Microcystic Adnexal Carcinoma

Forty-eight Cases, Their Treatment, and Their Outcome

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Background: Microcystic adnexal carcinoma, or sclerosing sweat duct carcinoma, is an uncommon cutaneous neoplasm associated with extensive local invasion. The standard of care with regard to the best excisional method in treating microcystic adnexal carcinoma has not been established.

Objectives: To perform a retrospective study comparing patients treated by Mohs micrographic surgery with those treated by wide excision and to elucidate the epidemiological features of microcystic adnexal carcinoma.

Patients and Methods: A retrospective analysis of a case series involving 48 primary and referral patients diagnosed as having microcystic adnexal carcinoma using standardized criteria. All cases were reviewed by the same dermatopathologists.

Results: Microcystic adnexal carcinoma predominantly affects the left side of the face of middle-aged women. Microcystic adnexal carcinoma is misdiagnosed 30% of the time. The recurrence rate is 1.98% per patient-year. Mohs micrographic surgery and simple excision show comparable complication rates. Clear margins were obtained in fewer procedures and, therefore, fewer office visits when the lesions were treated with micrographic surgery. The defect surface area after full extirpation following Mohs micrographic surgery was a mean of 4 times that of the clinically apparent size. The wide range of difference between the pre- and the post-Mohs micrographic surgery surface area noted in our data indicates that a margin cannot be safely predicted.

Conclusions: Microcystic adnexal carcinoma is a predominantly left-sided, locally aggressive facial tumor, which results in significant morbidity. Our data do not support the use of standardized predictable margins. Mohs micrographic surgery is a reasonable initial treatment, as it accomplishes cure in fewer office visits and does not rely on predicted margins.

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RESULTS

GENERAL

Forty-eight patients, each with 1 lesion, fulfilled the inclusion criteria. Thirty-three physicians from 5 specialties (dermatology, otorhinolaryngology, obstetrics, ophthalmology, and plastic surgery) were responsible for treatments.

The mean age of our study population at biopsy was 61.2 years (median, 65 years; range, 19-90 years) (Table 1). Female patients were diagnosed as having a lesion at a median age of 60 to 69 years, while male patients were diagnosed as hav-
PATIENTS AND METHODS

PATIENT IDENTIFICATION

Databases maintained by the UCSF Dermatopathology Service were used to identify patients with MAC. These included referrals and primary University of California, San Francisco, patients. All patients were diagnosed by 1 of 2 board-certified dermatopathologists (T.M.), using standardized microscopic criteria. All biopsy specimens stained with hematoxylin-eosin displayed a poorly circumscribed epithelial neoplasm with no more than slight cytologic atypia, with nests and clusters of neoplastic cells arranged within a densely sclerotic stroma. There were small keratinizing cysts and cuticle-lined ducts present. Other features, including clear cell changes, a “decapitation” secretion pattern, and perineural invasion, were variably present. Cases were excluded if the pathological diagnosis of the biopsy specimen was equivocal or if the excision specimen was unavailable or insufficient for review. If the biopsy and excisional specimens seemed contradictory, all specimens were obtained and rereviewed to resolve the conflict.

PATIENT INFORMATION

Medical records were reviewed for information regarding demographics, type of treatment, and follow-up. Information regarding prior irradiation exposure was not routinely documented. Operative reports were reviewed, and physician and patient interviews were conducted when medical records were incomplete. The margins taken for the simple excision group were not specified in the operative reports. For the MMS-treated group, sectioning was performed until tumor was absent from the surgical margin. No additional section was taken. The date of the biopsy that led to the diagnosis of MAC was the date used for follow-up calculations.

SURFACE AREA (SA) CALCULATIONS

The pretreatment SA was estimated by assuming a circular lesion, and using the following formula: \( R^2 \), where \( R = 0.5 \) (diameter of the clinical lesion). The posttreatment defect SA was derived from the MMS operative report by assuming an oval defect, and using the following formula: \( 0.5W(L) \), where \( W \) is the width and \( L \) is the length of the oval. Posttreatment defect sizes could not be calculated for simple excisions because of insufficient information.

STATISTICAL ANALYSIS

To compare surgical complications (hematoma, infection, cosmetic dissatisfaction, and/or functional limitation), pretreatment sizes, and recurrence rates, we partitioned patients into those who had never been treated with MMS vs those who had. Comparisons of dichotomous variables were performed using the binomial probability test, the \( \chi^2 \) test, or the Fisher exact test. Continuous variables were compared using the Kruskal-Wallis 2-sample test. Cox proportional hazards analysis was used to compare the likelihood of recurrence between treatment groups. All tests were 2-tailed.

TREATMENT AND COMPLICATIONS

Twenty-two patients (46%) were successfully treated with MMS, in an average of 2.6 stages (range, 1–4 stages). In contrast, of 23 patients initially treated with simple excision, 7 (30%) had to have at least a second surgical procedure, less than 45 days later, before excision was deemed complete. Of these, 3 underwent simple excision followed by curative MMS, while the remaining 4 underwent repeated simple excisions. Two of the remaining 4 patients required 2 excisions, the third required 3 excisions, and the fourth still was not tumor free after 4 simple excisions (Figure 2). Therefore, 33 procedures were required to treat these 23 patients. Furthermore, of 30 simple excisions, tumor was present at the margins in 14 specimens (47% of the time). There were no instances of MMS followed by simple excision.

Three patients had no further excisional type of treatment after the initial biopsy. One of these had clear margins from the biopsy, one refused treatment, and one was treated with electrodessication and curettage.

Many of the 22 lesions treated with MMS at onset (18 [82%]) were located on the face (Table 1). Most patients with facial lesions (20 [57%] of 35) underwent MMS at some point. Women tended to be treated more frequently with MMS at onset (17 [55%] of 31) than men (5 [29%] of 17).

Surgical complication rates were similar between the MMS (6 of 25 surgical procedures) and the simple excision (5 of 20 surgical procedures) groups. Six patients died during our follow-up period of causes unrelated to MAC.

DEFECT SIZE

Lesion pretreatment sizes were not statistically different from one treatment group to the next (MMS, 0.80 cm\(^2\) [range, 0.07–8.80 cm\(^2\)]; excision, 1.50 cm\(^2\) [range, 0.03–
Surgical defect SAs after MMS were a median of 4-fold larger (range, 0.23–40.00) than the corresponding pre-treatment SAs. Accurate posttreatment SAs were not available for simple excisions.

### Recurrences

The mean follow-up time was 3.2 years (range, 0-11.1 years) and was similar between treatment groups. There were 3 recurrences. The 25 patients treated with MMS developed 2 recurrences in 82.5 person-years of disease-free follow-up (2.4% per person-year). One recurrence developed among the 20 patients treated with simple excision in 65.2 years of disease-free follow-up (1.5% per person-year). The 3 untreated patients developed no recurrences in 4.8 years of disease-free follow-up (0% per person-year). The overall recurrence rate of 1.97% per person-year was, therefore, similar between treatment groups (MMS vs excision; \( P = .80 \)), and corresponds to a 10-year recurrence rate of 18%.

All 3 recurrences were in women in the head and neck region. Two of the recurrences were in patients treated with MMS, 1 of which was recurrent at diagnosis (after prior treatment with irradiation and simple excision) (Table 2). Both were subsequently treated with MMS, with no recurrence to date.

The third lesion was also recurrent at diagnosis (Table 2), and its surgical margins were involved after 4 simple excisions. The lesion recurred 1 year later, but the patient died before treatment.

If a data from the recurrent at diagnosis group were included (Figure 2), 26 total MMSs and 35 total simple excisions were performed on 45 treated lesions. Three lesions (12%) recurred after MMS, compared with 6 (17%) after simple excision. Also, 13 lesions (5 recurrent at diagnosis, 7 that underwent multiple excisions, and 1 recurrence) either had positive margins or recurred, of 35 (37%) that underwent simple excision, compared with 3 (1 recurrent at diagnosis and 2 recurrences) (12%) of 26 that underwent MMS.

### Comment

Microcystic adnexal carcinoma is an uncommon neoplasm that was fairly recently described. To our knowledge, this study of 48 patients is the largest MAC case series reported in the literature. Although previous literature reviews helped physicians understand the epidemiological features of MAC, diagnostic criteria were not standardized, and thus comparison between series is potentially problematic. We benefited from having all specimens reviewed by the same 2 senior dermatopathologists. Because our study population was treated by a wide spectrum of physicians with different surgical expertise, our results on recurrence and posttreatment wound size should be generalizable.
Our cases are similar to those previously reported in the literature17,18,19,20 for anatomic distribution and average age of onset. To our knowledge, our series includes the first genital lesion reported, although a perianal location has been previously described.21 We also describe MAC in a 19-year-old patient; interestingly, this is the third male patient diagnosed as having MAC during the second decade of life.10,22 To date, this young age at presentation is unique to men (Figure 1). The female predominance that was evident in our study has been observed, albeit inconsistently, in other series.14,18,19,23,24 Again, women also appeared to be affected at an older age than men. This age-sex interaction seems to be common among other adnexal neoplasms, especially syringomas and trichoblastomas.25

Microcystic adnexal carcinoma lesions in our series had a tendency to present as a left-sided facial lesion. To our knowledge, this has not been noted previously, and could indicate a relative predisposition for MAC to develop in UV-exposed areas. It would be interesting to compare this left-sided predominance with series obtained in Australia or England, where driving and facial sun exposure occur on the right. Prior associations of MAC and radiation therapy have been described,5,10,26,27 and thus induction of MAC by different forms of irradiation may be possible.

Microcystic adnexal carcinoma is frequently misdiagnosed, either clinically or pathologically.5,12,19 In our study, 13 (27%) of the 48 cases were not diagnosed correctly at initial biopsy. Microcystic adnexal carcinoma has a relatively bland microscopic appearance, especially in superficial biopsy specimens, which makes pathological identification difficult.5,28 Superficial biopsy specimens are commonly inadequate as they capture only the superficial cystic or ductal component, which may be misinterpreted as a benign adnexal neoplasm such as syringoma.

As with other nonmelanoma skin cancers, the recurrent at diagnosis lesions were more aggressive than primary lesions, as they made up 2 of the 3 recurrences (Table 2). Recurrent at diagnosis lesions had been mostly treated by simple excision in the past.

Of our 48 patients, 7 (15%) had a recurrence at some point (6 recurrences were at diagnosis, 2 of which recurred again, and 1 was newly diagnosed and treated with MMS). This is lower than that reported in the literature,17,18 and may be due to the fact that lesions in prior reviews were often identified precisely because of their persistence. This led to biased selection of more aggressive subtypes, a problem inherent to retrospective reviews.

It has long been suspected that, despite its bland microscopic appearance and its apparently small clinical size, the surgical treatment of MAC leads to large posttreatment defects.3,4,29 We demonstrated a median 4-fold in-

Table 2. Treatment of Lesions according to Type

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Newly Diagnosed (n = 35)</th>
<th>Recurrent at Diagnosis (n = 6)</th>
<th>Misdiagnosed But Not Excised (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMS (n = 25)</td>
<td>17†</td>
<td>4†</td>
<td>4</td>
</tr>
<tr>
<td>Excision (n = 20)</td>
<td>15</td>
<td>2†</td>
<td>3†</td>
</tr>
<tr>
<td>Biopsy only (n = 3)</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
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*The follow-up time was 3.2 years. The average time to recurrence was 2.35 years. MMS indicates Mohs micrographic surgery.
†A lesion within this group recurred during the study period.

Figure 2. Diagram depicting 48 microcystic adnexal carcinoma (MAC) cases according to treatment. There were 3 main therapeutic modalities: no excision, Mohs micrographic surgery (MMS), and excision. The upper right depicts the lesions that had been misdiagnosed before entering the study and their treatment. The bottom sums the total number of procedures, by treatment type, required to cure the 48 MAC lesions. BCC indicates basal cell carcinoma; SCC, squamous cell carcinoma.
crease in defect size when comparing pretreatment and posttreatment sizes in MMS-treated lesions. The wide range of change between pre- and post-MMS SAs renders the estimation of surgical safety margins unsafe. Although we are unable to compare posttreatment SAs and, therefore, unable to show tissue-sparing advantages from one treatment group to another, this finding supports the use of MMS, as this technique does not rely on such predicted margins. We suspect that the high complication rates in both treatment groups in this series are due precisely to these large defect sizes.

Mohs micrographic surgery is clearly advantageous with respect to the number of procedures required for cure. We were able to show that 30% (7/23) of patients treated with simple excision at onset will require at least one other procedure and, therefore, one other visit, compared with 0% (0/22) if treated with MMS. Since we also suspect that simple excision leads to defect sizes as large or larger than those left by MMS, we believe that MMS is a reasonable first-line therapeutic modality.

By adhering to specific, standardized, diagnostic criteria, we were able to clarify the epidemiological features and recurrence rate of MAC. This series provides the surgeon with important information regarding pretreatment and posttreatment defect sizes, number of procedures required, and frequency of recurrence.

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REFERENCES