountered, the surgeon may discontinue the resection. For these reasons, large tumors are best resected in a standard operating room using a team approach. The Mohs surgeon may excise peripheral margins, while deeper areas are removed by a surgeon familiar with the pertinent anatomy. The Mohs surgeon may continue to map the resection and examine the histopathologic sections. This team approach facilitates the procedure and minimizes communication problems that can arise be-

between two treating surgeons. This communication difficulty is one of the most significant potential problems that can arise from surgery in an office setting. Histologic examination of specimens presents four possible problems (6). First, frozen sections, although very good, may not be as reliable a guide to tumor margins in difficult cases as are permanent sections. For this reason, melanomas are not typically removed with Mohs surgery. Second, if the tumor is an unusual one, such as sebaceous cell carcinoma, malignant fibrous histiocytoma, or another less commonly encountered lesion, the Mohs surgeon may not be as familiar with the pathology, compared with that of basal cell carcinoma. Third, technical limitations, artifacts, orientation problems, and other errors can contribute to falsely negative margins (7,8). Fourth, some tumors may be multifocal or consist of areas connected by only thin cords of cells. These may be very difficult completely to excise using the microscopic mapping technique. Problems faced by a second reconstructive surgeon include time delays, odd-shaped defects, and beveled resection edges.

In a number of specific situations, surgeons need to be aware of high-risk tumors and consider the potential limitations of the Mohs procedure. These include large tumors, especially those involving perineural and lymphatic spaces, recurrent tumors that may exhibit multifocal or skip areas of tumor (9), previously irradiated tumors (10), unfavorable location of lesions, such as the medial canthus, and aggressive tumor types. For example, it has been calculated that in the case of a 10- to 20-mm morphoform basal cell carcinoma excised with 5-mm clinical margins, there is an 18% chance that margins will be positive (11). Many of these risk factors were present in our cases, and accordingly, problems of recurrence might well have been anticipated. On the other hand, these difficult cases are those in which the advantages of the Mohs technique would seem most applicable.

Five of our patients (cases 1, 2, 3, 4, and 6) were seen many months after the initial Mohs procedure. Reconstructive surgery for deformities such as lower lid ectropion and upper lid retraction were scheduled. Abnormal tissue was noted at surgery in each case and proved to be recurrent tumor. Therefore, it is important to be aware of possible “danger signs” in these patients. Subsequent lid or periorbital deformities, poor healing, or the presence of abnormal tissue at surgery suggest risk of harboring tumor and may indicate biopsy at the time of late reconstructive surgery. It is extremely important for a subsequent treating surgeon to be aware of the possibility of residual tumor or recurrent tumor. If tumor is known to persist (i.e., the Mohs procedure was terminated with known positive margins), accurate communication between the Mohs surgeon and subsequent treating surgeon is mandatory. It is also essential to follow-up on this communication and subsequent treatment so that both surgeons know what took place. Lack of specific communication and follow-up may have played a role in the poor outcomes of our first two cases. After the Mohs surgeon has referred a patient with known residual tumor, it is important for the subsequent treating surgeon adequately to extirpate the cancer. This may require extensive surgery, as was performed in cases 1, 3, and 4. The subsequent treating surgeon must be aggressive in managing these cases, both initially and in follow-up. Along these lines, in case 5 and after the second Mohs

**FIG. 11.** Case 5. Surgical defect after Mohs procedure, which was terminated with residual tumor known to persist on deep margins at the medial canthus.

**FIG. 12.** Case 5. Final postoperative appearance after excision of residual tumor and reconstruction.