Microcystic adnexal carcinoma: Collaborative series review and update

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Background: Microcystic adnexal carcinoma (MAC) is a malignant appendageal tumor first described in 1982. It can be clinically and histologically confused with other malignant and benign cutaneous neoplasms, leading to inadequate initial treatment. This neoplasm is locally aggressive and deeply infiltrating, characterized by high morbidity and frequent recurrence. Mohs micrographic surgery has been used to conserve tissue and improve the likelihood for cure.

Objective: We report our experience using Mohs micrographic surgery for the treatment of MAC and compare with earlier reports in the literature. In addition, we review the epidemiology, clinical and histologic characteristics, and optimal treatment of this rare neoplasm. We also describe a 15-year-old white male patient with MAC on the scalp occurring only 7 years after radiation exposure.

Methods: The medical records of 11 patients with MAC who were treated by Mohs micrographic surgery were reviewed at both departments, and follow-up data were obtained.

Results: In all patients treated with Mohs micrographic surgery, there were no recurrences after a mean follow-up of 5 years.

Conclusion: Mohs technique enables the detection of clinically unrecognizable tumor spread and perineural invasion often encountered with MAC. Aggressive initial treatment by microscopically controlled excision appears to offer the greatest likelihood of cure for this neoplasm, while providing conservation of normal tissue. In addition, we describe the second youngest patient with MAC and readdress the issue of previous radiotherapy as an important predisposing factor. (J Am Acad Dermatol 1999;41:225-31.)

Microcystic adnexal carcinoma (MAC) is a malignant appendageal tumor first described as a specific entity by Goldstein et al[1] in 1982. This neoplasm is locally aggressive and deeply infiltrating, characterized by high morbidity and frequent recurrence despite aggressive treatment with surgery, radiation therapy, or both. The ability of Mohs surgery to detect the microscopic tumor elements of MAC with tissue conservation makes this a therapeutic modality of great interest. There are currently 17 previous reports of Mohs surgery as a successful treatment modality for 34 cases of MAC in the literature. We report 11 additional cases of MAC treated with microscopically controlled excision.

MATERIAL AND METHODS

The medical records of 11 patients with MAC treated at the New York University Medical Center (P. R.) and the University of Tennessee Medical Center (R. A.) by Mohs micrographic surgery between 1986 and 1997 were reviewed. In each case, histologic diagnosis was confirmed by a dermatopathologist on the basis of sectioned, paraffin-embedded biopsy specimens stained with hematoxylin and eosin.

Mohs surgical excisions were performed and followed by sectioning and mapping of the tissue layer. After cryostat processing, histologic sections were cut horizontally and stained with hematoxylin and eosin. Additional Mohs stages were taken until tumor-free sections were obtained. After the final Mohs layer, an additional layer for permanent paraffin-embedded sections was sent for further margin control on the 4 patients treated at the New York University Medical Center (P. R.). The final Mohs layer was decolorized, restained with toluidine blue, and reexamined for tumor clearance on the 7

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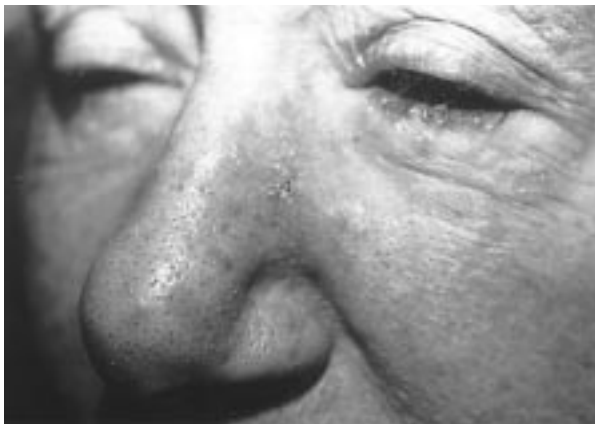

Fig 1. Case 5. Microcystic adnexal carcinoma of left nose; evidence of residual tumor after 2 primary excisions (*pointer*).

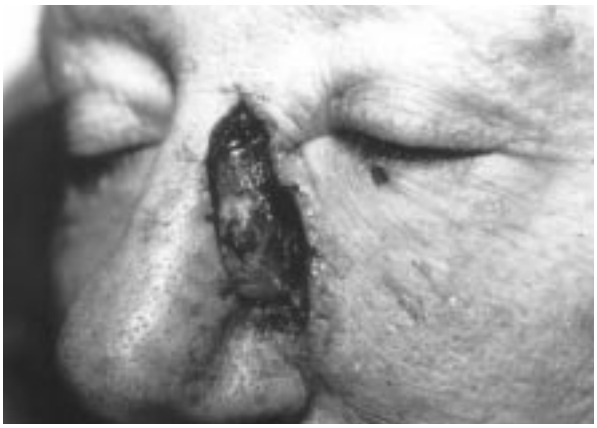

Fig 2. Case 5. Defect after 2 stages of Mohs micrographic surgery with margins free of tumor.

Table I. Clinical data for 11 patients with microcystic adnexal carcinoma treated with Mohs micrographic surgery

Patient No.	Age (y)	Sex	Location	Tumor	Stages	Defect size (cm)	Follow-up (y)
1*	80	F	R-NL fold	Primary	9	5×4	1
2	58	F	L-Nose	Primary	3	1.2×1.5	12.6
3	63	F	Columella	Primary	5	2.8×2.2	7.75
4	72	M	R-Jaw	Primary	2	4×2.5	12.6
5	83	F	L-Nose	Recurrent	2	3.4×3.2	5
6	83	F	R-Forehead	Recurrent	4	3×5	1.75
7	41	F	Upper lip	Primary	3	3×2.5	2
8	52	M	L-Conchal bowl	Primary	3	2.8×2.9	3.4
9	60	F	R-Dorsum nose	Primary	6	3.5×3.5	1.8
10	74	M	R-Temple	Primary	2	5.6×6.7	1.2
11*	15	M	L-Parietal scalp	Primary	2	4.5×4.5	2

NL, Nasolabial.
*Radiation exposure.
Cases 1-4 (NYU).
Cases 5-11 (UT).

patients treated at the University of Tennessee Medical Center (R. A.). Reconstruction of the Mohs surgery defects were then performed with primary closure, split-thickness skin grafting, local cutaneous flaps, or referral to plastic surgery.

The following variables were determined for each patient: age, sex, location, radiation exposure, recurrence by primary excision, stages and postoperative defect, and duration of follow-up.

RESULTS

The overall age of the patients ranged from 15 to 83 years (median, 63; mean, 62 years). The female-to-male ratio was 3.5:2. Tumors were located primarily on the head and neck area. Two of the patients experienced MAC at sites of previous radiotherapy. Of the 11 patients, 9 had primary tumor, and 2 presented with recurrence of MAC after primary excision. Tissue sections of all patients demonstrated tumor spreading several centimeters laterally beyond clinically apparent tumor tissue. The average number of stages required to clear the tumor was 3, with a maximum of 9 stages. During each stage, multiple histologic sections were required to analyze the peripheral margins. Tumor size as detected by Mohs technique ranged from 1.2×1.5 cm to 5.6×6.7 cm. Follow-up ranged from 1 to 12 years with an average follow-up of 5 years (Table I). All of the patients remained tumor free.

Selected case reports

Case 1. An 80-year-old woman with a history of

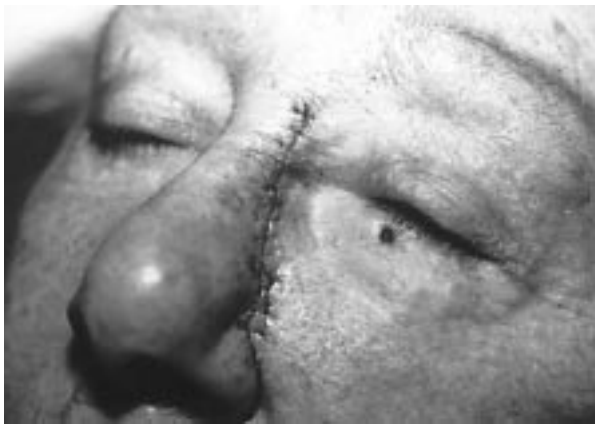

Fig 3. Case 5. Appearance after wound closure.

radiation therapy for teenaged acne was referred with a skin-colored nodule on the right nasolabial fold. The skin biopsy specimen showed a poorly circumscribed neoplasm of keratinizing nests and cords of epithelial cells with formation of cysts and ductlike structures to the base of the dermis, consistent with a diagnosis of MAC. She had radiation skin changes and a history of multiple basal cell and squamous cell carcinomas. The patient required 9 stages of Mohs surgery because of extensive tumor spread into the nasal cavity and septum, resulting in a 5.0 × 4.0 cm defect. She was subsequently referred for subtotal nasal reconstruction. At 1 year postoperatively, the patient had no evidence of recurrence.

Case 5. An 83-year-old woman with a history of actinic keratoses and excessive sun exposure as a child presented to her dermatologist with an asymptomatic lesion on the left side of her nose. The biopsy specimen was consistent with MAC and was managed initially by primary excision. There was evidence of residual tumor after 2 primary excisions (Fig 1). The patient was then referred for Mohs surgery, which showed tumor at the upper medial and lower lateral edge by frozen section. The residual tumor was cleared in 2 stages by microscopic control (Figs 2 and 3). There has been no evidence of recurrence 5 years after surgery.

Case 11. A 15-year-old boy presented with a history of acute T-cell lymphoblastic leukemia with central nervous system (CNS) involvement. His condition required 18 Gy of cranial irradiation at the age of 8 and 24 Gy at age 9, as well as etoposide as chemotherapy. The patient's leukemia underwent complete remission with this protocol. He presented with a 1-year history of a small indurated pruritic plaque on the scalp. The lesion measured 3 cm, and a skin biopsy specimen revealed MAC. The patient required 2 stages of micrographic surgery to reach a tumor-free plane measuring 4.5 × 4.5 cm. The tumor showed deep infiltration into the dermis and subcutis with perineural involvement. The patient remains free of tumor 2 years after surgery.

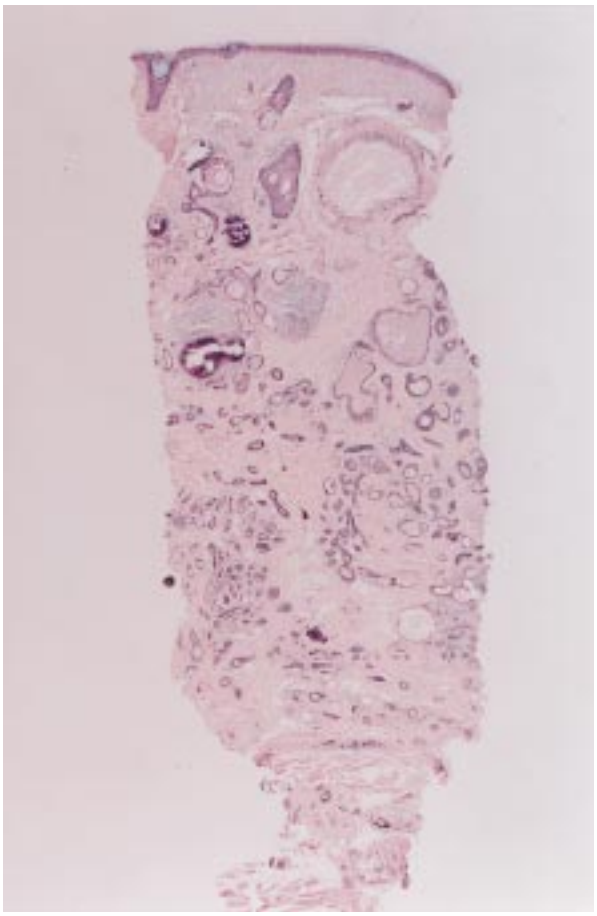

Fig 4. Scanning power reveals deeply infiltrating epithelial neoplasm extending to base of specimen; basaloid cells forming keratin-filled cystic and ductal structures. (Hematoxylin-eosin stain; original magnification ×25.)

DISCUSSION

MAC occurs predominantly on the head and neck, particularly in the centrofacial region. Involvement of the ear has been reported only twice previously,[2,3] and there are 3 cases of scalp involvement in the literature.[4-6] Of the 105 cases reported in the English language literature (including our 11 cases), the median age of presentation was 56 years. Of these cases, the sex distribution was approximately equal, 54 (51%) occurring in men and 51 (49%) occurring in women. This neoplasm occurs predominantly in the white population, with only 1 reported case in a black patient.[6] The clinical presentation is typically that of a slowly growing indurated nodule, plaque, or

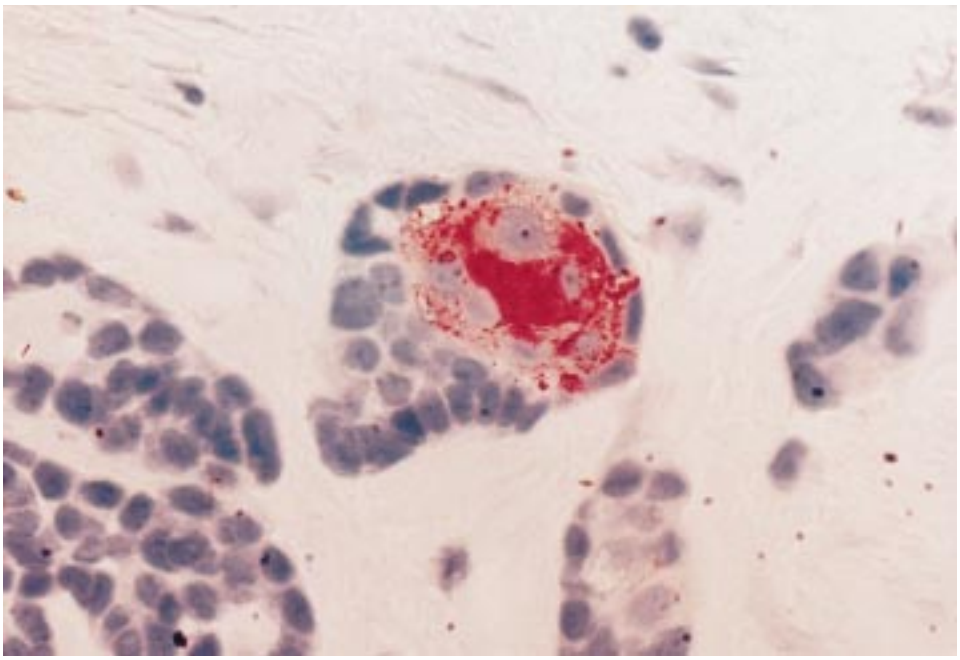

Fig 5. CEA stain. Ductlike structures consistent with eccrine differentiation. (Original magnification ×250.)

cystlike tumor that has often been present for many years. Average tumor size at presentation is 2 cm; however, MAC as large as 9 cm has been previously reported.[7] The lesions are usually asymptomatic without ulceration and are often ignored. Symptomatic lesions often manifest with numbness, tenderness, burning, anesthesia, or paresthesia. These symptoms are caused by the high frequency of perineural invasion.[8] The clinical differential diagnoses include basal cell carcinoma, squamous cell carcinoma, cyst, scar, and other adnexal tumors. The tumor is most often confused with morpheaform basal cell carcinoma because of the smooth surface and telangiectases.[9]

If a diagnosis of MAC is suspected, careful attention to a history of radiation therapy as a possible etiologic factor should be sought. Several reports indicate that there may be an association of this tumor with earlier exposure to radiation therapy. The literature contains 7 patients (8%) who experienced MAC on average 30 to 40 years after radiation exposure.[8,10-13] We report 2 additional cases of MAC occurring at sites of previous radiotherapy. Patient 11, the second youngest reported case, experienced MAC at the site of radiation exposure only 7 years after radiotherapy for CNS leukemia. The short latent period is likely because of the high irradiation doses used to treat the patient's leukemic condition,[14,15] or perhaps a synergistic effect between the irradiation and etoposide chemotherapy.[16] Patient 1 experienced MAC approximately 60 years after undergoing radiation therapy for acne, suggesting that the risk of carcinogenesis in irradiated skin persists for the life of the patient. The tumors in these patients with a history of radiation exposure have not been more aggressive or histologically more atypical than those without radiation exposure.[8]

MAC is locally aggressive and may invade adjacent tissue by expansion and infiltration,[17] accounting for the difficulty in obtaining local surgical control. Histologically, MAC is characterized by keratin-filled cysts, nests and cords of basaloid cells, and the formation of ductal structures within a desmoplastic stroma (Fig 4). The ductal structures are 1 to 2 cell layers thick and lined by flattened cells that may contain eosinophilic material in the lumen. The nests and ducts may have tail-like protrusions resembling the tadpole formations seen in syringomas.[18] The papillary to mid dermis reveals well-differentiated horn cysts and glandlike structures, whereas the reticular dermis contains strands of basaloid cells and small ductal structures. Immunohistochemical stains have supported both eccrine and pilar differentiation with carcinoembryonic antigen, epithelial membrane antigen, and cytokeratin being expressed most consistently (Fig 5).[19-21] The histopathologic differential diagnoses include benign and malignant tumors such as trichoadenoma, syringoma, desmoplastic trichoepithelioma,

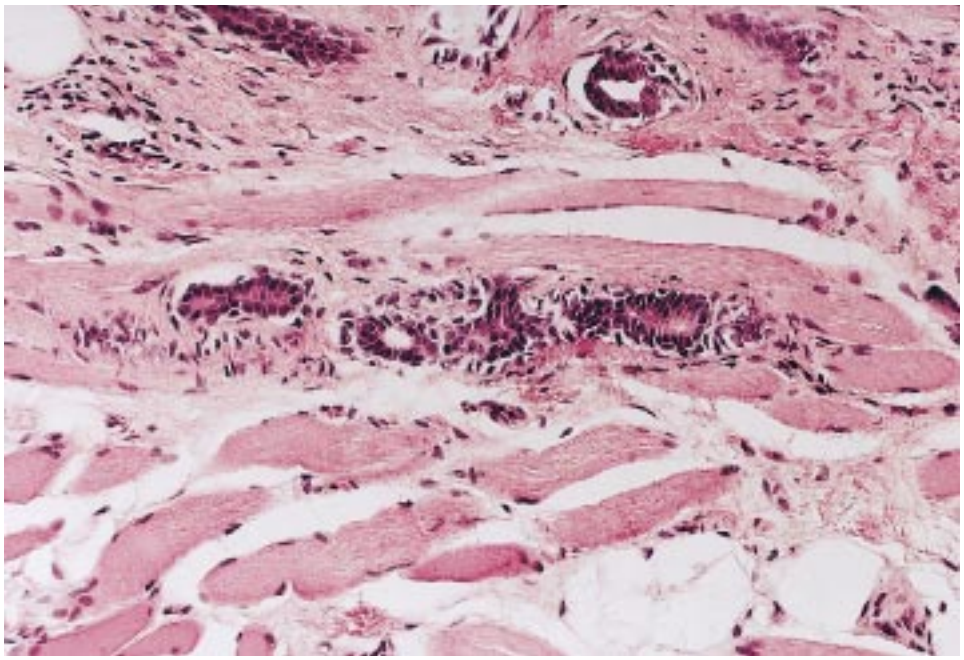

Fig 6. Small ductal structures infiltrating subcutaneous tissue and strands of skeletal muscle at base of biopsy. (Hematoxylin-eosin stain; original magnification ×100.)

Table II. Historical data for 34 patients with microcystic adnexal carcinoma treated with Mohs micrographic surgery

Authors	Year	No. of patients	Patients with local recurrence		Tumor	Average stages/ Defect size (cm)	Average follow-up (mo)
			No.	%			
Park et al[6]	1998	1	0	0	P	3/3 × 4.2	6
Billingsley et al[18]	1996	4	0	0	1P,3R	NS	31.4
Barlow et al[28]	1996	2	0	0	NS	1.5/NS	24
Hesse et al[29]	1995	1	0	0	1P	NS	24
Burns et al[30]	1994	10	0	0	6P,4R	NS	25
McAlvany et al[31]	1994	1	0	0	P	1/NS	32
Hazen and Bass[32]	1994	1	0	0	R	NS/6.1 × 3.0	42
Sebastien et al[8]	1993	1	0	0	R	NS/5.5 × 5.5	16
Futran et al[33]	1992	1	0	0	P	NS	1.5
Wallace et al[34]	1991	1	0	0	P	NS	18
Chow et al[4]	1989	1	0	0	P	NS/12 × 17	NS
Birkby et al[22]	1989	1	0	0	R	NS	18
Mayer et al[25]	1988	3	1	33	1P,2R	NS	NS
Hamm et al[10]	1987	3	0	0	1P,2R	NS	19
Nickoloff et al[19]	1986	1	0	0	P	4/2 × 1	13
Fleischmann et al[35]	1984	1	0	0	P	NS	7
Cooper and Mills[11]	1984	1	1	100	R	NS	8

NS, Not specified in records; *P,* primary; *R,* recurrent.

morpheaform basal cell carcinoma, squamous cell carcinoma, and metastatic breast carcinoma. Leboit and Sexton[5] reported 17 cases of MAC, 9 of which they found were initially misdiagnosed histologically. The authors noted that small biopsy specimens and bland cytologic features contributed to incorrect tissue diagnoses of benign tumors or less aggressive malignancies.

MAC is a poorly circumscribed and asymmetric tumor. It has an infiltrative growth pattern often associated with perineural involvement, emphasizing the importance of deep biopsy specimens for definitive diagnosis. In addition, involvement of the subcutis, muscle (Fig 6), and bone may occur. Computed tomography and magnetic resonance imaging have been used to detect extensive invasion by these tumors, allowing preoperative localization of the extent of tumor invasion.[7] Birkby, Argenyl, and Whitaker[22] reported the first case of direct bone involvement by a case of MAC of the lip, associated with extensive perineural invasion along the mental nerve. Hunt et al[3] reported tumor that tracked extensively along the facial nerve and from the parotid gland posteriorly through the temporomandibular joint and into the external auditory canal. Despite the invasive nature, the tumor cells are cytologically bland with rare or absent mitoses and lack of cell necrosis.[8] Cooper et al[23] reported increased cytologic atypia in his series of tumors associated with recurrences. Although MAC can be locally aggressive and destructive, only recently has there been a report of metastasis. Bier-Laning et al[24] reported a tumor that was detected in a regional lymph node in the contralateral neck of a patient, occurring 22 years after multiple courses of radiation therapy and surgery for recurrent MAC.

Treatment modalities for MAC have included radiation therapy, wide excision, and Mohs surgery. This tumor has largely been considered radioresistant with recurrence of most of the irradiated tumors.[7,25] The literature is limited but reflects an overall high MAC recurrence rate of 47% after traditional excisional surgery.[23,26] The margins reported for primary tumor excision have varied from a few millimeters to wide resections with 3- to 5-cm margins. Most recurrences have occurred within a median of 3 years[8]; however, MAC recurring as late as 30 years after treatment has been reported, emphasizing the need for prolonged follow-up.[27]

The Mohs technique has enabled the detection of clinically unrecognizable tumor spread several centimeters beyond clinically apparent tumor tissue by immediate frozen-section analysis of all margins. Hematoxylin-and-eosin staining is most commonly used in this setting; however, toluidine blue has also been effective, revealing tumor cells by staining the mucin present around ductal structures and detecting small collections of tumor cells involving small nerve branches.[9] Sending the final Mohs layer for permanent paraffin-embedded sections allows for further margin control, decreasing the risk of missing a single strand of tumor.[8] The data in the literature regarding the effectiveness of Mohs surgery in the treatment of MAC show it to be successful, providing accurate assessment of lateral and deep margins, but it is limited without long-term follow-up (Table II). Among these data, 17 cases of primary MAC were treated with Mohs surgery with no recurrence after 6 weeks to 36 months. In addition, there were 15 cases of recurrent MAC treated with Mohs surgery with no recurrence reported in 13 of these cases after 6 to 60 months. The extensive size and local destruction of the tumor prevented the achievement of tumor-free margins in 1 of the recurrences.[25]

Our review represents the largest and longest followed series of patients treated by Mohs surgery with no recurrences after an average follow-up of 5 years. This modality enabled the detection of clinically unrecognizable tumor spread and perineural invasion. Given the infiltrative nature of this neoplasm, location on the central face along embryonic fusion planes, and a high recurrence rate by primary excision per historical data, initial treatment by Mohs surgery appears to offer the greatest likelihood of cure for this neoplasm. In addition, we readdress the involvement of radiotherapy as an important risk factor given that 8.6% (including 2 of our cases) of the patients in the reviewed literature presented with a history of radiation exposure.

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