

ORIGINAL ARTICLES

Microcystic Adnexal Carcinoma: Mohs Micrographic Surgery as the Treatment of Choice

A. Martorell-Calatayud,^a C. Requena-Caballero,^a R. Botella-Estrada,^a S. Almenar-Medina,^b O. Sanmartín-Jiménez,^a B. Llombart-Cussac,^a E. Nagore-Enguíanos,^a C. Serra-Guillén,^a B. Echeverría-García,^a and C. Guillén-Barona^a

^aServicio de Dermatología, ^bServicio de Anatomía Patológica, Instituto Valenciano de Oncología, Valencia, Spain

Abstract. *Introduction and objectives.* Microcystic adnexal carcinoma is a rare and aggressive tumor that manifests clinically as a subcutaneous nodule located on the head or neck. The tumor can be confused clinically and histologically with other benign and malignant skin lesions, often leading to inappropriate initial treatment. The chief concern with microcystic adnexal carcinoma is the elevated morbidity and the high rate of recurrence after wide local excision. Recent preliminary studies point to higher cure rates with Mohs micrographic surgery.

Material and methods. We reviewed the medical histories of 6 consecutive patients with microcystic adnexal carcinoma who underwent Mohs micrographic surgery in our dermatology department between 1995 and 2007.

Results. In all cases, lesions were located on the head and were primary tumors. Seventy percent of the tumors were wrongly diagnosed initially as basal cell carcinoma. Perineural invasion was not detected in any patient, and all were free of recurrence after between 1 and 12 years of postoperative follow-up.

Conclusions. The absence of perineural involvement and substantial cell atypia can be attributed to the lesions being primary tumors. This would provide a rationale for definitive radical treatment of the primary tumor from the outset to avoid the complications associated with recurrence. The site and the absence of recurrence in all our patients who underwent Mohs micrographic surgery support the use of this technique as the treatment of choice in microcystic adnexal carcinoma.

Key words: microcystic adnexal carcinoma, Mohs surgery, perineural invasion.

CARCINOMA ANEXIAL MICROQUÍSTICO: LA CIRUGÍA MICROGRÁFICA DE MOHS COMO TRATAMIENTO DE ELECCIÓN

Resumen *Introducción y objetivos.* El carcinoma anexial microquístico (CAM) es un tumor raro y agresivo que clínicamente se manifiesta como un nódulo subcutáneo localizado en las regiones de cabeza y cuello. Esta tumoración puede ser clínica e histológicamente confundida con otras lesiones cutáneas benignas o malignas, lo que con frecuencia conduce a un tratamiento inicial erróneo. La principal complicación del CAM es la alta morbilidad y la elevada tasa de recurrencia tras escisión local amplia. Estudios preliminares recientes han mostrado unas mayores tasas de curación mediante cirugía micrográfica de Mohs (CMM).

Material y métodos. Se revisaron las historias clínicas de 6 pacientes consecutivos con CAM tratados mediante CMM en nuestro Servicio de Dermatología entre 1995 y 2007.

Resultados. Todos los casos se localizaron en la cabeza y el 100 % fue tumor primario. En el 70 % de los casos el tumor fue inicialmente mal diagnosticado de carcinoma basocelular. No se detectó invasión perineural en ninguno de los casos y la recurrencia estuvo ausente en todos los pacientes tras un periodo de seguimiento comprendido entre 1 y 12 años posteriores a la CMM.

Conclusiones. La ausencia de afectación perineural y de una importante atipia celular puede deberse al carácter primario de la tumoración. Ello justificaría la necesidad de un tratamiento definitivo radical inicial del tumor primario para evitar las complicaciones que implica una recidiva tumoral. La localización y la

ausencia de recurrencia en todos nuestros casos tratados mediante CMM apoyan el uso de esta técnica como el tratamiento de elección para el CAM.

Palabras clave: carcinoma anexial microquístico, cirugía de Mohs, invasión perineural.

Correspondence:
Antonio Martorell Calatayud.
C/ San José de la Montaña, 14, puerta 11
46008 Valencia, Spain
antmarto@hotmail.com

Introduction

Microcystic adnexal carcinoma (syngomatous carcinoma, malignant syringoma, desmoplastic carcinoma of the sweat glands)¹⁻³ is an uncommon skin tumor with 2 different types—glandular and follicular. It was first described by Goldstein et al⁴ in 1982.

It is characterized by its aggressive local nature, high infiltrating capacity, and marked neurotropism, all of which explain the high recurrence rate, despite administration of aggressive treatment.

There is currently some controversy over the best therapeutic option for complete eradication of microcystic adnexal carcinoma. The therapeutic and aesthetic advantages of Mohs micrographic surgery (MMS) could make it a treatment of choice for this tumor. However, experience with this technique in adnexal tumors is very limited.

We report a series of 6 cases of microcystic adnexal carcinoma treated using MMS in a single dermatology center. We analyze the various clinical and surgical parameters of the patients, as well as recurrence during long-term follow-up.

Material and Methods

We reviewed the medical and surgical history of 6 patients diagnosed at the dermatology department of the Instituto Valenciano de Oncología, Valencia, Spain, between 1995 and 2007. In each case, the histopathological diagnosis was confirmed by a pathologist using hematoxylin-eosin-stained biopsies.

The specimens were obtained and processed following the Mohs micrographic technique with 0.5-cm stages until there was no further involvement of the surgical margins. The technique was performed on paraffin-embedded specimens in 4 cases and on fresh frozen specimens in the other 2. In the fresh specimens, an additional stage was excised once the disease-free margins were reached.

For each patient we collected the following data: age, gender, site, time since onset, exposure to ionizing radiation, primary or recurrent lesion, size of the lesion in the preoperative clinical examination, number of MMS stages necessary to reach the disease-free margins, size of the postsurgical defect, follow-up period, and recurrence during follow-up.

After a PubMed search of the literature, we reviewed all cases of microcystic adnexal carcinoma treated using MMS between 1982 and 2007. From those reports, we recorded the following parameters: number of cases of microcystic adnexal carcinoma treated (divided into primary and recurrent cases), percentage of recurrences, mean number of surgical stages performed, and mean follow-up of patients treated.

Results

Table 1 shows the different clinical-surgical parameters of the 6 patients (5 women and 1 man, aged between 38 and 90 years [mean, 69 years]). All the tumors analyzed were primary tumors; none of the patients had previously undergone radiotherapy at the site of the lesion. Three of the cases had previously presented one or more basal cell carcinomas on the face. The tumor was on the face in all patients (3 on the cheek, 2 on the nasolabial crease, and 1 on the chin), and was right-sided in 4. The size of the lesion ranged between 0.5 cm × 0.6 cm and 2.0 cm × 2.0 cm.

The mean number of stages required to reach the disease-free margins was 1.4, and the size of the resulting surgical defect ranged between 1 cm × 1 cm and 4 cm × 3 cm.

All the patients underwent additional tests, including laboratory work-up (complete blood count, liver and renal function tests, and coagulation studies) and chest radiograph, all with normal results.

Follow-up varied between 1 year and 12 years (mean, 5 years). There were no recurrences.

Discussion

Microcystic adnexal carcinoma is a malignant adnexal tumor that appears most commonly in women aged 50 to 69 years.^{3,5-10} White and Asian individuals are more predisposed to the development of this tumor,¹¹ and few cases have been described in African American patients.^{2,6,12,13}

There seem to be several risk factors, including exposure to ultraviolet and/or ionizing radiation and underlying immunosuppression.³

Microcystic adnexal carcinoma takes the form of a stony-hard pseudocyst, plaque, or nodule. It is asymptomatic, grows slowly and progressively, and has a mean diameter of 2 cm at the time of diagnosis (Figure 1).¹⁴ The presence of soreness, paresthesia, or pain at the site of the tumor points to possible perineural involvement, which varies from 18% to 59% with this tumor.¹⁴

Microcystic adnexal carcinoma is found on the head and neck in up to 83% of cases.^{11,15} Seventy-three percent of these cases are found on the face, mainly in the area of the eyelid^{16,17} and the nasolabial crease.

The mean delay between onset of the lesion and the histopathological diagnosis varies with gender. Thus, whereas mean diagnostic delay is 1 year in women, in men it can reach as much as 5 years.¹¹ We found this delay to range from 6 months to 14 years; however, no relation with gender could be established, as the study population comprised mostly women.

Table 1. Characteristics of Patients Treated With Mohs Surgery in Our Department

Age/Sex	Course, y	Presenting Complaint	Previous Skin Cancer	Site	Physical Examination	Suspected Diagnosis	No. of Stages (Surgical Defect)	Follow-up, y/ Recurrence
69/Man	2	Asymptomatic plaque	No	Left cheek	Stony-hard, yellowish poorly delimited plaque measuring 1 × 1.5 cm	Adnexal tumor	2 (7 × 2 cm)	3/No
61/Woman	14	Asymptomatic indurated plaque	No	Right chin	Stony-hard plaque with a central depression measuring 2 × 2 cm	Adnexal tumor	2 (5 × 5 cm)	2/No
61/Woman	1	Indurated yellow plaque	BCC	Right nasolabial crease	Ivory-colored papule with telangiectasia measuring 1 × 1 cm	BCC	2 (3 × 3 cm)	1/No
52/Woman	3	Scarring	No	Right cheek	Yellowish papule measuring 2 × 1 cm	BCC	1 (3 × 3 cm)	1/No
81/Woman	1	Semihard nodule	BCC	Left cheek	Yellowish indurated papule measuring 0.5 × 0.6 cm	BCC	1 (1.5 × 1.5 cm)	12/No
48/Woman	11	Indurated yellowish nodule	BCC	Right nasal ala	Indurated papule measuring 1 × 1 cm	BCC	2 (2 × 2 cm)	9/No

Abbreviation: BCC, basal cell carcinoma

Microcystic adnexal carcinoma can penetrate deeper planes,¹⁸ and it frequently invades the subcutaneous tissue and underlying skeletal muscle. There have been reports of involvement of the perichondrium, periosteum, adventitia of the blood vessels, and even bone.¹⁹ Histologically, the tumor is characterized by sparing of the epidermis and occupation of the superficial reticular and papillary dermis by small cysts with keratinization of the isthmus and follicular infundibulum (Figure 2). In the middle and deep reticular dermis, the existence of multiple islets of basal cells is noteworthy. These cells show intracytoplasmic vacuolization and, in certain areas, they form ducts with well-defined lumens covered by flattened cells organized into 1 or 2 layers (Figure 3).^{20,21}

Perineural infiltration, which has been described in less than 5% of tumors of the head and neck,²²⁻²⁴ is a relatively frequent phenomenon in microcystic adnexal carcinoma, and has been detected after histopathology study in between 17.5%²³ and 59% of patients depending on the series.²⁵ This phenomenon appears mainly in



Figure 1. Poorly delimited ivory-colored plaque with telangiectasia on the right cheek.

recurrence of adnexal carcinoma (up to 87.5% of cases),¹⁸ and is uncommon in primary adnexal carcinoma; hence the importance of optimal initial therapy as a means of

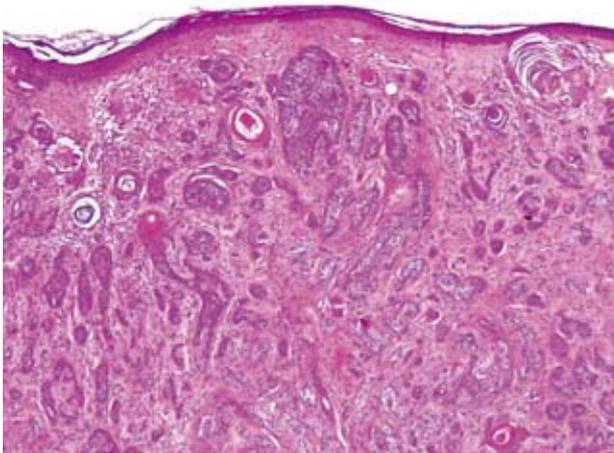


Figure 2. Epithelial islands and some horny cysts in the superficial dermis (hematoxylin-eosin, $\times 20$).

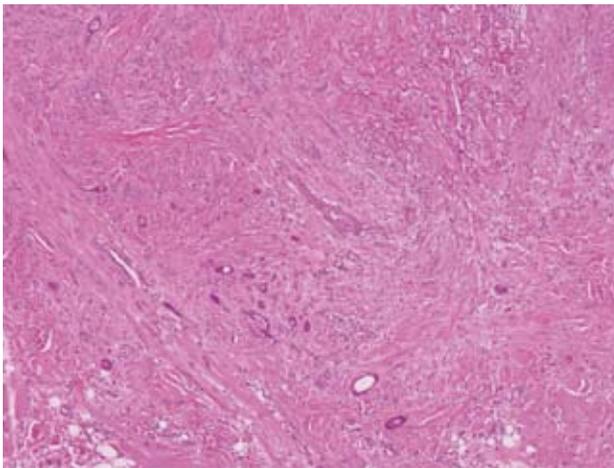


Figure 3. The mid-dermis has been invaded by small epithelial islands. Tubular structures can be seen in the deep dermis (hematoxylin-eosin, $\times 20$).

reducing the overall percentage of these tumors with perineural infiltration. None of our cases had perineural infiltration, possibly because all the tumors treated in our series were primary tumors.

Microcystic adnexal carcinoma is difficult to diagnose both from a clinical and from a histologic viewpoint.²⁶ In fact, depending on the series, between 25% and 53% of cases were incorrectly diagnosed clinically, with the most common initial diagnosis being sclerodermiform basal cell carcinoma.^{5,11} In many cases, the difficulty of the clinical diagnosis is compounded by errors in the histopathologic diagnosis, because shave biopsy specimens do not allow the characteristic stratified pattern of microcystic adnexal carcinoma to be analyzed.²⁷ In our study, 4 of the 6 cases were clinically diagnosed with basal cell carcinoma, and in 1 of these the histopathology

results supported this diagnosis. However, in this case, shave biopsy was performed, and the subsequent punch biopsy confirmed the diagnosis of microcystic adnexal carcinoma. Thus, in a sclerodermiform lesion in an exposed area, a tissue sample reaching the subcutaneous layer must be obtained.

The main problem with microcystic adnexal carcinoma is its locally aggressive behavior, which is seen in its marked invasive capacity and high frequency of perineural involvement,²⁸ leading to a high frequency of local recurrence after conventional excision, reaching 40% to 60%.^{5,28,29} Distant spread is very rare; only 5 cases of locoregional lymph node spread have been reported, 4 on the same side as the tumor³⁰ and 1 contralateral.³² Furthermore, systemic involvement is exceptional, with isolated cases in the lung,³² bone,²⁹ and liver.³³

The available therapeutic options for this tumor include radiotherapy and surgery, both for simple excision and for control of the surgical margins. Radiotherapy has been used to treat this tumor, either alone or in combination with surgery.^{33,34} The results obtained enable us to draw the following conclusions:

1. Radiotherapy should not be used alone for a primary microcystic adnexal carcinoma, since it has been shown that not only is it ineffective against this tumor, but it can also make the tumor clinically and histologically more aggressive.^{34,35}
2. Ionizing radiation can be considered as adjuvant therapy to surgical excision for tumors with disease-free margins in specific situations: recurrences; lymphatic, vascular, or perineural invasion; and muscle or bone invasion.^{15,36,37}

Conventional surgery requires a wide safety margin, both superficially and deep, in order to minimize the risk of incomplete excision. However, the definition of a "wide" margin is somewhat vague; therefore, it is impossible to evaluate the results of conventional surgery over a large number of studies. In addition, analysis of the surgical specimen obtained using this technique only enables 0.2% of margins to be evaluated, thus leading to a recurrence rate of 40% to 60% during the first 3 years after treatment.⁵

MMS is a more selective approach to the volume of tissue removed, and minimizes excision of healthy skin; therefore, the aesthetic result is better, which is particularly important given that this type of tumor tends to appear on the face.³⁸ Similarly, the mode of extracting the specimen and its analysis make it possible to evaluate almost 100% of the surfaces of the surgical specimen,²⁰ with the result that the risk of recurrence using this technique varies from 0%⁵ to 12%.^{2,6,39,42} The postsurgical defect can reach up to 4 times the size of the initial clinical lesion.^{5,43-45}

Table 2. Reports From the Literature of Patients With Microcystic Adnexal Carcinoma Treated With Mohs Surgery

	<i>No. of Cases</i>	<i>Recurrence Rate</i>	<i>No. of Stages</i>	<i>Mean Follow-up, mo</i>
Fleischmann et al ⁴⁵ , 1984	1	No	NS	7
Cooper and Mills ² , 1984	1 (recurrent)	Yes	NS	8
Nickoloff et al ⁸ , 1986	1	No	4	13
Hamm et al ³⁹ , 1987	3 (2 recurrent)	No	NS	19
Mayer et al ³⁵ , 1988	3 (2 recurrent)	Yes (1 case)	NS	NS
Chow et al ⁴³ , 1989	1	No	NS	NS
Birkby et al ⁴⁶ , 1989	1 (recurrent)	No	NS	18
Wallace and Bernstein ⁴⁷ , 1991	1 case	No	NS	18
Futran et al ⁴⁸ , 1992	1 case	No	NS	1.5
Sebastien et al ¹⁸ , 1993	1 (recurrent)	No	NS	16
Burns et al ⁴⁹ , 1994	10 (4 recurrent)	No	NS	25
McAlvany et al ⁵⁰ , 1994	1	No	1	32
Hazen and Bass ⁵¹ , 1994	1 (recurrent)	Yes	NS	42
Hesse et al ⁴⁴ , 1995	1	No	NS	24
Barlow et al ²⁷ , 1996	2	No	1.5	24
Billingsley et al ⁷ , 1996	4 (3 recurrent)	No	NS	31.4
Park and Parry ¹² , 1998	1	No	3	6
Friedman et al ³¹ , 1999	11 (2 recurrent)	No	3.5	60
Chiller et al ⁵ , 2000	25 (3 recurrent)	Yes (3 cases)	NS	38
Snow et al ⁵² , 2001	13 (3 recurrent)	No	NS	60
Abbate et al ⁵³ , 2003	6 (2 recurrent)	No	NS	23.3
Khachemoune et al ⁵⁴ , 2005	4	No	4	12
Leibovitch et al ¹⁴ , 2005	20 (4 recurrent)	No	2	60

Abbreviation: NS, not supplied.

Few series in the literature analyze patients treated with Mohs surgery, and the samples are small (Table 2). In our series, no patients presented signs of recurrence during the regular postsurgical follow-up, which ranged from 12 months to 12 years (mean, 5 years). The surgical defect reached 2-4 times the size of the initial clinical lesion.

Tumor recurrence in microcystic adnexal carcinoma is important, since, compared with primary microcystic adnexal carcinoma, recurrences present when larger in size, thus implying the need for a greater number of Mohs stages and a larger postsurgical defect. In histologic terms, greater cellular atypia is observed with a higher rate of

perineural invasion (up to 80% of cases). All 6 cases in our series presented primary adnexal tumors, which showed mild cellular atypia and no perineural infiltration in the histopathologic analysis.

Therefore, MMS should be considered the treatment of choice for this type of tumor.

At present, neither the follow-up interval nor the necessary complementary tests for these patients has been established. Given the greater risk of recurrence during the first 3 years after excision, follow-up is recommended every 3 to 6 months. After the first 3 years, lifetime monitoring should be started, since there have been

reports of recurrence up to 30 years after the lesion was first removed.

Conflict of Interest

The authors declare no conflicts of interest.

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